

Evert Bosdriesz

SYSTEMS BIOINFORMATICS, VRIJE UNIVERSITEIT AMSTERDAM
NETHERLANDS BIOINFORMATICS CENTER
e-mail: evert.bosdriesz@falw.vu.nl

Jan Berkhout

SYSTEMS BIOINFORMATICS, VRIJE UNIVERSITEIT AMSTERDAM

Frank Bruggeman

SYSTEMS BIOINFORMATICS, VRIJE UNIVERSITEIT AMSTERDAM
LIFE SCIENCES, CENTRE FOR MATHEMATICS AND COMPUTER SCIENCE

Douwe Molenaar

SYSTEMS BIOINFORMATICS, VRIJE UNIVERSITEIT AMSTERDAM

Bas Teusink

SYSTEMS BIOINFORMATICS, VRIJE UNIVERSITEIT AMSTERDAM

The cost and benefit of enzyme expression

The resources a microorganism has at its disposal are limited. Among other things, this implies that expressing enzymes is costly. Consider for instance the specific growth rate, which is the rate of biomass synthesis per unit biomass. Expressing a certain enzyme increases the total biomass and thus, unless it contributes in some way to the biomass synthesis rate, will decrease the growth rate. Indeed, it has been observed that expressing "dummy" proteins has a negative effect on the growth rate [1,2].

In order to quantify the cost and benefit of enzyme expression, we generalized a definition previously proposed by Dekel and Alon [1]. The benefit function is closely related to the flux control coefficient, the cost is directly related to the fraction of the resources dedicated to the enzyme. The flux is optimized if for each enzyme its control coefficient equals its contribution to the total resource usages. This is generalization of, and consistent with, earlier observations by Klipp and He [3].

The relation between the benefit function and the flux control coefficients allows us to intuitively understand the effects of kinetic parameters such as catalytic constants and Michaelis-Menten constants on the (optimal) flux, at least for small pathways. For instance, an enzyme with a high catalytic constant typically has a flux control coefficient that rapidly decreases with its concentration, and we expect this enzyme to have a low expression in the optimal state.

We are currently applying the cost-benefit analysis to self-replicator models [4].

REFERENCES

- [1] E. Dekel and U. Alon (2005), *Optimality and evolutionary tuning of the expression level of a protein* Nature **436** 588–92.
- [2] D. M. Stoebel, A.M. Dean, D.E. and Dykhuizen (2008), *The cost of expression of Escherichia coli lac operon proteins is in the process, not in the product* Genetics **178** 1653–60.
- [3] E. Klipp and R. Heinrich (1999), *Competition for enzymes in metabolic pathways: implications for optimal distributions of enzyme concentrations and for the distribution of flux control* Bio Systems **54** 1–14.
- [4] D. Molenaar, R. van Berlo, D. de Ridder and B. Teusink (2009), *Shifts in growth strategies reflect tradeoffs in cellular economics* Molecular Systems Biology **5**.