Christoph Kaleta - Research Group Theoretical Systems Biology, Friedrich Schiller University – Jena, Germany

Tuned for speed – Elucidation of strategies for rapid metabolic adaptations in prokaryotes

Martin Bartl[a], Gundían M. de Hijas-Liste[b], Martin Kötzing[a,c], Eva Balsa-Canto[b], Stefan Schuster[d], Julio R. Banga[b], Pu Li[a], Christoph Kaleta[c]

Microorganisms have to be able to quickly react to environmental challenges to survive in fluctuating environmental conditions. Dynamic optimization represents a suitable tool that allows one to identify regulatory mechanisms that provide prokaryotes with the capability to rapidly adapt after a change in environmental conditions. In this talk, I will address two works that have shed light onto such regulatory strategies. In the first work, Bartl et al. (2013), we show that protein abundance and protein synthesis capacity are key factors that determine the optimal strategy for the activation of a metabolic pathway. If protein abundance relative to protein synthesis capacity increases, the strategies shift from the simultaneous activation of all enzymes over a sequential activation of groups of enzymes to a sequential activation of individual enzymes along the pathway. In the case of pathways with large differences in protein abundance, even more complex pathway activation strategies with a delayed activation of low-abundant enzymes and an accelerated activation of high-abundant enzymes are optimal. We confirm the existence of these pathway activation strategies for a large number of metabolic pathways in several hundred prokaryotes. In the second work, de Hijas-Liste et al. (2013), we used dynamic optimization to identify optimal points of control in complex metabolic pathways. We find that in converging pathways no regulation is required around the converging reaction while in diverging pathways a regulation after the diverging reaction is necessary. Moreover, the speed at which proteins can be synthesized has a strong influence onto specific positions that are optimal for a precise control of a metabolic pathway. While organisms with a slow protein production favor the control of metabolic pathways toward the beginning of pathways, organisms with rapid protein production favor the regulation of metabolic pathways toward at the terminal step. We confirm the utilization of these regulatory strategies in a screen of several hundred prokaryotic metabolic networks.

References:

M. Bartl, M. Kötzing, S. Schuster, P. Li, C. Kaleta (2013). Dynamic optimization identifies optimal programs for pathway regulation in prokaryotes. *Nature Communications*, 4:2243.

G.-M. De Hijas-Liste, E. Balsa-Canto, J. Banga, C. Kaleta (2013). Optimal regulatory programs for the control of metabolic pathways: The case of feedback inhibition. *In preparation.*

Frank J. Bruggeman - Systems Bioinformatics, VU University,

Amsterdam, The Netherlands

Constraints, adaptability and optimality of metabolic networks

Microorganisms show a remarkable capacity to adjust their metabolic networks to changes in conditions to restore fitness. I will present the contours of a general theory of the evolution of metabolic networks under selective pressures that can be mimicked in laboratory evolution experiments. When nutrients are in excess during batch growth, natural selection favours microorganisms with the highest specific growth rate. In the last years, we have derived theory to understand the evolutionary outcome of this selective pressure in terms of the topology of the optimal metabolic network and the gene network that steers metabolism to optimal states in dynamic environments. I will contrast these findings for the microbial evolution under batch growth conditions with the evolutionary scenario in the chemostat, which has a qualitatively different selective pressure.