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Dynamic Optimization of Nitrogen Assimilation in Chlamydomonas reinhardtii

Optimization approaches are a useful tool to study principles behind dynamics observed in the regulation of metabolic pathways [1]. While earlier studies considered mostly steady-state systems [1, 2], the dynamic regulation, or just-in-time activation, of metabolic pathways has attracted increasing attention [3, 4] and was experimentally observed in the amino acid biosynthesis of *Escherichia coli* [4]. Using dynamic optimization by solving a nonlinear, dynamic optimal control problem with the quasi-sequential approach [5], we investigate the regulation of the nitrogen assimilation and the nitrogen metabolism [6] by the circadian clock [7] of the green algae Chlamydomonas reinhardtii. The aim of our analysis is to identify which enzymes within a drastically simplified model of the metabolism of C. reinhardtii need to be subjected to circadian control in order to adapt the organism to day-night rhythms. Moreover, the physiological and environmental constraints that imply the necessity of circadian regulation of different enzymes are investigated. Important components of such a model are appropriate kinetics of participating reactions as well as concentrations of enzymes and metabolites. We developed such a model focusing on nitrogen metabolism including assimilation, transport and processing in C. reinhardtii. This model was analyzed under different environmental conditions and provides first insights into the cause of the dynamics of metabolite and enzymes concentrations observed in the course of a day.

References

- Heinrich et al., Mathematical analysis of enzymic reaction systems using optimization principles. Eur J Biochem 201 1–21. 1991.
- [2] Heinrich R. and Schuster S., The Regulation of Cellular Systems New York: Chapman & Hall 1996
- Klipp et al., Prediction of temporal gene expression. Metabolic opimization by re-distribution of enzyme activities. Eur J Biochem 269 5406-5413. 2002.
- [4] Zaslaver et al., Just-in-time transcription program in metabolic pathways. Nat Genet 36 486– 491. 2004.
- [5] Hong et al., A quasi-sequential approach to large-scale dynamic optimization problems AIChE Journal 52 255–268. 2006.
- [6] Fernandez E. and Galvan A., Inorganic nitrogen assimilation in Chlamydomonas. J Exp Bot 58 2279–2287. 2007.
- [7] Mittag et al., The circadian clock in Chlamydomonas reinhardtii. What is it for? What is it similar to? Plant Physiol 137 399-409, 2005.

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