

Model Embedding

Combining Constraint-based & Kinetic Networks

Wolfram Liebermeister & Matthias König

Introduction

The main idea is the coupling of kinetic and constraint based models. Main test case will be the coupling of a kinetic model of hepatic glucose metabolism {[Koenig2012a](#), [Koenig2012b](#)} into a highly curated subnetwork of HepatoNet1 {[Gille2010](#)}.

Model Description

GlucNet - Human Hepatic Glucose Model

Kinetic model of the hepatic glucose metabolism comprising gluconeogenesis, glycolysis and glycogen metabolism integrated with the hormonal response via insulin and glucagon {[Koenig2012a](#), [Koenig2012b](#)} (Figure 1). The model will be referred to as GlucoNet.

Simulations

The model can simulate the switch between hepatic glucose production (HGP) and hepatic glucose utilization (HGU) under varying external glucose concentrations. The set of test simulations will comprise the kinetic simulations under varying glucose concentrations.

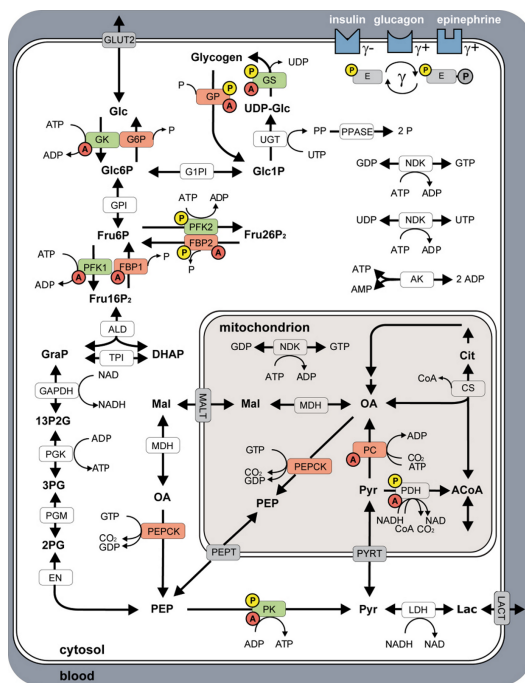


Figure 1 - GlucoNet model overview.

HepatoCore - Human Hepatic Core Metabolism

Highly curated subnetwork of HepatoNet1 {Gille2010} described in {Koenig2009} (Figure 2). The model will be referred to as HepatoCore.

Contains ...

Simulations

Wide range of functional tests of core hepatocyte functions. Different functional aspects of the core metabolism are tested.

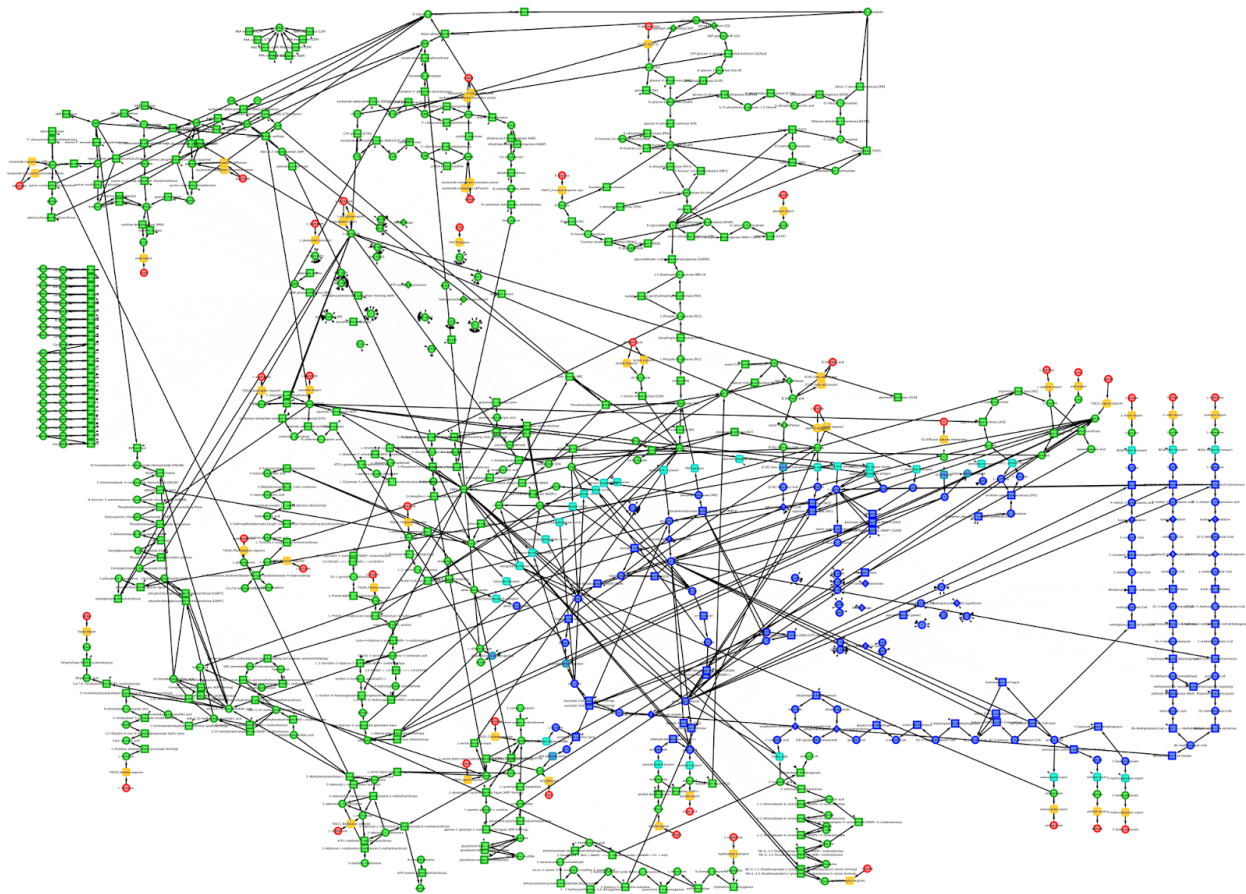


Figure 2 - HepatoCore model overview.

References

- Gille, C., Bölling, C., Hoppe, A., Bulik, S., Hoffmann, S., Hübner, K., et al. (2010). HepatoNet1: a comprehensive metabolic reconstruction of the human hepatocyte for the analysis of liver physiology. *Molecular systems biology*, 6(1).
- König, M., Bulik, S., & Holzhütter, H. (2012a). Quantifying the contribution of the liver to glucose homeostasis: a detailed kinetic model of human hepatic glucose metabolism. *PLoS computational biology*, 8(6), e1002577.
- König, M., & Holzhütter, H. (2012b). Kinetic modeling of human hepatic glucose metabolism in type 2 diabetes mellitus predicts higher risk of hypoglycemic events in rigorous insulin therapy. *Journal of Biological Chemistry*, 287(44), 36978-36989.
- König, M (2009). Metabolic network reconstruction of the human hepatocyte core metabolism. Diploma thesis, Humboldt University Berlin