Dynamic modeling of pyruvate dehydrogenase complex in mammalian cells (SysLogics WP7)

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Description:
The BMBF funded SysLogics project aims at the adaptation and development of modeling methods to reveal key metabolic and regulatory processes in mammalian cells. For this purpose, a neuronal cell line (AGE1.HN, Rose et al., 2005) provided by an industrial partner (ProBioGen AG, Berlin) is studied and characterized. This work package (WP7) focuses on the quantitative mathematical understanding of the regulation of the mammalian pyruvate dehydrogenase complex (PDC). The PDC is an enzyme complex located in the mitochondrial matrix of aerobic cells. It catalyzes oxidative decarboxylation of pyruvate and thus the exothermic and irreversible reaction from pyruvate to Acetyl-CoA. It plays as a key role in the metabolic flux from glycolysis to the TCA cycle, but also for the fatty acid synthesis pathway. It is tightly regulated depending on the energy requirements of the cell and its nutritional condition. The regulation is mainly performed based on three main processes: Reversible phosphorylation / desphosphorylation, acetyl-CoA / CoA ratio (Fig. 1), and transcriptional regulation of the regulatory enzymes. The implemented model is originally based on an algorithm developed earlier by the group (Zeng et al., 2002). It now incorporates the interaction between four different PDC kinase and two PDC phosphatase isoenzymes with the E1 unit of the PDC (Jandt et al., 2010). The corresponding enzyme kinetics are derived from literature. In cooperation with the other SysLogics cooperation partners, the computation results are adapted to proteomic and metabolomic data from high cell density cell cultivations conducted at TUHH.

References:

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