# Analysis of metabolic profiles using model-driven metabolite ratios

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## Abstract

**Background:** Metabolic profiles can be valuable indicators of an organism's phenotype, since metabolite levels display endpoints of characteristic biological reactions. For a better understanding of the relationship between phenotypic and metabolic profiles under specific physiological conditions, we analyze plasma metabolite measurements of the Human Metabolome (HuMet, `http://www.humet-tum.de`) study. In this survey 15 male volunteers underwent a 24 hours fasting challenge. Under such conditions mitochondrial beta-oxidation, the catabolic breakdown of fatty acids, is the main physiological process which provides energy to the cell. In a recurring sequence of enzymatic catalyzed reactions, fatty acid chains are shortened by two carbon atoms during each round of the degradation cascade.

**Results:** Here we construct a mathematical model that describes the fatty acid beta-oxidation pathway approximately as a linear cascade of subsequent, irreversible first-order reactions with varying metabolite input. If this model is solved for steady state conditions, derived conversion rates are proportional to specific metabolite concentration ratios. Investigating the relationship between individual phenotypic and metabolic profiles reveals that, compared to absolute

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metabolite concentrations, model-driven ratios greatly improve statistical correlation with physiological parameters like blood sugar and free carnitine, but also for anthropometric parameters like body mass index and total fat mass.

**Conclusion:** Metabolite ratios have recently been used to link metabolic reactions with genetic variants in a genome-wide association study (Illig et al., 2010; Suhre et al., 2011). Our results show that metabolite ratios, which are derived from models of biochemical pathways, can be used to improve the characterization of distinct metabolic phenotypes. We suggest that model-driven analysis of metabolic systems under perturbations such as fatty acid beta-oxidation under fasting conditions allows for a better investigation of the relationship between individual physiological phenotypes and biological pathways.

## References


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