# Modeling Method for Increased Precision and Scope of Directly Measurable Fluxes at a Genome-Scale - DTU Orbit (09/11/2017)

**Modeling Method for Increased Precision and Scope of Directly Measurable Fluxes at a Genome-Scale**

Metabolic flux analysis (MFA) is considered to be the gold standard for determining the intracellular flux distribution of biological systems. The majority of work using MFA has been limited to core models of metabolism due to challenges in implementing genome-scale MFA and the undesirable trade-off between increased scope and decreased precision in flux estimations. This work presents a tunable workflow for expanding the scope of MFA to the genome-scale without trade-offs in flux precision. The genome-scale MFA model presented here, iDM2014, accounts for 537 net reactions, which includes the core pathways of traditional MFA models and also covers the additional pathways of purine, pyrimidine, isoprenoid, methionine, riboflavin, coenzyme A, and folate, as well as other biosynthetic pathways. When evaluating the iDM2014 using a set of measured intracellular intermediate and cofactor mass isotopomer distributions (MIDs),(1) it was found that a total of 232 net fluxes of central and peripheral metabolism could be resolved in the *E. coli* network. The increase in scope was shown to cover the full biosynthetic route to an expanded set of bioproduction pathways, which should facilitate applications such as the design of more complex bioprocessing strains and aid in identifying new antimicrobials. Importantly, it was found that there was no loss in precision of core fluxes when compared to a traditional core model, and additionally there was an overall increase in precision when considering all observable reactions.

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Authors: McCloskey, D. (Ekstern), Young, J. D. (Ekstern), Xu, S. (Ekstern), Palsson, B. (Intern), Feist, A. (Intern)
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