

REMI: CONSTRAINT-BASED METHOD FOR INTEGRATING RELATIVE EXPRESSION AND RELATIVE METABOLITE LEVELS INTO A THERMODYNAMICALLY CONSISTENT METABOLIC MODEL

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Flux balance analysis (FBA) allows steady-state flux predictions using optimization principles and often does not result in a unique steady-state flux distribution. Therefore, integration of omics data, such as transcriptomics, metabolomics has been employed as additional constraints to reduce the solution space of feasible flux phenotypes. Here, we present a computational method, termed REMI, which integrates relative expression along with relative metabolomics into genome-scale metabolic models (GEMs) to estimate the differential fluxes at GS level. First, we integrated relative expression data into an E.coli GEM using our approach and an existing GX-FBA method (Navid & Almaas, 2012; Orth et al, 2011). The results of our method are more robust and in better agreement with experiments as compared to GX-FBA, because our method facilitates alternative solution enumeration. High frequency solutions analysis between the alternatives may guide in understanding of a biological system physiology. Furthermore, to further reduce the flux space and obtain predictions closer to actual physiological state first we add thermodynamic constraints into models and then employed relative expression as well as relative metabolomics as additional constraints (Henry et al, 2007). The constraint model, resulted in reduced feasible flux space as one can expect, and predicts flux distributions that were in better agreement with experiments.

References

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