

## The COBRA Toolbox: a comprehensive and powerful modelling resource

Hulda S. Haraldsdóttir<sup>1</sup>, Hoai Minh Le<sup>1</sup>, Longfei Mao<sup>1</sup>, Ines Thiele<sup>1</sup> and Ronan M. T. Fleming<sup>3\*</sup>  
([ronan.mt.fleming@gmail.com](mailto:ronan.mt.fleming@gmail.com)).

<sup>1</sup>Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg

<https://opencobra.github.io/cobratoolbox/>

**Project Goals: This project aims to develop COBRA Toolbox: a package of methods to simulate, analyse, predict and visualise a variety of metabolic phenotypes using genome-scale models.**

Over the past decade, COntstraint-Based Reconstruction and Analysis (COBRA) methods have widely been used in several fields including microbial metabolic engineering, modelling of gene expression and metabolism at genome-scale on modelling transcriptional and signaling networks. The COBRA Toolbox, a MATLAB package of COBRA methods, provides systems biology researchers with a high-level interface to a variety of methods for constraint-based modelling of genome-scale stoichiometric models of cellular biochemistry. The first version of COBRA Toolbox, released in 2007, contains a variety of methods, such as flux variability analysis, growth-rate optimisation, robustness analysis, gene essentiality analysis and model curation tools. Version 2.0 [3] expanded the first version by adding new functions including network gap filling, C13 analysis, metabolic engineering, omics-guided analysis and visualisation. The COBRA Toolbox has now gained widespread use and has become a leading software package for genome-scale analysis of metabolism. The success of COBRA Toolbox has been used in more than 500 studies. The COBRA Toolbox has rapidly developed in recent years based on contributions from a growing number of researchers. Our recently contributed functions to the COBRA Toolbox include: (i) consistent estimation of Gibbs energy using component contributions [2], (ii) identification of conserved moieties in metabolic networks [1], (iii) reconstruction context-specific metabolic network models from generic reconstructions [5], (iv) robust flux balance analysis [4], (v) Cell Designer - Matlab interface for parsing and editing files, and (vi) tools for conversion of a reconstruction into a COBRA model in a quality controlled manner. The latest version of The COBRA toolbox is available at <https://github.com/opencobra/cobratoolbox> and includes contributions from a community of >25 developers: <https://github.com/opencobra/cobratoolbox/graphs/contributors>.

## References

- [1] Hulda S. Haraldsdóttir and Ronan M. T. Fleming. Identification of conserved moieties in metabolic networks by graph theoretical analysis of atom transition networks. *Submitted*, 2015.
- [2] Elad Noor, Hulda S. Haraldsdóttir, Ron Milo, and Ronan M. T. Fleming. Consistent Estimation of Gibbs Energy Using Component Contributions. *PLoS Comput Biol*, 9(7):e1003098, July 2013.
- [3] Jan Schellenberger, Richard Que, Ronan M. T. Fleming, Ines Thiele, Jeffrey D. Orth, Adam M. Feist, Daniel C. Zielinski, Aarash Bordbar, Nathan E. Lewis, Sorena Rahmanian, Joseph Kang, Daniel R. Hyduke, and Bernhard Ø Palsson. Quantitative prediction of cellular metabolism with constraint-based models: the COBRA Toolbox v2.0. *Nature Protocols*, 6(9):1290–1307, September 2011. 00182.
- [4] Yuekai Sun, Ronan MT Fleming, Ines Thiele, and Michael A. Saunders. Robust flux balance analysis of multiscale biochemical reaction networks. *BMC Bioinformatics*, 14(1):240, July 2013. 00000 PMID: 23899245.
- [5] Nikos Vlassis, Maria Pires Pacheco, and Thomas Sauter. Fast reconstruction of compact context-specific metabolic network models. *PLoS Comput Biol*, 10(1):e1003424, January 2014. 00001.

*This work was supported by the U.S. Department of Energy, Offices of Advanced Scientific Computing Research and the Biological and Environmental Research as part of the Scientific Discovery Through Advanced Computing program, grant #DE-SC0010429.*