

Quadruple-precision solution of genome-scale models of Metabolism and macromolecular Expression

Ding Ma¹, Laurence Yang², Ines Thiele³, Bernhard Palsson², **Ronan M. T. Fleming**^{3*}(ronan.mt.fleming@gmail.com), Michael Saunders¹

¹Dept of Management Science and Engineering, Stanford University, Stanford, CA, USA; ²Dept of Bioengineering, University of California, San Diego, CA, USA; ³Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Luxembourg.

<http://stanford.edu/group/SOL/multiscale/>

Project Goals: Development and biological applications of industrial quality linear and nonlinear optimization solvers for Constraint-Based Reconstruction and Analysis of multiscale mechanistic models of biochemical networks.

Constraint-Based Reconstruction and Analysis (COBRA) is currently the only methodology that permits integrated modeling of Metabolism and macromolecular Expression (ME) at genome-scale. Linear optimization can be used to compute steady-state flux solutions to ME models. Special care must be taken when computing such solutions as they contain fluxes that are spread over many orders of magnitude. Standard floating point solvers may return inaccurate solutions, or may have difficulty determining whether a feasible solution exists. Genome-scale ME models contain upwards of 70,000 variables and continue to increase in size, so accurate but inefficient exact simplex solvers are an impractical option. We developed qMINOS, a quadruple-precision version of MINOS, our industrial quality linear and nonlinear optimization solver. We tested the performance of qMINOS on a range of multiscale linear optimization problems and established a sequential solution procedure involving double- and quadruple- precision simplex solvers that together achieve a balance between efficient and reliable solution to ME models. The prior existence of efficient numerical optimization algorithms enabled the exponential growth in biological applications of metabolic models. Likewise, qMINOS now guarantees the accurate solution to linear, nonlinear, genome-scale and multi-scale ME models in reasonable time. Platform specific compiled qMINOS code has been disseminated to the community via the latest version of The COBRA Toolbox [1], available at <https://github.com/opencobra/cobratoolbox>.

References

- [1] Schellenberger J, Que R, Fleming RMT, Thiele I, Orth JD, et al. (2011) Quantitative prediction of cellular metabolism with constraint-based models: the COBRA Toolbox v2.0. *Nature Protocols* 6: 1290–1307.

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.