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

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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 squential 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 guaruntees 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.

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