

Creation and analysis of biochemical constraint-based models using the COBRA Toolbox v.3.0

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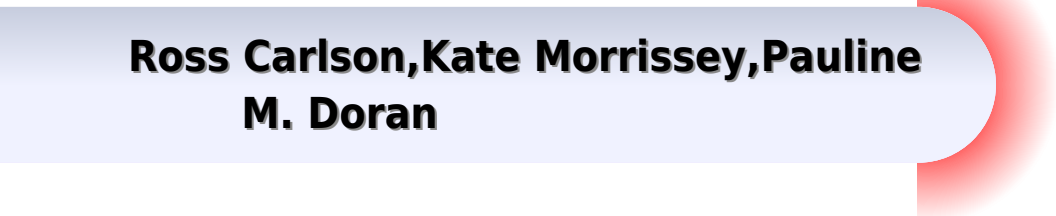
Constraint-based reconstruction and analysis (COBRA) provides a molecular mechanistic framework for integrative analysis of experimental molecular systems biology data and quantitative prediction of physicochemically and biochemically feasible phenotypic states. The COBRA Toolbox is a comprehensive desktop software suite of interoperable COBRA methods. It has found widespread application in biology, biomedicine, and biotechnology because its functions can be flexibly combined to implement tailored COBRA protocols for any biochemical network. This protocol is an update to the COBRA Toolbox v.1.0 and v.2.0. Version 3.0 includes new methods for quality-controlled reconstruction, modeling, topological analysis, strain and experimental design, and network visualization, as well as network integration of chemoinformatic, metabolomic, transcriptomic, proteomic, and thermochemical data. New multi-lingual code integration also enables an expansion in COBRA application scope via high-precision, high-performance, and nonlinear numerical optimization solvers for multi-scale, multi-cellular, and reaction kinetic modeling, respectively. This protocol provides an overview of all these new features and can be adapted to generate and analyze constraint-based models in a wide variety of scenarios. The COBRA Toolbox v.3.0 provides an unparalleled depth of COBRA methods.

This protocol is an update to *Nat. Protoc.* 2, 727–738 (2007): <https://doi.org/10.1038/nprot.2007.99> and *Nat. Protoc.* 6, 1290–1307 (2011): <https://doi.org/10.1038/nprot.2011.234>

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Cobra Toolbox Manual

**Ross Carlson, Kate Morrissey, Pauline
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