Abstract:
Systems biology has long been interested in models capturing both metabolism and expression in a cell. In a recent paper, Salvy and Hatzimanikakis (2020) proposed an implementation of the metabolism and expression model formalism (ME-models), which they call ETFL, for Expression and Thermodynamics Flux models. ETFL is a hierarchical model formulation, from metabolism to RNA synthesis, that allows simulating thermodynamics-compliant intracellular fluxes as well as enzyme and mRNA concentration levels. ETFL formulates a mixed-integer linear problem (MILP) that enables both relative and absolute metabolite, protein, and mRNA concentration integration. ETFL is compatible with standard MILP solvers and does not require a non-linear solver, unlike the previous state of the art. It also accounts for growth-dependent parameters, such as relative protein or mRNA content. The authors validated ETFL using results obtained from a well-characterized E. coli model. They show that ETFL is able to reproduce proteome-limited growth. It is also possible to subject the model to other analyses, including the prediction of feasible mRNA and enzyme concentrations and gene essentiality.