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# Dynamic regulatory on/off minimization infers key regulators of the Calvin cycle under internal temporal perturbations

Flux balance analysis (FBA) together with its dynamic extension, DFBA, have proven instrumental for analyzing the robustness of metabolic networks. Under the assumption of minimization of metabolic adjustment, DFBA has recently been employed to analyze the transition between metabolic states at systemic level. Here we propose a suite of novel methods for analyzing the dynamics of perturbed metabolic networks and quantifying their robustness without knowledge of kinetic parameters. Following the biochemically meaningful premise that metabolite concentrations exhibit smooth temporal changes, the proposed methods rely on minimizing the significant fluctuations of metabolic profiles to predict the time-resolved metabolic state characterized by both fluxes and concentrations. On a model of the Calvin cycle, we demonstrate that the principle of regulatory on/off minimization (ROOM) coupled with DFBA can accurately predict the changes in metabolic states. Our methods outperform the existing DFBA-based modeling alternatives, and help in revealing the mechanisms for maintaining robustness of dynamic processes in metabolic networks over time.