Model Invalidation and Parameter Estimation of Biochemical Reaction Networks via Semidefinite Programming

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Abstract: Validating the model structure as well as identifying model parameters of biochemical reaction networks is a challenging task. Often competing reaction mechanisms and structural hypothesis, limited, typically varying uncertain measurements, as well as nonlinearities appearing render the use of classical estimation and validation methods infeasible or lead to poor results, since the the special structure of biochemical reaction networks is not directly taken into account. In the frame of this work we present a new set-based approach for model invalidation, parameter and state estimation. Basically the invalidation task is reformulated as an feasibility problem, taking directly the measurement and parameter bounds as constraints into account. The resulting feasibility problem is in general non-convex. As shown, taking the polynomial or rational structure that is typically present in biochemical reaction systems, it is possible to relax the non-convex feasibility problem into a convex semidefinite program (SDP). This can then be solved efficiently, e.g. via interior point methods. As the relaxation process is conservative, infeasibility of the original feasibility problem can be certified via the corresponding SDP. This approach allows to obtain conclusive results on model invalidity based on the certification of non-existence of a feasible parametrization even if only imprecise or sparse measurements are available. Competing model alternatives can thus be discriminated by proving inconsistency with the available data for (some of) the wrong alternatives. To provide estimates of parameter and state sets being consistent with the measurements, subregions in the surrounding are certified as infeasible and discarded. Herefore, the initial parameter or state space is partitioned and the partitions are checked for infeasibility. In order to reduce the overall computational cost, we provide a bisection algorithm, so as to check groups of partitions simultaneously. The derived method is exemplified considering simple biochemical reaction networks.

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