Global optimization of biochemical pathways: the parameter estimation problem

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ABSTRACT

Here we address the problem of parameter estimation (inverse problem) of nonlinear dynamic biochemical pathways. This problem is stated as a non-linear programming (NLP) problem subject to non-linear differential-algebraic constraints. These problems are known to be frequently ill-conditioned and multimodal. Thus, traditional (gradient-based) local optimization methods fail to arrive to satisfactory solutions. In order to surmount this limitation, the use of several state-of-the-art deterministic and stochastic global optimization methods is explored. A case study considering the estimation of 36 parameters of a nonlinear biochemical dynamic model is taken as a benchmark. Only a certain type of stochastic algorithms, evolution strategies (ES), are able to solve this problem successfully. Although these stochastic methods can not guarantee global optimality with certainty, their robustness, plus the fact that in inverse problems have a known lower bound for the cost function, make them the best available candidates.

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