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Identification of Parameters in Large Scale Models of Systems Biology.

Inverse problem for the identification of parameters for large scale systems of nonlinear ODEs arising in systems biology is analyzed. In a recent paper in *Math. Biosci.*, 305(2018), 133-145, the authors implemented the numerical method suggested by one of the authors in *J. Optim. Theory Appl.*, 85, 3(1995), 509-526 for identification of parameters in moderate scale models of systems biology. This method combines Pontryagin optimization with sensitivity analysis and Tikhonov regularization. We suggest modification of the method by embedding a method of staggered corrector for sensitivity analysis and by enhancing multi-objective optimization which enables application of the method to large scale models with practically non-identifiable parameters based on multiple data sets, possibly with partial and noisy measurements. We apply the method to benchmark model of a three-step pathway modeled by 8 nonlinear ODEs with 36 parameters. The numerical results demonstrate geometric convergence with a minimum of five data sets and with minimum measurements per data set. Software package *qlopt* is developed. MATLAB package AMIGO2 is used to demonstrate advantage of *qlopt* over most popular methods/software such as *lsqnonlin*, *fmincon* and *nl2sol*. (Received August 31, 2019)