

# SBML ODE Solver Library: Extensions for Inverse Analysis

Rainer Machné<sup>1</sup>, James Lu<sup>2,\*</sup>, Stefan Mueller<sup>2</sup>, Christoph Flamm<sup>1</sup>

1. Institute for Theoretical Chemistry, University of Vienna, Austria

2. Johann Radon Institute for Computational and Applied Mathematics, Linz, Austria

\*E-mail: james.lu@oeaw.ac.at

## Abstract

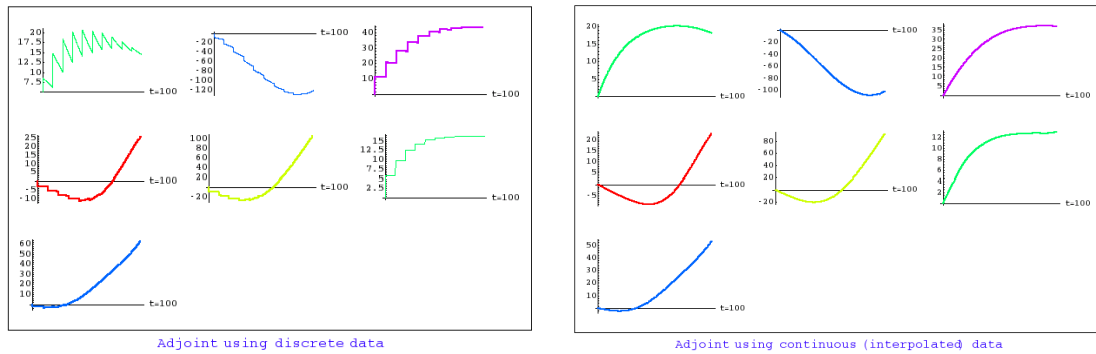
The SBML ODE Solver Library (SOSLib) [1] is a C/C++ programming library for the construction, symbolic and fast numerical analysis of a system of ordinary differential equations (ODEs) derived from a biochemical reaction network encoded in the Systems Biology Markup Language (SBML) [2]. Its native API provides fine-grained interfaces to all internal data structures, symbolic operations and numerical routines. Thus, SOSLib allows for direct interfaces to all variable and parameter values support an easy integration of its numerical routines into hybrid (stochastic-deterministic) solvers or into multi-scale modeling applications [3].

Recent efforts in the development of SOSLib has been focused on extensions that allow one to perform not only *forward* analysis but also the *inverse* analysis of biochemical models. In particular, adjoint capabilities of SOSLib has been extended to enable the identification of parameters from "noisy" experimental data. Currently, many cases of identification problems can be handled by SOSLib : the "parameters" to be identified may either be the various kinetic constants in the model or initial conditions associated with the ODE system; the data may either be in the form of continuous-time measurements or experimental values at given discrete time points. Another aspect that has been addressed is the efficiency of SOSLib. Since inverse analyses typically requires many evaluations of the forward operator, in the study of high-dimensional, complex biological models it is necessary to decrease the time needed for the numerical integration of the associated ODE systems. Due to the fact that a significant portion of the compute time required for solving stiff ODE systems is typically associated with the evaluations of the right-hand sides and Jacobians, on-the-fly compilation of these functions using either tcc or gcc compilers have recently been implemented. Numerical studies show that this results in approximately a factor of 4 speed up of both the forward and the adjoint solvers, thereby allowing for high-throughput analyses of large biological systems.

Via the SOSLib API for the computation of arbitrary user-defined objective functions and the associated sensitivity analysis, identification or optimization of biochemical processes can be easily performed. In particular, we demonstrate examples of parameter identification for biological models using Ipopt [4] as the local optimizer (which implements an interior point method) in combination with a scatter-search strategy as a globalization method.

## References

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(a) experimental data at discrete time points      (b) experimental data continuously measured

Figure 1: The adjoint solution profiles: MAP kinase model [5]

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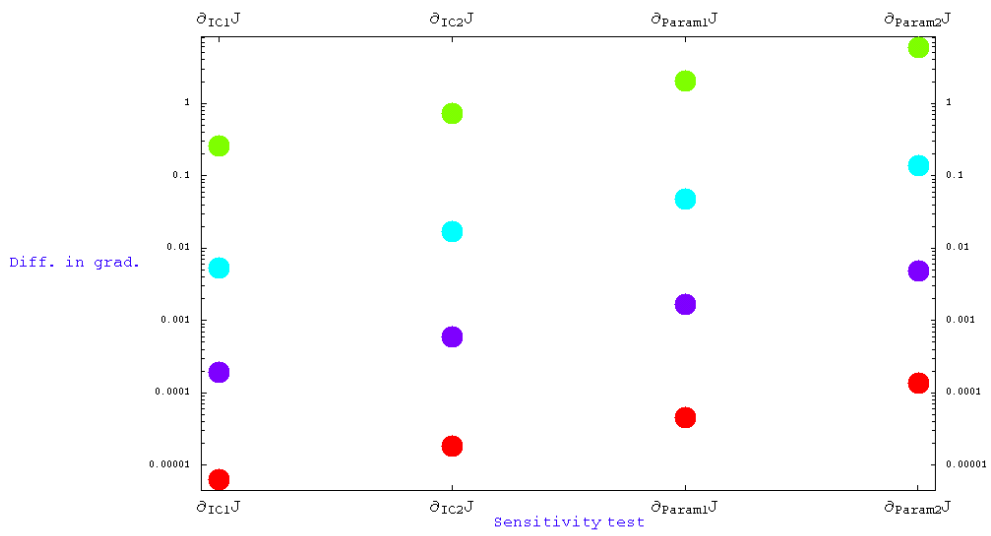


Figure 2: Convergence of objective gradients, computed via adjoint solutions for discrete and continuous data: MAP kinase model [5]