Scientific Report

First name / Family name	Ralf Hannemann-Tamás
Nationality	German
Name of the *Host Organisation*	MTA SZTAKI
First Name / family name of the *Scientific Coordinator*	Katalin Hangos
Period of the fellowship	01/03/2012 to 28/02/2013

I – SCIENTIFIC ACTIVITY DURING YOUR FELLOWSHIP

The model complexity reduction problem of large chemical reaction networks under isobaric and isothermal conditions was considered. Together with the host research group, I have developed a method to attack a version of the complexity reduction problem. This method is sketched in the following.
With a given detailed kinetic mechanism and measured data of the key species over a finite time horizon, the complexity reduction is formulated in the form of a mixed-integer quadratic optimization problem where the objective function is derived from the parametric sensitivity matrix. The proposed method sequentially eliminates reactions from the mechanism and simultaneously tunes the remaining parameters until the pre-specified tolerance limit in the species concentration space is reached. The computational efficiency and numerical stability of the optimization are improved by a pre-reduction step followed by suitable scaling and initial conditioning of the Hessian involved. We successfully tested the proposed complexity reduction method using three well-known case studies taken from reaction kinetics literature. With respect to results above on model complexity reduction, we could publish one conference paper (publication 2) and one full journal paper (publication 1).

Furthermore I worked on software tools for higher-order adjoint sensitivity analysis of Modelica models and was able to publish a conference paper at the Modelica Conference 2012 (publication 3), concerning higher-order adjoint sensitivity analysis of large-scale models in the Modelica modeling language.

II – PUBLICATION(S) DURING YOUR FELLOWSHIP

1. **Ralf Hannemann-Tamás, Attila Gábor, Gábor Szederkényi, Katalin M. Hangos:** ***Model complexity reduction of chemical reaction networks using mixed-integer quadratic programming*****, Computers & Mathematics with Applications, pp. 1-21. Available online 22 December 2012, DOI:** .http://dx.doi.org/10.1016/j.camwa.2012.11.024
Abstract: "The model complexity reduction problem of large chemical reaction networks under isobaric and isothermal conditions is considered. With a given detailed kinetic mechanism and measured data of the key species over a finite time horizon, the complexity reduction is formulated in the form of a mixed-integer quadratic optimization problem where the objective function is derived from the parametric sensitivity matrix. The proposed method sequentially eliminates reactions from the mechanism and simultaneously tunes the remaining parameters until the pre-specified tolerance limit in the species concentration space is reached. The computational efficiency and numerical stability of the optimization are improved by a pre-reduction step followed by suitable scaling and initial conditioning of the Hessian involved. The proposed complexity reduction method is illustrated using three well-known case studies taken from the reaction kinetics literature."

2. **Attila Gábor, Ralf Hannemann-Tamás, Katalin Hangos:** ***Convex mixed integer quadratic program approach to model reduction in chemical reaction networks.*** **In: 12th International PhD Workshop on Systems and Control, Veszprem, 2012. aug. 27, University of Pannonia, 2012. (ISBN 978-615-5044-71-7)**, pp. 1-6 (on CD). University of Pannonia.
Abstract: "In this paper a new approach to model reduction in chemical reaction networks is presented. Instead of minimizing the order of the system – i.e. the number of ordinary differential equations – our method subsequently omits reactions from the network such that the modeling error, i.e. the difference

between the concentrations in the original and in the reduced system, remain below a user specified tolerance."

3. **Ralf Hannemann-Tamás, Jana Tillack, Moritz Schmitz, Michael Förster, Jutta Wyes, Katharina Nöh, Eric von Lieres, Uwe Naumann, Wolfgang Wiechert, Wolfgang Marquardt:** ***First- and Second-Order Parameter Sensitivities of a Metabolically and Isotopically Non-Stationary Biochemical Network Model.*** **In: Martin Otter and Dirk Zimmer (Eds.): Proceedings of the 9th International Modelica Conference, pp. 641-648, 2012.**
Abstract: "The Jülich-Aachen Dynamic optimization Environment (JADE) is employed for computing first- and second-order parameter sensitivities of a metabolically and isotopically non-stationary biochemical network model. Based on a Modelica representation of the model, code generation, algorithmic differentiation and first- and second-order adjoint sensitivity analysis are employed for computing the gradient and the Hessian of a parameter estimation objective function. In particular, we use composite adjoints, an extension of the classical adjoint sensitivity analysis, and a numerical integrator based a modification of second-order discrete adjoints of the extrapolated linearly-implicit Euler method. Therewith, the 116 × 116-Hessian of the objective function with respect to 116 model parameters can be computed at the cost equivalent to only 18 objective function evaluations, while computing the same Hessian with the cheapest finite difference formula would require 6845 evaluations of the objective function."

III – ATTENDED SEMINARS, WORKHOPS, CONFERENCES

1. Internal group seminar of the Process Control Research Group, Budapest, Hungary, 2011 August 9, 13:00-14:00, *Modelica and Sensitivity Analysis for Parametric Hybrid Differential-Algebraic Equations*.

2. ERCIM ABCDE seminar and ABCDE Review, Sophia Antipolis, France, 2012 October 24, 16:30-16:35 and October 26, 9:50-10:00, *Ralf Hannemann-Tamás.*

3. 5th PROST Seminar, Department of Engineering Cybernetics, NTNU Trondheim, Norway, 2012 June 26, 13:15-14:00, *Second-order Sensitivity Analysis of Modelica Models and Model Reduction of Chemical Reaction Networks.*

IV – RESEARCH EXCHANGE PROGRAMME (REP)

Not applicable.