Science and Technology Group

Annual Report FY2014: André Leier

Dr. André Leier

Science and Technology Associate

1 Introduction

My research agenda has two branches. The first one is purely theoretical and mainly refers to the applicability of available mathematical tools as well as the development of new mathematical methods for analyzing the dynamics of chemical reaction networks in time and space. The other branch involves the development of mathematical and computational models for concrete biological and physiological processes.

In FY 2014, I worked on a number of projects. For the sake of brevity, I only report on those that either have been published (see references below) or submitted or are in the process of submission.

2 Activities and Findings

In Leier et al. (2014), we extend our methodology published in 2013 on exact reduction of linear chains of reactions with delay distributions in two ways. First, we report that it is now possible to deal with fully bi-directional monomolecular systems, including degradations, synthesis and generalized bypass reactions. Second, we provide all derivations of associated delays in analytical, closed form. Both advances have a major impact on further reducing computational costs, while still retaining full accuracy.

In Ghosh et al. (2015), we compare sample paths and moments of trajectorial solutions of RDME and Spatial Chemical Langevin Equation (SCLE). The SCLE is the spatial version of the CLE, a stochastic differential equation that is considered reasonably accurate for medium to large numbers of molecules. It is also considerably faster than other existing methods for simulation of stochastic biochemical networks.

In a combined experimental and computational study, my collaborators (Piehler Lab, University of Osnabrück; Prof. Marquez Lago, OIST) and I have succeeded in determining the lifetime of individual interferon receptor dimers at physiological cell surface expression levels using single quantum dot tracking. Strikingly, we identified a substantially enhanced complex stability as compared with molecular interactions studied in artificial membranes, which is caused by plasma membrane microcompartmentalization, based on the cortical actin skeleton (MSK). A self-consistent spatial-stochastic model, based entirely on

experimentally derived parameters, reproduced these functional properties. Importantly, the tight integration of our computational model and experiments was key to discovering a two-tiered plasma membrane compartmentalization being directly involved in regulating receptor stability. The manuscript has been submitted to *PNAS*.

Trajectories obtained from a Delay Stochastic Simulation Algorithm (DSSA) are exact representations of the underlying Delay Chemical Master Equation (DCME). However, in contrast to the CME, no closed form solutions have so far been derived for any kind of DCME. Prof. Marquez Lago and I recently got a manuscript accepted for publication in the Proceedings of the Royal Society A, describing for the first time direct and closed solutions of the DCME for simple reaction schemes.

In collaboration with Prof. Marquez Lago and Dr. Forte, I contributed to the development of a new spatial-stochastic reaction-diffusion algorithm, applicable both in the reaction-limited and the diffusion-limited regime. The manuscript has been already undergone final revisions and will soon be submitted.

Lastly, together with Prof. Marquez Lago I have been co-supervising the project work of Dr. Klingbeil. Based on our specifications, Dr. Klingbeil has programmed a software package featuring a hybrid genetic programming and simulated annealing approach to support the in-vitro design/in-silico study of biological circuits. A first draft of an application node has been revised and submission will follow shortly.

3 Collaborations

I have been and still are involved in various collaborations, in particular with Prof. Marquez Lago and her unit but also with researchers and groups outside OIST.

4 Publications and other output

Leier, A., Barrio, M., Marquez-Lago, T. (2014), Exact model reduction with delays: Closed-form distributions and extensions to fully bi-directional monomolecular reactions. Journal of the Royal Society Interface, 11(95):20140108.

Ghosh, A., **Leier, A.**, Marquez-Lago, T. (2015), The Spatial Chemical Langevin Equation and Reaction Diffusion Master Equations: Moments and Qualitative Solutions. Theoretical Biology and Medical Modelling, 12:5.

4.1 Conference Presentations/Invited Talks/Seminars

Bock Laboratories, University of Wisconsin at Madison, USA, May 9, 2014
Seminar: Modeling of spatio-temporal processes on the plasma membrane
ECMTB 2014, June 15-19, 2014
Talk: The effect of plasma membrane compartmentalization on receptor assembly dynamics
JSMB/SMB 2014, July 28 - August 1 2014
Invited Talk: The stabilizing effect of plasma membrane compartmentalization on IFN type I receptor assembly dynamics
ICSB 2014, September 14-18 2014
Talk: The effect of plasma membrane compartmentalization on receptor assembly dynamics