Sino-German Workshop on Multiscale spatial computational systems biology

Beijing, October 08 – 12, 2015

Monika Heiner

Brandenburg Technical University, Germany
monika.heiner@b-tu.de

Fei Liu

Harbin Institute of Technology, China
liufei@hit.edu.cn

October 11, 2015

Acknowledgement

This workshop has been funded by The Sino-German Center for Research Promotion (Grant no. GZ1203) The workshop is jointly held by the Harbin Institute of Technology and the Brandenburg Technical University Cottbus-Senftenberg.

Contents

Part I

GERMAN PARTICIPANTS

1 Mary-Ann Blätke

contact details

Otto-Von-Guericke University Magdeburg
Regulatory Biology
Pfälzer Straße 5, Carnot-Gebäude (Geb. 25)
39106 Magdeburg, Germany

maryann.blaetke@ovgu.de

http://www.regulationsbiologie.de/members/profiles/blaetke.php

talk

A Framework for Modular Biomodel Engineering

abstract. The biomodelkit framework allows to modular compose multi-scale biomodels from a set of modules. A module is defined as a Petri net describing the functionality of a single genetic component (gene, mRNA, protein) and its interactions with other components. Next to the Petri net, each module encloses rich annotations to be compliment with MIRIAM (Minimum Information Required in the Annotation of Models) standards. Both, the Petri net and the annotations are explicitly stored in a MySQL-Database with a public web-interface. Using the web-interface of the biomodelkit framework the user can submit and curate modules, browse through the modules and their structure, compose modular models and generate alternative models by applying model mutation algorithms. A new feature addressing the spatial aspects of multi-scale biomodel engineering allows to extend a modular composed model with spatial properties. The spatial transformation includes the conversion of the flat Petri net model to a coloured Petri net, to represent an arbitrary number of instances for each component in the modular composed model. Furthermore, the spatial transformation equips each component with a local position, which can be changed to represent its movement on a defined grid. The grid itself is scalable and can either be of discrete or continuous character in 1-, 2- or 3-dimensions. The formation of complexes, respectively the interactions among components, are restricted by their local positions. To move components forming a complex, the local positions of the involved components

have to be updated simultaneously. By using this spatial transformation approach the mechanisms and components in the composed models can be mapped to different cellular arrangement, as well as different cell geometries. Thus, the biomodelkit framework based on modular concept using Petri nets and supported by a web-accessible database offers a powerful tool for multi-scale biomodel engineering.

research interests

Petri nets, systems biology, system medicine, personalised medicine, computational biology, modelling standards, model ontology

publications

- MA Blätke, M Heiner and W Marwan: BioModel Engineering with Petri Nets; In Algebraic and Discrete Mathematical Methods for Modern Biology, (R Robeva, Ed.), Elsevier Inc., 2015.
- MA Blätke, C Rohr, M Heiner and W Marwan: A Petri Net based Framework for Biomodel Engineering; In Large-Scale Networks in Engineering and Life Sciences, (Benner, P, Findeisen, R, Flockerzi, D, Reichl, U and Sundmacher, K, Eds.), Springer, Birkäuser Mathematics, pages 317-366, December 2014.
- F Liu, MA Blätke, M Heiner and M Yang: Modelling and simulating reaction-diffusion systems using coloured Petri nets; Computers in Biology and Medicine, 53:297-308, October 2014 (online July 2014).
- MA Blätke, A Dittrich, C Rohr, M Heiner, F Schaper and W Marwan: JAK/STAT signalling - an executable model assembled from molecule-centred modules demonstrating a module oriented database concept for systems and synthetic biology; Molecular BioSystem, 9(6):1290-1307, 2013.
- W Marwan, MA Blätke: A module-based approach to biomodel engineering with Petri nets. In Proceedings of the 2012 Winter Simulation Conference (WSC 2012), Berlin, IEEE, 978-1-4673-4781-5/12, 2012.
- MA Blätke, M Heiner, W Marwan: Predicting Phenotype from Genotype through Automatically Composed Petri Nets Proc. 10th International Conference on Computational Methods in Systems Biology (CMSB 2012), London, Springer, LNCS/LNBI, volume 7605, pages 87-106

2 Thomas Buder

contact details

TU Dresden
Dep. of Innovative Methods of Computing Center for High Performance Computing
01062 Dresden, Germany

thomas.buder@tu-dresden.de

http://imc.zih.tu-dresden.de/imc/index.php?page=members&who=buder

http://imc.zih.tu-dresden.de/imc/index.php?page=cancer

talk

Mathematical model for pilocytic astrocytoma growth and progression provides clinical decision support

abstract. Pilocytic astrocytoma (PA) is the most common brain tumor in children and often only partial resection is possible due to the location of the tumor. In that case, spontaneous regression, regrowth, or progression to a more aggressive form have been observed. We developed a stochastic mathematical model for pilocytic astrocytoma growth and progression that allows to quantitatively predict the regression probability after partial resection based on epidemiological and volumetric data.

research interests

stochastic models of cancer progression; stochastic models of field cancerization; modeling and simulation environment Morpheus

publications

- T. Buder, B. Klink, A. Deutsch, A. Voss-Böhme. Mathematical Model for Pilocytic Astrocytoma Can Provide Clinical Decision Support, Cancer Research

Submitted and under revision.

- T. Buder, A. Deutsch, A. Voss-Böhme. Modelling Field Cancerization In The Human Colon, Journal of the Royal Society Interface, *Submitted*.

3 Fiete Haack

contact details

University of Rostock
Institute of Computer Science, Modeling and Simulation Group
Albert-Einstein- Str. 22
D-18059 Rostock, Germany

fiete.haack@uni-rostock.de

http://www.inf.uni-rostock.de/en/llm/graduate-network/scholarship-students/fiete-haack/

talk

Exploring the spatio- temporal dynamics of WNT/Beta-Catenin Signaling in-silico and in-vitro

abstract. The cell membrane plays a major role in signal transduction. It directly interacts with the extracellular space and cytosolic signaling components through transmembrane proteins and receptors. This talk addresses the impact of lipid rafts on the spatial organization of the cell membrane. Lipid rafts are small dynamic domains of locally concentrated sphingolipids and cholesterol in the membrane that significantly slow down receptor mobility. Based on a Cellular Automata model, the question of how lipid rafts and varying raft characteristics change the diffusion and localization of membrane-bound receptors as well as protein-receptor binding kinetics is elucidated. Our results demonstrate that in particular processes with slow dissociation and binding kinetics are promoted by lipid rafts, whereas fast binding processes are slightly hampered. Further, a combined in vitro and in silico approach is applied to evaluate the involvement of lipid rafts in the spatio-temporal regulation of WNT/Beta-catenin signaling. Based on experimental data retrieved from human neural progenitor cells (hNPCs), we built a stochastic WNT/Beta-catenin signaling model that, for the first time, correctly combines membrane-related and intracellular processes. Subsequent simulation studies indicate that the nuclear Beta-catenin dynamics observed experimentally can only by explained by a concisely regulated interplay between redox-dependent and

raft-dependent auto-/paracrine WNT signaling.

research interests

cellular signal transduction pathways, specifically cell surface receptor dynamics and membrane organization with current focus on lipid rafts and intracellular signal mediators in canonical WNT signaling during early neural differentiation; modeling and simulation with focus on Cellular Automata and rule based modeling

publications

- F Haack, H Lemcke, R Ewald, T Rharass, AM Uhrmacher (2015): Spatio-temporal model of endogenous ROS and raft- dependent Wnt/beta-catenin signaling driving cell fate commitment in human neural progenitor cells. - PLOS Computational Biology, 11(3):e1004106.
- M. Luboschik, S. Rybacki, F. Haack, and H.-J. Schulz (2014). Supporting the integrated visual analysis of input parameters and simulation trajectories. 2014. Comput. Graph. (39), 37-47.
- F Haack, K Burrage, R Redmer, AM Uhrmacher (2013): Studying the role of lipid rafts on protein receptor bindings with Cellular Automata. - IEEE/ACM Transactions on computational biology and bioinformatics, 10(3):760- 770.
- F. Haack, K. Fackeldey, S. Röblitz, O. Scharkoi, M. Weber, and B. Schmidt. Adaptive spectral clustering with application to tripeptide conformation analysis. 2013. J. Chem. Phys. (139), 194110.
- AT Bittig, F Haack, C Maus, AM Uhrmacher (2011): Adapting Rule-based Model Descriptions for Simulating in Continuous and Hybrid Space. - In: Proceedings of the 9th International Conference on Computational Methods in Systems Biology, pp. 161-170, New York, NY, USA, ACM. CMSB '11.
- S. Rybacki, J. Himmelspach, F. Haack, and A.M. Uhrmacher (2011). WorMS-a framework to support workflows in M&S. 2011 Proceedings of the 2011 Winter Simulation Conference, ed. by S. Jain and R. R. Creasey and J. Himmelspach and K. P. White and M. Fu,, Piscataway, New Jersey, Institute of Electrical and Electronics Engineers, Inc.

4 Monika Heiner

contact details

Brandenburg Technical University (BTU) Cottbus-Senftenberg
Institute of Computer Science
Walther-Pauer-Str. 2
03046 Cottbus, Germany

monika.heiner@b-tu.de

http://www-dssz.informatik.tu-cottbus.de/DSSZ/Main/MonikaHeiner

talk

From Petri Nets to Partial Differential Equations

abstract. Petri nets offer a graphical and intuitive notation for biochemical networks, which can be immediately executed and interpreted in different modelling paradigms. Our unifying Petri net framework developed over the last 15 years comprises the traditional time-free Petri nets (PN) as well as quantitative, i.e. time-dependent Petri nets such as stochastic Petri nets (SPN), continuous Petri nets (CPN), and hybrid Petri nets (HPN), as well as their their coloured counterparts.

Coloured Petri nets permit, among others, the convenient and flexible encoding of spatial attributes, and thus the modelling of processes evolving in time and space, which are usually considered as stochastic or deterministic reaction-diffusion systems by help of stochastic or deterministic partial differential equations (PDE). In our approach, the discretisation of space already happens on the modelling level, while traditionally the discretisation is left for the PDE integration method (FEM, FDM, FVM).

Our framework is supported by a related Petri net toolkit consisting of Snoopy, Charlie and Marcie. It has been applied to a couple of case studies; some of them will be sketched in this talk.

research interests

design and application of computational modelling and analysis techniques for systems and synthetic biology, with focus on spatial and temporal multiscale systems, efficient analysis and simulation techniques deploying (coloured qualitative, stochastic, continuous, hybrid) Petri nets, tool development (Snoopy, Marcie, Charlie);

publications

- MA Blätke, M Heiner, W Marwan: BioModel Engineering with Petri Nets; In Algebraic and Discrete Mathematical Methods for Modern Biology, (R Robeva, Ed.), Elsevier Inc., 2015.
- F Liu, MA Blätke, M Heiner and M Yang: Modelling and simulating reaction-diffusion systems using coloured Petri nets; Computers in Biology and Medicine, 53:297-308, October 2014 (online July 2014).
- M Heiner, D Gilbert: BioModel Engineering for Multiscale Systems Biology; Progress in Biophysics and Molecular Biology, 111(2-3): 119-128, 2013.
- MA Blätke, A Dittrich, C Rohr, M Heiner, F Schaper and W Marwan: JAK/STAT signalling - an executable model assembled from molecule-centred modules demonstrating a module oriented database concept for systems and synthetic biology; Molecular BioSystem, 9(6):1290-1307, 2013.
- M Heiner, D Gilbert: How Might Petri Nets Enhance Your Systems Biology Toolkit; Proc. PETRI NETS 2011, LNCS 6709, Springer, 17-37, 2011.

tools:

- M Heiner, M Schwarick and J Wegener: Charlie – an extensible Petri net analysis tool; In Proc. PETRI NETS 2015, Brussels, Springer, LNCS, volume 9115, pages 200-211, June 2015.
- M Herajy and M Heiner: A Steering Server for Collaborative Simulation of Quantitative Petri Nets; In Proc. PETRI NETS 2014, Tunis, Springer, LNCS, volume 8489, pages 374-384, June 2014.
- M Heiner, C Rohr and M Schwarick: MARCIE – Model checking And Reachability analysis done effiCIEntly; In Proc. PETRI NETS 2013, Milano, Springer, LNCS, volume 7927, pages 389-399, June 2013.
- M Heiner, M Herajy, F Liu, C Rohr and M Schwarick: Snoopy – a unifying Petri net tool; In Proc. PETRI NETS 2012, Hamburg, Springer, LNCS, volume 7347, 398-407, June 2012.

5 Christian Klukas

contact details

LemnaTec GmbH
Pascalstraße 59
52076 Aachen, Germany

previously
Leibniz Institute for Plant Genetics and Crop Plant Research (IPK)
Gatersleben, Germany, `http://www.ipk-gatersleben.de/en`

`christian.klukas@lemnatec.de`

`http://www.lemnatec.com`

talk

New approaches for analyzing multi-channel image data and post-processing of phenotypic data

research interests

information system for the storage and analysis of high-throughput image data; infrastructure for the automated movement and imaging of plants; investigate developmental changes and differences in the phenotype of plants

publications

- C Klukas, JM Pape, D Chen: Integrated Analysis Platform: An Open-Source Information System for High-Throughput Plant Phenotyping. Plant Physiol. 2014 165
- D Chen, ..., C Klukas: Dissecting the Phenotypic Components of Crop Plant Growth and Drought Responses Based on High-Throughput Image Analysis.

Plant Cell tpc.114.129601 (2014)

- BH Junker, C Klukas and F Schreiber (2006): VANTED: A system for advanced data analysis and visualization in the context of biological networks. BMC Bioinformatics, 7:109

6 Heinz Koeppl

contact details

Technische Universitaet Darmstadt
Rundeturmstraße 12
64287 Darmstadt, Germany

heinz.koeppl@bcs.tu-darmstadt.de

http://www.bcs.tu-darmstadt.de/biocomm/people_1/professor/heinzkoeppl.en.jsp

talk

Stochastic multi-scale models of biomolecular networks

abstract. Cellular reaction networks are often multi-scale in nature due to wide variation in the species abundance and reaction time scales. Traditional deterministic or stochastic modeling of such systems do not exploit this multi-scale feature and will either be inaccurate or computationally expensive for simulation or inference purposes. This necessitates developing simplified hybrid models combining both stochastic and deterministic approaches that can substantially speed up simulation of such reaction networks. In the talk I will present a layered partitioning approach which splits the reaction set into a fast and a slow group. We lay out a mathematical framework for objectively identifying these groups and performs a rigorous error analysis for the approximation proposed. We furthermore discuss a further partitioning of fast reactions into fast and super fast, where the latter is modelled according to ordinary differential equations. Coupling signal transduction with gene expression and metabolism is an important application domain for such multi-scale approximations.

research interests

systems biology, synthetic biology, statistical inference, Markovian population models, spatial models, single cell analysis, cell-to-cell variability, stochastic and hybrid

simulation algorithms;

publications

- Huang, L. ; Hjalmarsson, H. ; Koeppl, H. : Almost sure stability and stabilization of discrete-time stochastic systems. ScienceDirect, Systems and Control Letters (82)2015, pp. 26-32.
- C. Zechner, M. Unger, S. Pelet, M. Peter and H. Koeppl. Pooling single cell recordings: Scalable inference through heterogeneous kinetics. Nature Methods, 11, 197202, 2014.
- Koeppl, H.: Uncoupled analysis of stochastic reaction networks in fluctuating environments. PLOS Computational Biology, 10 (12) 2014, DOI: 10.1371/journal.pcbi.1003942.
- M. Klann and H. Koeppl. Reaction schemes, escape times and geminate recombinations in particle-based spatial simulations of biochemical reactions. Physical Biology, 10(4):046005, 2013.
- Koeppl, H. ; Hafner, M. ; Lu, J.. Mapping behavioral specifications to model parameters in synthetic biology. BMC Bioinformatics, 14 S9, 2013
- C. Zechner, J. Ruess, P. Krenn, S. Pelet, M. Peter, J. Lygeros, and H. Koeppl. Moment-Based Inference Predicts Bimodality in Transient Gene Expression. Proceedings of the National Academy of Sciences USA (PNAS),vol. 109, issue 21, pages 8340-8345, 2012.

7 Benjamin Kormeier

contact details

Bielefeld University
Faculty of Technology, Bioinformatics/Medical Informatics Department
P.O.-Box 10 01 31, (Universitätsstraße 25)
33501 Bielefeld, Germany

bkormeie@techfak.uni-bielefeld.de

http://www.techfak.uni-bielefeld.de/ags/bi/staff/groupmembers/kormeier_benjamin/

talk

Visualization of biological networks based on a data warehouse

abstract. The progress in the area of biological research in recent years leads to a multiplicity of different databases and information systems. For this purpose the BioDWH data warehouse integration infrastructure was developed. Information must be visualized in a clear and understandable way. With the help of DAWIS-M.D. (Data Warehouse Information System for Metabolic Data) it is possible for the scientist to search quickly and efficiently in large data sets. In addition, we present a software framework for visualizing and modeling biological networks VANESA. Moreover based on the database integration we present a web-based decision support system GraphSAW which analyzes and evaluates drug interactions and side effects.

research interests

data warehouse, database integration, information system, network modelling, network visualization, drug interactions, drug side effects;

publications

- Shoshi A, Hoppe T, Kormeier B, Ogultarhan V, Hofestädt R (2015): GraphSAW: A web-based system for graphical analysis of drug interactions and side effects using pharmaceutical and molecular data. BMC Medical Informatics and Decision Making 15:15.
- Kormeier B.: Data Warehouses in Bioinformatics; In: Approaches in Integrative Bioinformatics - Towards the Virtual Cell; Chen M, Hofestädt R (eds), ISBN:3642412807, Springer Verlag Heidelberg New York Dordrecht London, (2014)
- Sommer B, Kormeier B, Demenkov PS, Arrigo P, Hippe K, Ates Ö, Kochetov AV, Ivanisenko VA, Kolchanov NA, Hofestädt R (2013): Subcellular localization charts: a new visual methodology for the semi-automatic localization of protein-related data sets; Journal of Bioinformatics and Computational Biology 11(1): 1340005.

8 Jens Krüger

contact details

University of Tübingen
Applied Bioinformatics, Department of Computer Science
Sand 14
72076 Tübingen, Baden-Württemberg, Germany

krueger@informatik.uni-tuebingen.de

https://abi.inf.uni-tuebingen.de/People/krueger

talk

Molecular Simulations using Workflows and Science Gateways

abstract. Research in structural bioinformatics and computational chemistry relies on a tremendous amount of different tools, applications and software suites. Their correct and reproducible usage represents a considerable hurdle for scientific users. The talk will highlight, how simulation protocols can be represented as scientific workflows, improving transparency and reproducibility just in the sense of good lab practice. Furthermore the benefits of science gateways for hosting these workflows such as the MoSGrid portal will be presented, including aspects like data handling and user management. Finally the positive impact of science gateways on teaching bioinformatics and related courses will be demonstrated.

research interests

molecular simulations, ion channels, membrane proteins, allosteric modulation, science gateways, simulation protocols as workflows, high performance computing;

publications

- M. Avbelj, O. O. Wolz, O. Fekonja, M. Bencina, M. Repic, J. Mavri, J. Krüger, C. Schärfe, M. Delmiro Garcia, G. Panter, O. Kohlbacher, A. N. R. Weber, R. Jerala: Activation of lymphoma-associated MyD88 mutations via allostery-induced TIR domain oligomerization, Blood 2014, doi:10.1182/blood-2014-05-573188.
- A. K. Hildebrandt, D. Stöckel, N. M. Fischer, L. de la Garza, J. Krüger, S. Nickels, M. Röttig, C. Schärfe, M. Schumann, P. Thiel, H. P. Lenhof, O. Kohlbacher and A. Hildebrandt: ballaxy: web services for structural bioinformatics, Bioinformatics 2014, doi:10.1093/bioinformatics/btu57.
- J. Krüger, R. Grunzke, S. Gesing, S. Breuers, A. Brinkmann, L. de la Garza, O. Kohlbacher, M. Kruse, W.E. Nagel, L. Packschies, R. Müller-Pfefferkorn, P. Schäfer, C. Schärfe, T. Steinke, T. Schlemmer, K. Warzecha, A. Zink and S. Herres-Pawlis: The MoSGrid Science Gateway – A Complete Solution for Molecular Simulations, Journal of Chemical Theory and Computation 2014, 10 (6), 2232-2245, DOI: 10.1021/ct500159h.
- G. Lukat, J. Krüger and B. Sommer: APL@Voro: A Voronoi-Based Membrane Analysis Tool for GROMACS Trajectories, Journal of Chemical Information and Modeling 2013, 53(11): 2908-2925.
- X. G. Zong, S. Krause, C. C. Chen, J. Krüger, C. Gruner, X. C. Cao-Ehlker, S. Fenske, C. Wahl-Schott, and M. Biel: Regulation of HCN channel activity by cyclic cytidine 3', 5'- monophosphate (cCMP), Journal of Biological Chemistry, 287(32): 26506-26512, 2012.
- O. Niehörster, A. Brinkmann, A. Keller, C. Kleineweber, J. Krüger and J. Simon: Cost-Aware and SLO-Fulfilling Software as a Service, Journal of Grid Computing, 10(3): 553-577, 2012.

9 Xin Lai

contact details

Friedrich-Alexander University Erlangen-Nuremberg
University Hospital Erlangen, Laboratory of Systems Tumour Immunology, Department of Dermatology
Building D4, Hartmannstraße 14
91052 Erlangen, Germany

xin.lai@uk-erlangen.de

http://sysbiomed-erlangen.weebly.com/members.html

talk

Mathematical modelling of the communication between alveolar macrophages and epithelial cells during Legionella pneumophila infection

abstract. Pneumonia is an acute inflammatory lung disease provoked by infection with different pathogens, including Legionella *pneumophila (L. pneumophila)*. The invading of *L. pneumophila* into the lung triggers the response of resident alveolar macrophages, which produce pro-inflammatory cytokines, such as IL-1β. However, the mechanism by which the macrophages communicate with surrounding epithelial cells in the lung to keep a tight control of the local inflammatory response remains to be further elucidated. In this study, we combined experimental data with mathematical modelling to dissect the features of the NF-κB signalling mediated process underlying this mechanism. We found that alveolar macrophages can cause the tolerance of lung epithelial cells via IL-1β. After recognising IL-1β, quick degradation of IRAK1 protein happens within the epithelial cells and blocks further stimulation by bacterial factors, such as flagellin. Moreover, we used the data-driven model to assess the influence of clinically relevant factors, such as single nucleotide polymorphisms (SNPs) within the IRAK1 gene altering its protein stability, on the lung inflammatory response induced by *L. pneumophila*.

research interests

Dynamic system, ODE models, Parameter estimation, Parameter identifiability, Network biology, Microarray data analysis, MicroRNA, Cellular signal transduction pathways & decisions, Melanoma

publications

- U Schmitz, X Lai, F Winter, O Wolkenhauer, J Vera, SK Gupta (2014). Cooperative gene regulation by microRNA pairs and their identification using a computational workflow. Nucleic Acids Research, 42, 7539-52.
- X Lai, A Bhattacharya, U Schmitz, M Kunz, J Vera, O Wolkenhauer (2013). A systems biology approach to study microRNA-mediated gene regulatory networks. BioMed Research International, 7038-49.
- J Vera, U Schmitz, X Lai, D Engelmann, FM Khan, O Wolkenhauer, BM Pützer (2013). Kinetic modeling-based detection of genetic signatures that provide chemoresistance via the E2F1-p73/DNp73-miR-205 network. Cancer Research, 73, 3511-3524.
- X Lai, U Schmitz, SK Gupta, A Bhattacharya, M Kunz, O Wolkenhauer, J Vera (2012). Computational analysis of target hub gene repression regulated by multiple and cooperative microRNAs. Nucleic Acids Research, 40, 8818-8834.

10 Adelinde M. Uhrmacher

contact details

University of Rostock
Institute of Computer Science
Albert-Einstein Str. 21
18055 Rostock, Germany

adelinde.uhrmacher@uni-rostock.de

http://mosi.informatik.uni-rostock.de/4379.html?&L=1

talk

The Role of Domain Specific Languages For Spatial, Multi-Level Modeling and Simulation

abstract. Domain specific languages offer the possibility of a compact, succinct description of models and experiments likewise. Particularly, given the complexity of spatial multi-level models and the experiments executed to validate these models, additional support is required. We present two rule-based domain specific external languages for modeling, ML-Rules and ML-Space. Both are aimed at multi-level modeling of cells from intra-cellular up to tissue level. Whereas their syntax is rather similar, their semantics is different. Its hybrid spatial semantics allows ML-Space to take excluded volumes and species moving in continuous space into account, in addition to providing support for compartmental, e.g., the merging and splitting of cells, and reaction-diffusion systems dynamics. The CTMC semantics gives ML-Rules more freedom in specifying compartmental as well as reaction-diffusion systems dynamics. Both languages add to the family of external domain specific rule-based modeling languages like BioNetgen or Kappa.

Domain-specific languages can also be used for specifying experiments. SESSL (Simulation Experiment Specification via a Scala Layer), an internal domain-specific language for simulation experiments, supports multiple simulation systems and offers various features (e.g., for experiment design, performance analysis, result reporting, simulation-based optimization or statistical model checking). Being simulation system

agnostic, it enables a reuse of functionality across simulation systems.

Describing models or experiments in a domain specific language tailored to the requirements at hand promises a higher transparency, better reproducibility, and easier reuse of simulation results. However, as any language, domain-specific languages used for modeling or simulation have to meet requirements like compactness, composability, ease of use, and flexibility. The evaluation of which is not trivial but important for the field to mature.

position statement

Future – Trends – Open Issues in Systems Biology

abstract. I have been asked for a short list of challenges to start the workshop.

Number one I called the obvious one, because executing spatial models is known to be expensive, up to the point to prevent thorough validation experiments. Trading accuracy for speed automatically and carefully in hybrid approaches will provide part, but likely only part, of the answer.

Number two I called the notorious one. Spatial models have to be validated based on real data. If we are interested in spatial phenomena, those need to be accessible and quantified to compare the simulation results with.

Number three I called the glorious one, as it is fun to develop modeling approaches for these systems. However, the question is whether domain-specific languages, extending existing formalism, or multi-formalisms approaches are the way to go. In any case, the evaluation of languages to determine their suitability and value needs more work.

As last in this row, I would like to mention, being aware that more exist of course, the problem of reproducibility. Given the problems to reproduce often simpler models and the various extensions of SBML referring to compartmental, spatial, or variable structure models that are rather slow in converging, how do we ensure that these highly complex spatial models being realized in often hand-tailored tools can be reused in other tools and the experiments be repeated achieving similar results.

research interests

Developing modeling and simulation methods and their applications. Among the applications, cell biology has played a central role for more than a decade. Her methodological research aims at developing modeling formalisms and languages for multi-level modeling, efficient execution algorithms and intelligent support for executing simulation experiments.

publications

- A. T. Bittig, C. Matschegewski, J. B. Nebe, S. Stahlke, and A. M. Uhrmacher. Membrane related dynamics and the formation of actin in cells growing on microtopographies: A spatial computational model. BMC Systems Biology, 8:106, 2014.
- M. Jeschke, R. Ewald, and A. M. Uhrmacher. Exploring the performance of spatialstochastic simulation algorithms. Journal of Computational Physics, 230(7):2562-2574, 2011.
- C. Maus, S. Rybacki, and A. M. Uhrmacher. Rule-based multi-level modeling of cell biological systems. BMC Systems Biology, 5:166, October 2011.

Part II

CHINESE PARTICIPANTS

11 Ming Chen

contact details

Zhejiang University
Yuhangtang Rd. 866
Hangzhou 310058, China

mchen@zju.edu.cn

talk

Genome-wide multilevel spatial interactome model of rice

abstract. Multi-omics data brings us a challenge to develop appropriate computational systems biology approaches to model complex biological systems at spatial and temporal scales. In this talk, we will describe multi-omics data available for rice cellular interactome modeling. Biological networks on multiple levels such as gene regulations, protein interactions, noncoding RNA regulations and metabolic reactions are reconstructed. A systematic identification and quantification of rice proteins in various tissues and organs are introduced. To better understand the interactions of proteins in rice, we developed PRIN, a predicted rice interactome network. We presented a novel integrative approach (PSI) that derives the wisdom of multiple specialized predictors via a joint-approach of group decision making strategy and machine learning methods to achieve better prediction results of protein subcellular localization. A genome-wide multiple level of interactome model of rice is integratively built. Furthermore, a database RiceNetDB is developed for systematically storing and retrieving the genome-scale multi-level network of rice to facilitate biomolecular regulatory analysis and gene-metabolite mapping. A virtual rice cell model in three dimensions will be developed via international collaborations.

research interests

systems biology, computational and functional analysis of transcriptomics, and bioinformatics research and application for plant sciences

publications

- Zhao Zhang, Li Jiang, Jingjing Wang, Peizhen Gu, Ming Chen (2014) MTide: an integrated tool for the identification of miRNA-target interaction in plants. Bioinformatics, doi:10.1093/bioinformatics/btu633.
- D Chen, Liang-Yu Fu, Zhao Zhang, Guoliang Li, Hang Zhang, Li Jiang, Andrew Harrison, Hugh Shanahan, Christian Klukas, Hong-Yu Zhang, Yijun Ruan, Lingling Chen, Ming Chen (2014) Dissecting the chromatin interactome of microRNA genes. Nucleic Acids Research, 42(5):3028-3043.
- L Liu, L Jiang, M Chen (2014) The Organelle-focused Proteomes and Interactomes in Rice. Current Protein & Peptide Science, 15(6): 583-590.

12 Gang Guo

contact details

National University of Defence Technology
Institute of Simulation Engineering, College Of Information System And Management
No.137 Yanwachi Street
Changsha Hunan 410073, China

hndzgg@aliyun.com

http://www.researchgate.net/institution/National_University_of_Defense_Technology/members/3

talk

Monte Carlo simulation of anomalous diffusion and its accuracy analysis

abstract. Anomalous diffusion observed in numerous physical, chemical and biological systems in recent years turns out to be quite ubiquitous which is characterized by a nonlinear behavior for the mean square displacement as a function of time. For anomalous diffusion described by fractional partial differential equation, lattice Monte Carlo (LMC) simulation is an important and effective method when it is difficult to get analytical solutions or necessary to track the trajectory of particles. We discuss some typical anomalous diffusions which are widely used in real applications, i.e., the Galilei-invariant fractional diffusion-drift equation, the Galilei-variant fractional diffusion-drift equation, and the modified fractional diffusion equation with two time scales. The first task is to derive the analytical solutions with different initial and boundary conditions, the first passage time distributions (FPT) and the corresponding Laplace transforms. The LMC simulation algorithms can be designed and developed based on the theory of continuous time random walk (CTRW). The study attempts to determine if there exists a separable CTRW model with a fixed lattice step in its structure function that is equivalent to the anomalous diffusion distribution in the sense of finite order moments or discrete integral transformations. Both the macroscopic and the microscopic accuracy of the LMC simulation algorithm will be analyzed and verified quantitatively by means of the difference between the higher order moments and the distribution func-

tions respectively with the help of stochastic simulation and numerical calculation. The goal is to reveal partly the microscopic mathematical and physical mechanism and the very nature of the typical anomalous diffusion as well as to provide rigorous mathematical theory and core algorithm for the application of stochastic simulation with high accuracy.

research interests

publications

- Guo Gang, Li Kun, Wang Yuhui, Exact solutions of a modified fractional diffusion equation in the finite and semi-infinite domains, Physica A (417), 193-201, 2015.
- Guo Gang, Qiu Xiaogang, First passage time distributions of anomalous biased diffusion with double absorbing barriers, Physica A (411), 80-86, 2014.
- Guo Gang, Qiu Xiaogang, Accuracy of lattice Monte Carlo simulation of biased diffusion models, Physical Review E (90), 043305, 2014.

13 Rui Jiang

contact details

Tsinghua University
FIT 1-107
Beijing 100084, China

ruijiang@tsinghua.edu.cn

http://bioinfo.au.tsinghua.edu.cn/member/ruijiang/english/index.html

talk

Identification of disease-causing single nucleotide variants in exome sequencing studies

abstract. Exome sequencing has been widely used in detecting pathogenic nonsynonymous single nucleotide variants (SNVs) for human inherited diseases. However, traditional statistical genetics methods are ineffective in analyzing exome sequencing data, due to such facts as the large number of sequenced variants, the presence of non-negligible fraction of pathogenic rare variants or de novo mutations, and the limited size of affected and normal populations. Here, we propose two bioinformatics approach SPRING and GLINTS for identifying pathogenic nonsynonymous SNVs for a given query disease. SPRING, abbreviation for *Snv PRioritization via the INtegration of Genomic data*, integrates six functional effect scores calculated by existing methods and five association scores derived from a variety of genomic data sources to calculate the statistical significance that an SNV is causative for a query disease. This method is designed to use with a set of seed genes known as associated with the disease of interest, and thus is suitable for studies on diseases with some prior knowledge. GLINTS, meaning *GLobal INference of disease-causing single nucleotide varianTS*, further incorporates three disease phenotype similarity data to facilitate the detection of causative SNVs without any knowledge of seed genes for a query disease. This method is therefore suitable for research on diseases whose genetic bases are completely unknown. With a series of comprehensive validation experiments, we demonstrate the effectiveness of both methods, not only in simulation studies, but also in detecting causative *de novo*

mutations for autism, epileptic encephalopathies and intellectual disability.

research interests

precision medicine, gene regulation network construction, deep learning;

publications

- Mengmeng Wu, Jiaxin Wu, Ting Chen, Rui Jiang, Prioritization of nonsynonymous single nucleotide variants for exome sequencing studies via integrative learning on multiple genomic data, Scientific Reports, In press, 2015
- Rui Jiang, Walking on multiple disease-gene networks to prioritize candidate genes, Journal of Molecular Cell Biology, 7(3):214-230, 2015
- Shining Ma, Tao Jiang, Rui Jiang, Differential regulation enrichment analysis via the integration of transcriptional regulatory network and gene expression data, Bioinformatics, 31(4): 563-571, 2015
- Jiaxin Wu, Yanda Li, Rui Jiang, Integrating multiple genomic data to predict disease-causing nonsynonymous single nucleotide variants in exome sequencing studies, PLoS Genetics, 10(3): e1004237, 2014
- Yong Chen, Jingjing Hao, Wei Jiang, Tong He, Xuegong Zhang, Tao Jiang, Rui Jiang, Identifying potential cancer driver genes by genomic data integration, Scientific Reports, 3:3538, 2013
- Feng Zeng, Rui Jiang, Ting Chen, PyroHMMsnp: a SNP caller for Ion Torrent and 454 sequencing data, Nucleic Acids Research, 41(13):e136, 2013
- Y Chen, T Jiang, R Jiang, Uncover disease genes by maximizing information flow in the phenome-interactome network, Bioinformatics, 27:i167-i176, 2011
- Wanwan Tang, Xuebing Wu, Rui Jiang, Yanda Li *, Epistatic module detection for case-control studies: A Bayesian model with a Gibbs sampling strategies, PLoS Genetics, 5(5): e1000464, 2009
- Xuebing Wu, Qifang Liu, Rui Jiang, Align human interactome with phenome to identify causative genes and networks underlying disease families, Bioinformatics, 25(1):98-104, 2009
- Rui Jiang, Zhidong Tu, Ting Chen, Fengzhu Sun, Network motif identification in stochastic networks, Proc Natl Acad Sci USA, 103(25): 9404-9409, 2006

14 Taijiao Jiang

contact details

Chinese Academy of Sciences
Institute of Biophysics
15 Datun Rd. Chaoyang District
Beijing 100101, China

taijiao@moon.ibp.ac.cn

http://english.ibp.cas.cn/ibp_pi/HK/201311/t20131113_112605.html

just moved to
Chinese Academy of Medical Sciences (CAMS),
Suzhou Institute of Systems Medicine
http://www.ismsz.cn

talk

Modeling influenza virus evolution in big data era

abstract. The advancement of high throughput sequencing technology coupled with internet technology has enabled us to acquire massive genomic data for in-depth understanding of disease mechanisms, facilitating more effective strategies for disease prevention and treatment. In our lab, by focusing influenza viruses, we have developed a series of methods [1-5] to model influenza evolution from the massive gene data collected during influenza surveillance carried out by Chinese Center for Disease Control and Prevention (China CDC). Furthermore, we have proposed network-based approaches for effective seasonal influenza vaccine strain selection [4], and found the genetic pathways towards the generation of the novel H7N9 viruses occurred in East China of 2013. No doubt, the effective mining of the big genomic data related to diseases will not only greatly facilitate the prevention and control of infectious diseases but also advance the precision medicine for complex diseases like malignant tumors.

research interests

studying gene and protein networks involved in infectious diseases by network analysis and structural modeling; modeling of protein structures and complex biological systems, including novel computational methods to model the genetic and antigenic evolution of seasonal influenza virus;

development of novel computational methods for protein structure prediction, genomic co-evolution analysis, bio-medical data mining and complex network modeling; integration of computation and experiments to understand the molecular events underlying complex diseases including infectious diseases. discovery of disease bio-markers for diseases classification, early diagnosis and precision medication.

publications

- Lizong Deng, Aiping Wu, Wentao Dai, Tingrui Song, Ya Cui, and Taijiao Jiang. Exploring protein domain organization by recognition of secondary structure packing interfaces. Bioinformatics. 2014 May 10. pii: btu327. [Epub ahead of print]
- Aiping Wu, Chunhu Su, Dayan Wang, Yousong Peng, Mi Liu, Sha Hua, Tianxian Li, George F Gao, Hong Tang, Jianzhu Chen, Xiufan Liu, Yuelong Shu, Daxin Peng, Taijiao Jiang. Sequential Reassortments Underlie Diverse Influenza H7N9 Genotypes in China. Cell Host & Microbe 2013, DOI: 10.1016/j.chom.2013.09.001
- Xiangjun Du, Libo Dong, Yu Lan, Yousong Peng, Aiping Wu, Ye Zhang, Weijuan Huang, Dayan Wang, Min Wang, Yuanji Guo, Yuelong Shu, Taijiao Jiang. Mapping of H3N2 influenza antigenic evolution in China reveals a strategy for vaccine strain recommendation. Nature Communications, 28 Feb 2012; 3:709. DOI: 10.1038/ncomms1710.
- Aiping Wu, Yousong Peng, Xiangjun Du, Yuelong Shu, Taijiao Jiang. Correlation of Influenza Virus Excess Mortality with Antigenic Variation: Application to Rapid Estimation of Influenza Mortality Burden. PLoS Computational Biology, 2010 Aug 12; 6(8):e1000882.
- Xiangjun Du, Zhuo Wang, Aiping Wu, Lin Song, Yang Cao, Haiying Hang, Taijiao Jiang. Networks of genomic co-occurrence capture characteristics of human influenza A (H3N2) evolution. Genome Research, 2008 Jan 1; 18(1):178-87.

15 Fangting Li

contact details

Peking University
School of Physics, Center for Quantitative Biology
No. 5, Yiheyuan street, Haidian district
Beijing, 100871, China

lft@pku.edu.cn

http://cqb.pku.edu.cn/en/kxdw/zxjs/fangtingli/253614.shtml

talk

The cell cycle model in budding yeast

Yeast cells produce daughter cells through a DNA replication and mitosis cycle associated with checkpoints and governed by the cell cycle regulatory network. To ensure genome stability and genetic information inheritance, this regulatory network must be dynamically robust against various fluctuations. Here we construct a simplified cell cycle model for a budding yeast to investigate the underlying mechanism that ensures robustness in this process containing sequential tasks (DNA replication and mitosis). We first establish a three-variable model and select a parameter set that qualitatively describes the yeast cell cycle process. Then, through nonlinear dynamic analysis, we demonstrate that the yeast cell cycle process is an excitable system driven by a sequence of saddle-node bifurcations with ghost effects. We further show that the yeast cell cycle trajectory is globally attractive with modularity in both state and parameter space, while the convergent manifold provides a suitable control state for cell cycle checkpoints. These results not only highlight a regulatory mechanism for executing successive cell cycle processes, but also provide a possible strategy for the synthetic network design of sequential-task processes.

research interests

quantitative biology of the cell cycle process in yeast; quantitative biology of the DNA damage response in yeast; modeling the immune system response;

publications

- Lv Cheng, Li Xiaoguang, Li Fangting, Li Tiejun (2014) Constructing the Energy Landscape for Genetic Switching System Driven by Intrinsic Noise. PLoS ONE 9(2): e88167. doi:10.1371/journal.pone.0088167.
- Lin Hou, Lin Wang, Minping Qian, Dong Li, Chao Tang, Yunping Zhu, Minghua Deng, and Fangting Li (2011) Modular Analysis of the Probabilistic Genetic Interaction Network. Bioinformatics, 27:853-859.
- Fangting Li, Ning Tan (2006) Genetic and logic networks with signal-inhibitor-activator structure are dynamical robust. Progress in Natural Science. 16:1329-1336.
- Fangting Li, Xun Jia (2006) Dynamical Analysis of Protein Regulatory Network in Budding Yeast Nucleus. Chinese Physics Letters. 23:2307-2310.
- Y. Zhang, M. Qian, Q. Ouyang, M. Deng, F. Li, C. Tang (2006) A stochastic model of the yeast cell cycle network. Physica D, 219: 35-39.
- Fangting Li, Ying Lu, Tao Long, Qi Ouyang, Chao Tang (2006) Dynamical properties of cell cycle and life cycle networks in budding yeast. In: Network: from biology to theory, edited by J. Feng, J. Jost and M. Zhang. Springer-Verlag. Page 221-230.
- Fangting Li, Tao Long, Ying Lu, Qi Ouyang, Chao Tang (2004) The yeast cell cycle network is robustly designed. Proc. Natl. Acad. Sci. USA 101:4781-4786.

16 Fei Liu

contact details

Harbin Institute of Technology, Control and Simulation Center
Room 210, Building E1, Harbin Institute of Technology Science Park Yikuang Str. 2
Harbin, 150080, China

liufei@hit.edu.cn

http://homepage.hit.edu.cn/pages/liufei

talk

Colored Petri nets for multiscale systems biology

bstract. Systems biology aims to understand the behavior of a biological system at the system level by means of investigating the behavior and interactions of all the components in the system. Due to the ability to produce data of one and the same phenomenon at different scales, the modeling of biological systems is moving from single scales to multiple scales, e.g., from the molecular scale to the cell, tissue, and even the whole organism level. In this report, we will present a colored Petri net pproach to modeling and analyzing multiscale systems biology. Specifically, in this report you will see what are colored Petri nets, what challenges of multiscale systems biology can be tackled by colored Petri ets, a colored Petri net framework for multiscale systems biology, and a couple of case studies.

research interests

Modeling and simulation for (multi-scale) Systems Biology and Synthetic Biology; Colored qualitative, stochastic, continuous, and hybrid Petri nets; Stochastic/PDE/ODE/hybrid simulation algorithms

publications

- F Liu, M Heiner and M Yang: Representing Network Reconstruction Solutions with Colored Petri Nets; Neurocomputing, 2015.
- F Liu, M Heiner and M Yang: Modeling and analyzing biological systems using colored hierarchical Petri nets, illustrated by C. elegans vulval development. WSPC Journal of Biological Systems, 22(3):463-493, online May 2014..
- F Liu and M Heiner: Petri Nets for Modeling and Analyzing Biochemical Reaction Networks. In "Approaches in Integrative Bioinformatics", (M Chen and R Hofestädt, Eds.), Springer, 23 Oct 2013: 245-272.
- F Liu, MA Blätke, M Heiner and M Yang: Modelling and simulating reaction-diffusion systems using coloured Petri nets; Computers in Biology and Medicine, 53:297-308, October 2014 (online July 2014).
- D Gilbert, M Heiner, F Liu and N Saunders: Colouring Space - A Coloured Framework for Spatial Modelling in Systems Biology; In Proc. PETRI NETS 2013, Milano, Springer, LNCS, volume 7927, pages 230-249, June 2013.
- Q Gao, D Gilbert, M Heiner, F Liu, D Maccagnola and D Tree: Multiscale Modelling and Analysis of Planar Cell Polarity in the Drosophila Wing; IEEE/ACM Transactions on Computational Biology and Bioinformatics, 10(2):337-351, 2013 (online 01 August 2012).
- F Liu and M Heiner: Modeling membrane systems using colored stochastic Petri nets; Nat. Computing, 12(4):617 - 629, 2013.
- F Liu, M Heiner and M Yang: An efficient method for unfolding colored Petri nets; In Proceedings of the 2012 Winter Simulation Conference (WSC 2012), Berlin, IEEE, 978-1-4673-4781-5/12, 2012.

17 Zujian Wu

contact details

Jinan University
Center of Computation, College of Information Science and Technology
No.601, Huangpu Dadao Xi, Tianhe District
510632, Guangzhou, Guangdong, China

zujian.wu@jnu.edu.cn

http://ming.jnu.edu.cn/zwu.html

talk

An integrated qualitative and quantitative biochemical model learning framework using evolutionary methodologies

abstract. Both qualitative and quantitative model learning frameworks for biochemical systems have been studied in computational systems biology. In this talk, after illustrating two forms of pre-defined component patterns to represent biochemical models, I will introduce an integrative qualitative and quantitative modelling framework for inferring biochemical systems. Interactions between reactants in the candidate models for a target biochemical system can be evolved and eventually identified by the application of a qualitative model learning approach with an evolution strategy. Kinetic rates of the models generated from qualitative model learning are then further optimised by employing a quantitative approach with simulated annealing. Experimental results indicate that our proposed integrative framework is feasible to learn the relationships between biochemical reactants qualitatively and to make the model replicate the behaviours of the target system by optimising the kinetic rates quantitatively. Moreover, potential reactants of a target biochemical system can be discovered by hypothesising complex reactants in the synthetic models. Based on the biochemical models learned from the framework, biologists can further perform experimental study in wet laboratory. In this way, natural biochemical systems can be better understood.

research interests

publications

- Z. Wu, W. Pang, and G. M. Coghill. An integrated qualitative and quantitative biochemical model learning framework using evolutionary strategy and simulated annealing. Cognitive Computation, DOI:10.1007/s12559-015-9328-x. (2015)
- Z. Wu, W. Pang, and G. M. Coghill. An integrative top-down and bottom-up qualitative model construction framework for exploration of biochemical systems. Soft Computing, pp. 1-16, 2014. ISSN: 1432-7643, DOI:10.1007/s00500-014- 1467-6. (2014)
- Z. Wu, W. Pang, and G. M. Coghill. Stepwise modelling of biochemical pathways based on qualitative model learning. In Y. Jin and S. A. Thomas (eds), Proceeding of the 13th UK Workshop on Computational Intelligence. Computational Intelligence (UKCI 2013), 2013 13th UK Workshop on, Surrey, UK, 9-11 September. IEEE Xplore, pp. 31-37, IEEE Catalog Number CFP1348L-ART, ISBN 978-1-4799-1568-2. (2013).

18 Ziding Zhang

contact details

China Agricultural University
College of Biological Sciences
Yuanmingyuan xilu 2, Haidian District
Beijing 100193 China

zidingzhang@cau.edu.cn

talk

Understanding Plant Immunity through Integrative Network Analysis

abstract. Plants have evolved a sophisticated immune system that enables each cell to monitor every possible destructive invasion by microbe and to mount an appropriate defense response when necessary Pattern-triggered immunity (PTI) and effector-triggered immunity (ETI) are two primary immune defense modes in plants. Up to now, genome-wide gene network organizing principles leading to quantitative differences between PTI and ETI have remained elusive. With the increasing availability of genome, proteome, and interactome data, network biology is becoming an important approach to decipher the molecular mechanism of plant immunity. Recently, we developed an advanced machine learning method and modular network analysis to systematically characterize the organization principles of Arabidopsis PTI and ETI. In this talk, we report our major findings from three network resolutions. At a single network node/edge level, we ranked important genes and gene interactions for immune response and successfully identified many known immune regulators for PTI and ETI, respectively. Topological analysis showed that important gene interactions tend to link network modules. At a subnetwork level, we identified a subnetwork shared by PTI and ETI, which covers 1159 genes and 1289 interactions. In addition to being enriched with interactions linking network modules, it is also a hotspot attacked by pathogen effectors. The subnetwork likely represents a core component to coordinate multiple biological processes in the transition from development to defense. Finally, we constructed modular network models for PTI and ETI to explain the quantitative differences from

the global network architecture. Our results show defense modules appeared to be interdependently connected in PTI, but independently connected in ETI, providing an explanation for the robustness of ETI to genetic mutations and effector attacks. Taken together, the multiscale comparisons between PTI and ETI provide a systems biology point of view to understand plant immunity, and highlight the coordination among network modules to establish a robust immune response.

research interests

plant, pattern-triggered immunity, effector-triggered immunity, network, machine learning, systems biology

publications

- Dong X, Zhang Y-J, Zhang Z (2013) Using weakly conserved motifs hidden in secretion signals to identify type-III effectors from bacterial pathogen genomes. PLoS ONE, 8: e56632.
- Li Z-G, He F, Zhang Z, Peng Y-L (2012) Prediction of protein-protein interactions between Ralstonia solanacearum and Arabidopsis thaliana. Amino Acids, 42: 2363-2371.
- He F, Zhou Y, Zhang Z (2010) Deciphering the Arabidopsis floral transition process by integrating a protein-protein interaction network and gene expression data. Plant Physiol, 153: 1492-1505.

Part III

THIRD COUNTRY PARTICIPANTS

19 David Gilbert

contact details

Brunel University London
Computational Design Group, Systems Biology
Uxbridge, UB8 3PH, United Kingdom

david.gilbert@brunel.ac.uk

http://people.brunel.ac.uk/~csstdrg

talk

Model checking for multiscale biological systems

abstract. I will present recent work from our group on the development of a model checking methodology and associated software for multiscale biological systems. These techniques are derived from extensions of standard model checking using temporal logic combined with a form of multidimensional spatial logic and a tree-based architectural description of multilevel biological systems. The method is implemented using simulative model checking, and can be applied to checking the behaviour of not only models but of multiscale biological systems themselves, and thus can be employed as part of the design-implementation process of complex synthetic biological systems. The approach is generic in that it can easily be applied to model checking other non-biological systems.

I will briefly illustrate this approach with the application of our techniques to some case studies.

research interests

model checking, temporal logic, systems biology, synthetic biology, computational design, multidimensional, multilevel.

publications

- O Parvu, D Gilbert, M Heiner, F Liu, N Saunders and S Shaw: Spatial-temporal modelling and analysis of bacterial colonies with phase variable genes; ACM Transactions on Modeling and Computer Simulation (TOMACS), 2015
- O. Parvu, D. Gilbert (2014): Automatic validation of computational models using pseudo-3D spatio-temporal model checking. BMC Systems Biology 2014, 8:124
- O. Parvu, D. Gilbert (2014): Implementation of linear minimum area enclosing triangle algorithm. Computational and Applied Mathematics pp 1-6, November 2014.
- X. Liu, S. J. E. Taylor, N. Mustafee, J. Wang, Q. Gao, D. Gilbert (2014): Speeding up systems biology simulations of biochemical pathways using condor. Concurrency and Computation: Practice and Experience. Volume 26, Issue 17, pages 2727-2742.
- Q Gao, D Gilbert, M Heiner, F Liu, D Maccagnola and D Tree: Multiscale Modelling and Analysis of Planar Cell Polarity in the Drosophila Wing; IEEE/ACM Transactions on Computational Biology and Bioinformatics, 10(2):337-351, 2013.
- D. Gilbert, M. Heiner, F. Liu and N. Saunders: Colouring Space - A Coloured Framework for Spatial Modelling in Systems Biology. In Proc. PETRI NETS 2013. Springer LNCS, volume 7927, pages 230-249, June 2013.
- M. Heiner and D. Gilbert: BioModel Engineering for Multiscale Systems Biology; Progress in Biophysics and Molecular Biology, 11:2-3, 119-128, 2013. DOI 10.1016/j.pbiomolbio.2012.10.001

20 Mostafa Herajy

contact details

Port Said University
Faculty of Science, Mathematics and Computer Science Dept.
23rd December street
Port Said, Egypt

mm_herajy@hotmail.com

talk

Efficient Simulation of Hybrid Petri Nets

abstract. Petri nets are promising tools for modelling and analyzing biological systems. They can help with the understanding of complex biological pathways by graphically depicting the underlying reaction networks. Nevertheless, with the increasing interest in modelling complex biological systems, basic place/transition nets tend to be inefficient to tackle emergent issues due to challenges coming with the modelling of multiscale reaction networks. Thus new classes of Petri nets are devised with a special aim to aid systems biologists in studying intricate reaction networks. Among these classes are Hybrid Petri nets (HPN) and Coloured Hybrid Petri nets (HPN^C). HPN permit the representation and simulation as well as the interplay of discrete stochastic and continuous deterministic components in one and the same model, while HPN^C allow for the efficient modelling of spatiotemporal systems exposing multiple time-scales.

During this talk, an overview of modelling multi-scale biological systems using (coloured) Hybrid Petri nets is presented. Moreover, the different simulation algorithms used to execute hybrid models are discussed highlighting the various issues that hamper the efficient simulation of (coloured) Hybrid Petri nets and how to work at them.

research interests

Hybrid Modelling; (Coloured) Hybrid Petri Nets; Multi-timescale modelling, Stochastic and continuous simulation

publications

- M Herajy, M Heiner: Modeling and Simulation of Multi-scale Environmental Systems with Generalized Hybrid Petri Nets; Frontiers in Environmental Science, 3(53), 2015 (accepted for publication: 13 July 2015).
- M. Herajy, M. Heiner. A Steering Server for Collaborative Simulation of Quantitative Petri Nets. In G Ciardo and E Kindler, editors, Proc. PETRI NETS 2014, volume 8489 of LNCS, pages 374-384. Springer, June 2014
- M Herajy, M Heiner: Petri Net-Based Collaborative Simulation and Steering of Biochemical Reaction Networks; Fundamenta Informaticae, 129(1-2):49-67, 2014.
- M. Herajy, M. Schwarick, M. Heiner. Hybrid Petri nets for modelling the eukaryotic cell cycle. ToPNoC, Special Issue, VIII(2):123-141, 2013.
- M. Herajy, M. Heiner. Hybrid representation and simulation of stiff biochemical networks. Nonlinear Analysis: Hybrid Systems, 6(4):942-959, 2012.
- M Heiner, M Herajy, F Liu, C Rohr, M Schwarick: Snoopy – a unifying Petri net tool; In Proc. PETRI NETS 2012, Hamburg, Springer, LNCS, volume 7347, 398-407, June 2012.

21 Björn Sommer

contact details

Faculty of Information Technology, Monash University, New Horizons, Building 82, AU

bjoern@CELLmicrocosmos.org

https://monash.edu/research/people/profiles/profile.html?sid=7304948&pid=11563

talk

Immersive Cell Exploration and Membrane Modeling

abstract The CELLmicrocosmos project provides different approaches to model biological cells at the mesoscopic level and membranes at the molecular level. It is possible to create different cell models, associate them with protein-related networks based on different localization databases, as well as to generate membrane patches or vesicles. Whereas in the recent years the modeling process was in the focus of our research, recently the visualization and especially exploration was improved. For this purpose, 3D interaction was integrated, as well as optional large-scale visualization capabilities compatible to, e.g., CAVE2.

research interests

to support Bioinformatics-related research by interdisciplinary visualization and modeling approaches; CELLmicrocosmos project (http://www.cellmicrocosmos.org) which provides different tools supporting the visualization and modeling of cells, cell compartments and cell membranes.

publications

- Sommer, B., C. Bender, T. Hoppe, C. Gamroth, and L. Jelonek. Stereoscopic Cell Visualization: From Mesoscopic to Molecular Scale. Journal of Electronic Imaging 23, no. 1 (2014): 011007-1-011007-10. doi:10.1117/1.JEI.23.1.011007.
- Sommer, B., 2014, Network analysis and integration in a virtual cell environment, in Approaches in Integrative Bioinformatics. Towards the Virtual Cell, in Ming Chen, Ralf Hofestaed (eds), Springer, Heidelberg Germany, pp. 275-297.
- Sommer, B., B. Kormeier, P. S. Demenkov, P. Arrigo, K. Hippe, Ö. Ates, A. V. Kochetov, V. A. Ivanisenko, N. A. Kolchanov, and R. Hofestädt. Subcellular Localization Charts: A New Visual Methodology for the Semi-Automatic Localization of Protein-Related Data Sets. Journal of Bioinformatics and Computational Biology 11, no. 1 (2013): 1340005.
- Sommer, B., T. Dingersen, C. Gamroth, S. E. Schneider, S. Rubert, J. Krüger, and K. J. Dietz. CELLmicrocosmos 2.2 MembraneEditor: A Modular Interactive Shape-Based Software Approach to Solve Heterogeneous Membrane Packing Problems. Journal of Chemical Information and Modeling 5, no. 51 (2011): 1165-82.