Yamaguchi Workshop on Computational Network Biology

Program
Check Out Our Workshop Plan.

Date: Monday, March 21, 2016
Venue: Lecture room No. 11
Place: Faculty of Science in Yoshida campus, Yamaguchi University
13:00 - 13:05 Opening Talk
   Prof. Dr. Hiroshi Matsuno

13:05 - 13:40 Invited Talk1
   Prof. Dr. Monika Heiner
   Analysis and repair of whole genome bacterial metabolic models for synthetic biology

13:40 - 15:15 Invited Talk2
   Ms. Pauline Traynard
   Logical model of the mammalian cell cycle analyzed with model-checking

15' Coffee Break

15:30 - 15:55 Session Talk1
   Dr. Sohei Ito
   Qualitative analysis of gene regulatory networks using temporal logic

15:55 - 16:20 Session Talk2
   Dr. Fei Liu
   Colored Hybrid Petri Nets for Modeling and Simulating the Delta-Notch Dependent Boundary Formation in the Drosophila Large Intestine

16:20 - 16:45 Session Talk3
   Dr. Heewon Park
   Statistical methodologies for high-dimensional genomic data analysis

15' Coffee Break

17:00 - 17:25 Session Talk4
   Dr. Adrien Fauré
   Towards a new definition of circuit functionality

17:25 - 17:45 Student Talk1
   Mr. Masashi Kubota
   Analyses of artificial genetic flip-flop circuits based on ordinary differential equation
17:45 - 18:05 Student Talk2
Mr. Atsushi Mizuta
Properties of Uniqueness on Dependent Shrink for Retention-Free Petri Nets

18:05 - 18:10 Closing Talk
Dr. Manabu Sugii
Analysis and repair of whole genome bacterial metabolic models for synthetic biology

Synthetic biology is a rapidly expanding field, concerned with the rigorous engineering of organisms with the aim of modifying their metabolic systems to enhance the production of target substances such as biofuels, medicines, plastics, etc. Engineering rigour can be achieved by the use of whole genome metabolic models to act as designs. These models can be large; for example the model for the K-12 strain of E.coli comprises over 3000 metabolic reactions (transitions) and just under 2000 metabolites (places), which calls for a mechanised approach for analysis and correction. Traditionally, whole genome metabolic models are analysed by constraint-based methods which exploit elementary modes, corresponding to T-invariants in the Petri net world. The models approved by constraint-based approaches do not necessarily respect the biologically motivated requirements of behavioural analysis by model simulation.

We describe a method to automatically analyse and correct large Petri net models of the dynamic behaviour of whole genome metabolism of bacteria. A particular challenge is the detection and elimination of bad siphons. Computational difficulties are due to the algorithmic complexity of the structural analysis, as well as in terms of time required for dynamic analysis.
Ms. Pauline Traynard

Institut de Biologie de l'Ecole Normale Supérieure, Computational Systems Biology Lab., FRANCE

**Logical model of the mammalian cell cycle analyzed with model-checking**

The molecular networks controlling cell cycle progression have been predominantly modelled using differential equations, an approach which demands to define complex regulatory terms with poorly characterised kinetic parameters. In contrast, qualitative dynamical models are easier to define, analyze and compose. We revisit a boolean model for the core network behind the mammalian cell cycle (Fauré et al. Bioinformatics, 2006), taking into account recent advances in the characterisation of the underlying molecular networks to obtain a better qualitative consistency between simulations and documented mutants features.

We evaluate the dynamical properties of the resulting model with synchronous and asynchronous simulations using the software GINsim (http://www.ginsim.org). We also have designed temporal logic queries, enabling an efficient and automatic verification of key dynamical properties such as conditions on the activation of components or the order of changes of their levels, with the symbolic model checker NuSMV. Moreover, adding transition probabilities allow a stochastic simulation of the model with the software MaBoSS and provides new insights into the dynamical behavior of the system.
Session Talk
Learn About our Work & Culture.

Talk1: Dr. Sohei Ito
National Fisheries University, JAPAN

Qualitative analysis of gene regulatory networks using temporal logic

Current biological information is mainly accumulated in qualitative forms such as metabolic pathway, protein-protein interaction network and gene regulatory network. It is desirable to model and analyse biological systems from such qualitative information. We proposed a novel framework to model and analyse gene regulatory networks (GRNs) using temporal logic. We capture behaviours of a GRN as state transition systems and characterise its possible behaviours by a temporal logic formula. A biological property of interest is also described in temporal logic. We can analyse whether a property holds in the possible behaviours of a GRN by checking satisfiability of the formula. This framework is extended to analyse biological homeostasis of GRNs, using the notion of realisability in the paradigm of reactive system verification. In this talk I will introduce our framework and demonstrate its usefulness.

Talk2: Dr. Fei Liu
Control and Simulation Center, Harbin Institute of Technology, CHINA

Colored Hybrid Petri Nets for Modeling and Simulating the Delta-Notch Dependent Boundary Formation in the Drosophila Large Intestine

The modeling of the boundary formation in the Drosophila large intestine is a typical multiscale problem, and it is either time-consuming or hardly addressed by common modeling and simulation tools. As a powerful multiscale modeling and analysis tool for large-scale biological systems, colored hybrid Petri nets can be used to cope with such system.
In this talk, we will talk about a colored hybrid Petri net approach to model the boundary formation in the large intestine of Drosophila embryo. We validate the model in the wild-type conditions and use the model to make predictions in different over-expression rates of Notch proteins, which well match the experimental observations in vivo. We have shown that colored Petri nets are very appropriate to model such multicellular systems, and our model is scalable and thus we can easily study the model behavior on different size of intestinal tissues.

Talk3: Dr. Heewon Park
Faculty of Global Science Studies, Yamaguchi University, JAPAN

Statistical methodologies for high-dimensional genomic data analysis

Much research is currently underway to understand the complexity of the heterogeneous genetic networks underlying cancer. We consider statistical modeling strategies for high-dimensional genomic data analysis to reveal heterogeneous system of cancer. The L1-type regularization approaches (e.g., lasso, elastic net, etc.) have drawn a large amount of attention in the field of bioinformatics. Although the existing L1-type regularization methods have been widely applied to genomic data analysis, the methods cannot incorporate the biological knowledge and possess several drawbacks. We first demonstrate the demerits of the existing L1-type approaches and introduce novel statistical strategies to effectively analyze high-dimensional genomic data analysis. Monte Carlo simulations and analysis of various large scale omics project (e.g., The Cancer Genome Atlas (TCGA), Sanger Genomics of Drug Sensitivity in Cancer dataset from the Cancer Genome Project, etc.) are conducted to show the effectiveness of the proposed novel strategies. The proposed methods provide reliable and biologically relevant results for genomic data analysis, especially cancer driver gene selection.
Towards a new definition of circuit functionality

In the wake of the seminal work of René Thomas and co-workers, the notion of circuit functionality has focused on the asymptotic behavior "generated" by simple positive and negative regulatory circuits: multistationarity and oscillations, respectively. In spite of some important theoretical and practical results, such as proofs of Thomas’s conjectures and identification of stable states, this approach has left major questions unanswered, including the full decomposition of a network into functional modules and the very definition of what "generate" exactly means.

In an attempt to clarify those issues we are currently investigating the possible role of symmetry in the dynamics of a model as a marker of circuit functionality. In this presentation I will discuss current definitions of functionality, their limitations and our efforts to connect them with symmetric patterns in the state transition graph of logical networks.
Talk1: Mr. Masashi Kubota

Faculty of Science, Yamaguchi University, JAPAN

**Analyses of artificial genetic flip-flop circuits based on ordinary differential equation**

The artificial gene circuit is a network of genes, whose expression timings and these amounts are designed in advance by a certain pre-designed method. So far, several genetic circuits including a toggle switch by Gardner (2000), an adder circuit, and an oscillation circuit. In this presentation, after giving a design of two-toggle switch and an extended version of it with inducer functions using GINSim and Scilab, analytic results of flip-flop (FF) circuits, RS-FF and JK-FF, will be performed using these two tools.

Talk2: Mr. Atsushi Mizuta

Faculty of Science, Yamaguchi University, JAPAN

**Properties of Uniqueness on Dependent Shrink for Retention-Free Petri Nets**

We have investigated the relation of transitions based on dependency of transitions and proposed dependent shrink algorithm for retention-free Petri net models of signaling pathways. In this paper, we define a dependent relation and investigate properties of firing relation. Finally, we show the uniqueness of dependent shrink algorithm operation based on the properties of the dependent relation.
Organizers

Learn About our Team.

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