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Computational Methods in Systems Biology

12th International Conference, CMSB 2014
Manchester, UK, November 17-19, 2014
Proceedings

Springer

Volume Editors

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Preface

This volume contains the papers presented at CMSB 2014. The 12th International Conference on Computational Methods in Systems Biology was held during November 17–19, 2014, at the Manchester Institute of Biotechnology of the University of Manchester.

The conference is an annual event that brings together computer scientists, biologists, mathematicians, engineers, and physicists from all over the world who share an interest in the computational modeling and analysis of biological systems, pathways, and networks. It covers computational models for all levels, from molecular and cellular, to organs and entire organisms.

There were 31 regular and 18 poster submissions. Each regular submission was reviewed by at least two, and on average 2.77, Program Committee members. Each poster submission was reviewed by an average of 1.38 Program Committee members. Selected poster flashes were all reviewed by three Program Committee members. The committee decided to accept 16 regular papers, and all the submitted posters. The program also included three invited talks, by Ruth Baker, Dagmar Iber, and Magnus Rattray.

We thank the Program Committee for their hard work in reviewing submissions. We especially thank François Fages, Monika Heiner, and Carolyn Talcott for their advice on matters relating to the organization of the conference. We acknowledge support by the EasyChair conference system during the reviewing process and the production of these proceedings, see http://www.easychair.org (managed by our Manchester colleague Andrei Voronkov and his team). We thank Tommaso Mazza and the IEEE Computer Society Technical Committee on Simulation for supporting the best student paper award. We thank the Manchester Institute of Biotechnology for providing the conference venue.

September 2014

Pedro Mendes
Joseph O. Dada
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Invited Talks
(Abstracts)

Experimental and Modelling Investigation of Monolayer Development with Clustering

Ruth Baker

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Abstract. Standard differential equation models of collective cell behaviour, such as the logistic growth model, invoke a mean-field assumption which is equivalent to assuming that individuals within the population interact with each other in proportion to the average population density. Implementing such assumptions implies that the dynamics of the system are unaffected by spatial structure, such as the formation of patches or clusters within the population. Recent theoretical developments have introduced a class of models, known as moment dynamics models, that aim to account for the dynamics of individuals, pairs of individuals, triplets of individuals, and so on. Such models enable us to describe the dynamics of populations with clustering, however, little progress has been made with regard to applying moment dynamics models to experimental data. Here, we report new experimental results describing the formation of a monolayer of cells using two different cell types: 3T3 fibroblast cells and MDA MB 231 breast cancer cells. Our analysis indicates that the 3T3 fibroblast cells are relatively motile and we observe that the 3T3 fibroblast monolayer forms without clustering. Alternatively, the MDA MB 231 cells are less motile and we observe that the MDA MB 231 monolayer formation is associated with significant clustering. We calibrate a moment dynamics model and a standard mean-field model to both data sets. Our results indicate that the mean-field and moment dynamics models provide similar descriptions of the 3T3 fibroblast monolayer formation whereas these two models give very different predictions for the MDA MD 231 monolayer formation. These outcomes indicate that standard mean-field models of collective cell behaviour are not always appropriate and that care ought to be exercised when implementing such a model.

From Networks to Function — Computational Models of Organogenesis

Dagmar Iber

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Abstract. One of the major challenges in biology concerns the integration of data across length and time scales into a consistent framework: how do macroscopic properties and functionalities arise from the molecular regulatory networks and how do they evolve? Morphogenesis provides an excellent model system to study how simple molecular networks robustly control complex pattern forming processes on the macroscopic scale in spite of molecular noise, and how important functional variants can evolve from small genetic changes. Recent advancements in 3D imaging technologies, computer algorithms, and computer power now allow us to develop and analyse increasingly realistic models of biological control. To also incorporate cellular dynamics and cell-cell interactions in our simulations, we have now also developed a software tool that allows us to solve our regulatory network models on dynamic 2D and 3D tissue domains at cellular resolution. I will present our recent work where we use data-based modeling to arrive at predictive models to address the mechanism of branching in lungs and kidneys, the mechanism by which an asymmetry emerges in our hand (thumb to pinky), as well as a mechanism by which proportions are maintained in differently sized embryos.

Integrating mRNA and Polymerase Time Course Data to Model the Dynamics of Transcription

Magnus Rattray

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Abstract. We are developing methods to model transcription using mRNA expression (RNA-Seq) and RNA polymerase (pol-II ChIP-Seq) time course data. In our first application we model the motion of RNA polymerase during pre-mRNA elongation. We model the pol-II dynamics by using a spatio-temporal Gaussian process to described changes in pol-II density profiles across sites of the transcribed region [1]. We apply our model to infer the elongation speed and promoter-proximal pol-II activity for early targets of estrogen receptor in MCF7 breast cancer cells. Bayesian methods are used to infer the model parameters and associate our parameter estimates with levels of confidence. By clustering the inferred promoter-proximal pol-II activity profiles we can associate early-activated target genes with specific transcription factor binding patterns.

In our second application we link the pol-II dynamics with mRNA production and degradation in the same system using a simple linear differential equation. We again represent the pol-II dynamics as a Gaussian process and are able to exactly compute the data likelihood by exploiting the fact that a linear operation on a Gaussian process remains a Gaussian process. We find that for a certain number of target genes it is necessary to include an RNA-processing delay to get a reasonable fit to the data. We use Bayesian inference to infer the delay parameter and identify genes with strong evidence of a significant delay, about 11% of the genes where the signal is strong enough to fit the model. This delay appears to be related to splicing: we find that short genes tend to exhibit longer splicing-associated delay and there is also a positive association with genes that have a relatively long final intron.

References

1. wa Maina, C., Matarese, F., Grote, K., Stunnenberg, H.G., Reid, G., Honkela, A., Lawrence, N., Rattray, M.: Inference of RNA Polymerase II Transcription Dynamics from Chromatin Immunoprecipitation Time Course Data. PLoS Computational Biology 10(5), e1003598

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