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Special Issue – Selected papers from the First q-bio Conference on Cellular Information Processing

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Editorial

Selected papers from the First q-bio Conference on Cellular Information Processing

This special issue consists of 12 original papers and 4 reviews that elaborate on work presented at the *First q-bio Conference on Cellular Information Processing* [1], which was held on the campus of St. John's College in Santa Fe, New Mexico, USA, 8-11 August 2007.

The conference was attended by roughly 200 participants from around the world and included 35 invited talks, 10 contributed talks, 11 poster spotlight talks, two tutorial talks and 85 poster presentations. The purpose of the conference was to advance predictive mathematical/computational modelling of cellular regulatory systems, quantitative experimental studies of these systems, and identification of general principles of cellular information processing. Presentations covered a range of biological phenomena: from morphogenesis and development to cellular adaptation to host-pathogen interactions to diseases caused by molecular changes of cellular regulatory systems. Nevertheless, each report of work combining experimental and theoretical/computational approaches seemed to be highly regarded and widely appreciated regardless of the system studied. Many participants expressed a new-found appreciation for commonalities and similarities in the approaches used and the information processing phenomena observed across diverse systems. For example, many of the talks, such as the opening talk, emphasised the use of information theory and signal processing approaches to elucidate design principles of cellular regulation.

During the course of planning and preparing for the conference, the organisers began using the term 'q-bio' to succinctly refer to research efforts directed at predictive modelling of cellular regulatory systems. This term eventually became part of the conference name. Besides the economy of expression afforded by this jargon, the organisers were attracted to the term for several reasons. First, 'q-bio' is an abbreviation of 'quantitative biology', a term that aptly describes a distinguishing feature of the type of work that the conference aims to advance. The development of predictive models is often dependent on quantitative experiments. Second, the reference 'quantitative biology', a long used term, recognises that the type of work emphasised at the conference is not new, although it does seem to be reaching a new level of maturity as technological advances allow biological systems to be probed and monitored quantitatively with unprecedented control, scope, and resolution. Finally, 'q-bio' is something of a nod to pioneering efforts in science that have started or caught fire in Los Alamos, such as scientific computing. The term 'q-bio', to the best of our knowledge, was first used by Paul Ginsparg as the name of one of the archives in the physics e-print server, `arXiv.org`, which began its existence in Los Alamos and provided a visionary model of open scientific publishing. We use 'q-bio' in the name of the conference with the permission of Ginsparg and the `arXiv.org` project, now at Cornell University. The name reflects a hope that the conference will help spark a revolution that will bring the prominence of quantitative work in biology up to the level of that in fields such as chemistry and physics.

Why another systems biology conference? The answer is that we were dissatisfied with the emphasis on high-throughput technologies seen at many systems biology conferences. In organising the q-bio Conference, we wanted to emphasise the other side of systems biology: modelling, simulations, focused experiments and deep theoretical understanding of underlying principles of

biological regulation. Although such work is routinely presented at systems biology conferences, it is usually not the focus, except at smaller and/or irregular meetings. We thought q-bio was ready for something bigger. We wanted to promote complete stories and recognise the complementary roles that theorists and experimentalists play in the development of predictive understanding of a complex biological system. It seems to have been an experiment that worked. Many complete stories were told at the conference, with these stories coming from individual groups that emphasise both modelling and experimentation, as well as multidisciplinary teams of collaborating research groups.

The Special Issue at a Glance

The original idea of this special issue was to document a representative selection of the work presented at the conference in one place and to provide a snapshot of the q-bio field. However, we must acknowledge that this idea was only partially realised. The papers in this special issue are biased toward the theoretical and computational end of the q-bio spectrum, even though they are contributed by researchers dedicated to the q-bio ideal of complete stories and include contributions from research groups that are well known for their experimental work. Like the conference itself, this special issue was something of an experiment, as papers generally do not accompany presentations at biological meetings to the same extent as in other fields, such as computer science. Thus, the contributors of the papers collected here are truly pioneers.

The individual papers in this special issue, which we have arranged loosely into four blocks, speak for themselves. We encourage the readers to inspect them directly, and the introductions below are deliberately brief.

Reviews

In *Network integration and graph analysis in mammalian molecular systems biology*, Ma'ayan provides a detailed review of graph-theoretic and network-analysis methods in modern systems biology, whether high throughput or not. The focus is on methods with a broad domain of application. In contrast, Resnekov et al. in *The Alpha Project: a model system for systems biology research*, review experimental and computational efforts focused on understanding a single model system. The two remaining reviews in the issue, *Relevance of phenotypic noise to adaptation and evolution* by Furusawa and Kaneko and *Protein–protein/DNA interaction networks: versatile macromolecular structures for the control of gene expression* by Saiz and Vilar, are focused on the theory and modelling cornerstones of q-bio research. The former review is focused on phenomenological aspects of evolution and regulation, and the latter is focused on detailed structural models of protein-DNA interactions.

Modelling

The second block of papers in the special issue revolves around building detailed mathematical models of specific regulatory systems. For example, Wilson et al. develop an agent-based reaction-diffusion model for ErbB receptor signalling in *Stochastic simulations of ErbB homo and heterodimerisation: potential impacts of receptor conformational state and spatial segregation*. In related work, Resat et al. develop and study ordinary differential equations that describe receptor signalling in *System theoretical investigation of human epidermal growth factor receptor–mediated signalling*. Turning to modelling of bacterial phenomena, Kulkarni and Xu add a new page to our understanding of the underlying biology of the well-studied MinD system in their paper *Modelling of processes governing subcellular localisation of MinD in Escherichia coli*. Finally, Dreisigmeyer et al. rationalise the results of numerous studies of bistability in *lac* operon regulation in their paper *Determinants of bistability in induction of the Escherichia coli lac operon*.

Theory

In the next block of papers, the authors explicitly focus on theoretical results and universal phenomena, even though they may be studied initially in a limited context. The results are expected to be broadly applicable and useful for guiding an understanding of a variety of biological systems. For example, in his paper *Satisfiability, sequence niches and molecular codes in cellular signalling*, Myers uses physical and information-theoretic arguments to derive properties of molecular recognition codes. A somewhat similar information-theoretic analysis in *Serially regulated biological networks fully realise a constrained set of functions* by Mugler et al. allows the authors to determine to what extent the topology of a biochemical regulatory network affects its function and information-processing capabilities.

Methods

The largest block (6 papers) in the special issue deals with development of methods for simulations of large biochemical networks. The methods and techniques presented are diverse; ranging from approximations to stochastic dynamical evolution with rigorous, guaranteed error bounds studied by Munsky and Khammash in *Transient analysis of stochastic switches and trajectories with applications to gene regulatory networks*, to comparative numerical work of Cao and Liu in *Detailed comparison between StochSim and SSA*. We are particularly pleased to have four contributions that deal with systematic approaches for modelling of large biochemical reaction networks, including, in particular, selection of models with the necessary complexity. These approaches (Borisov et al. *Domain-oriented reduction of rule-based network models*, Loew et al. *Virtual Cell modelling and simulation software environment*, Blinov et al. *Complexity and modularity of intracellular networks: a systematic approach for modelling and simulation*, and Atlas et al. *Incorporating genome-wide DNA sequence information into a dynamic whole-cell model of*

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Escherichia coli: application to DNA replication) have the potential to provide new insights into complex biological systems. This collection of articles represents an authoritative reference on biochemical network simulation methods.

Looking into the future

The q-bio Conference is planned to continue as an annual event. The Second q-bio Conference took place on 6–9 August 2008 on the campus of St. John's College, which provides an environment that is highly conducive to interactions. A second special issue in *IET Systems Biology* is already planned, and we hope that it will include papers as exciting as the ones in the present collection. The Third q-bio Conference is scheduled for 5–8 August 2009.

Acknowledgments

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(Los Alamos, New Mexico, July 2008)

Reference

[1] EDWARDS J.S., FAEDER J.R., HLAVACEK W.S., JIANG Y., NEMENMAN I., WALL M.E.: 'q-bio 2007: a watershed moment in modern biology', *Mol. Syst. Biol.*, **3**, p. 148

Dr Ilya Nemenman received a PhD in theoretical physics from Princeton University. He has been further trained as a postdoctoral scientist at the NEC Research Institute and the Kavli Institute for Theoretical Physics, and as an Associate Research Scientist at the Columbia University School of Medicine. He is currently a technical staff member at the Computer, Computation, and Statistical Sciences Division at Los Alamos National Laboratory, where he studies information processing in stochastic cellular regulation and neural systems.

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