

The Logic of Life

The Human Genome Project and recent advances in proteomics and DNA microarray technology highlight the need for systems-level integration of experiments and theory in order to understand the logic of life. This is the ambitious goal for systems biology, the quantitative study of biological processes as integrated systems rather than as isolated parts.

This issue of *Genome Research* comprises a selection of articles (see References) presented at the 3rd International Conference on Systems Biology 2002 (ICSB2002), held at Karolinska Institute, Stockholm, December, 13 to 15, 2002. The organizers of ICSB2002 were Karolinska Institute, Uppsala University, Swedish Institute of Computer Science and Linköping University. The first ICSB conference was held in Tokyo, Japan, in November 2000, on the initiative of Hiroaki Kitano, who has played a major role in the launching of the field and who chairs the program committee. ICSB2002 lived up to the high expectations from the previous meetings, including the second meeting, which was held at Caltech in November 2001 and organized by Mel Simon, John Doyle, and Hiroaki Kitano with a scientific program comprising keynote speakers, other talks, and a large poster session.

ICSB2002 had a strong focus on combining quantitative experimental analysis with mathematical models to deepen the understanding of the biological processes. This was reflected in the list of keynote speakers, invited speakers, and presentations. Keynote speakers were Mark Ptashne (Memorial Sloan-Kettering Cancer Center), Yoshihide Hayashizaki (RIKEN Yokohama Institute), Stanislas Leibler (Rockefeller University), Uri Alon (Weizmann Institute), and John Doyle (California Institute of Technology). Other talks were by George Church, Boris Shraiman, Trey Ideker, Hiroaki Kitano, Marileen Dogterom, Bernhard O. Palsson, Naama Barkai, John Reinitz, Howard C. Berg, David A. Fell, Lilia Alberghina, Keith Amonlirdviman, Hanspeter Herzl, Martin Howard, André Levchenko, Mads Kaern, Armindo Salvador, Stefan Schuster, An-Ping Zeng, Terence Hwa, and Lucy Shapiro. Because the field has recently been dominated by North America and Japan, we were pleased both that the conference could attract so many outstanding speakers from overseas and also that we had so many great talks contributed by Europe-based researchers.

The scientific committee reviewed 26 papers, out of which 13 were selected for this special issue. In addition, more than 130 posters were presented in a lively and well-attended session. The poster abstracts and the abstracts for the talks can be downloaded from the conference Web site at www.icsb2002.org. In conjunction with the conference, three parallel tracks of tutorials were held on December 11, 2002. December 12 was devoted to workshops on "Formal methods and Biological Reasoning," "Reverse engineering gene networks," and "Software Platforms for Systems Biology". In addition, Masaru Tomita, Keio University, organized a satellite meeting on "The Metabolome Analysis and Systems Biology" on December 16.

The conference was elegantly opened by Mark Ptashne, first keynote speaker, who discussed the role of regulated recruitment in the regulation of genes and intracellular signaling events (Ptashne and Gann 2002). Yoshihide Hayashizaki gave a keynote presentation in which he surveyed the dynamic transcriptome of the mouse. Hayashizaki has led the RIKEN/FANTOM project to

characterize full-length cDNAs in the mouse. He presented awesome results, including the identification of >10,000 new non-coding RNAs and >2000 sense-antisense pairs, and conjectured that these transcripts can be a mechanism of mutually pairwise regulated mRNA degradation. Stan Leibler started the second day of the conference. In his presentation on "Tinkering of Genetic Networks," he showed how unpredictable very small networks built from the most well studied components can be when operating in vivo. Uri Alon described fascinating theoretical work on how some simple kinetic motifs are favored by evolution, as well as experimental work on temporal ordering in transcriptional regulation of biosynthetic pathways. On the last day of the conference, John Doyle gave a talk on the similarity between biological systems and complex engineered systems. He emphasized how evolution constrains biological systems to be robust to uncertainty in environment and to failure of components. He further discussed how this should be accommodated in the theoretical framework of systems biology. Apart from these keynote addresses, many other memorable presentations were given. Lucy Shapiro presented beautiful results on the importance of regulation of gene expression in time and space during cell cycle. We specifically remember how the spatial positioning of a gene in relation to the origin of replication directs its temporal expression during DNA replication. Abstracts of these presentations can be found at www.icsb2002.org. That many of the contributors of the conference have been doing what we now call systems biology for many years can be summarized by the opening line of John Reinitz' talk (we think we have the quote right): "Being a developmental biologist who is not afraid of math, I think I have always been doing systems biology, only before it had to be kept under wraps somehow."

The conference was held in the darkness characteristic of Swedish winter. However, according to Swedish tradition, darkness is challenged and for a moment driven away by Lucia, appearing with her escort of candle-bearing singing attendants in white robes on the morning of December 13. The organizing committee is grateful to Lucia for appearing and dispensing her rays of light to the conference. The other main event outside the scientific program was the conference Banquet, held in the hall of the Vasa museum in Stockholm, next to the hull of a 230-ft battleship that sunk on her maiden voyage in 1630 while still in sight of the naval shipyards of Stockholm. A memento mori on the importance of stability and robustness in the design of complex systems!

In his memorable closing remarks, Uri Alon indeed summarized the conclusions from ICSB2002 by alluding to the fate of VASA, in which the name was used as an acronym for Very Automated Systems Approach.

—The ICSB 2002 Scientific Organizing Committee
 Måns Ehrenberg (Chair)
 Erik Aurell
 Johan Elf
 Rickard Sandberg
 Jesper Tegnér

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