

SBMC 2006:
The challenges of Systems Biology
July 12 – 14, 2006
Heidelberg, Germany

The SBMC2006 conference took place in the heart of the beautiful Old Town Heidelberg, on the banks of the Neckar River and has been very well organized by HepatoSys, the Federal German research initiative on Systems Biology of hepatocytes supported by the German Ministry of Education and Research (BMBF) along with numerous industrial as well academic sponsors.

Because of the interdisciplinary collaborations between important institutions such as DKFZ, EMBL, EML, BIOQUANT, Heidelberg is now claiming a prominent role among the most important centers for Systems Biology.

The aim of the conference was to provide insights into some aspects of Systems Biology techniques for analyzing the mammalian cells behavior, in particular cell regulation of gene expression and signal transduction networks.

Areas of biology covered included quantitative life cell imaging, proteomics, dynamic modeling of signaling pathways in primary cells systems such as hepatocytes.

Among the speakers of high international profile are worth mentioning:

Session Proteomics:

L. Cantley (Division of Signal Transduction Harvard Institutes of Medicine, Boston).

It is becoming increasingly clear that Systems Biology will catalyze fundamental changes in the future of health care. Lewis Cantley's recent research focuses on a systems biology analysis approach in order to understand the biochemical pathways that regulate normal mammalian cell

growth and the defects in signal transduction that cause cell transformation. A logical network and the regulation of metabolic energy lead to cell growth control in response to growth factors, nutrient availability and cellular energy status, and play a critical role in cancers.

Session Life Cell Imaging:

N. Hiroi (JST ERATO-SORST - Kitano Symbiotic Systems Project, Tokyo) presented a new reaction-diffusion modeling method (Dimension Restricted Reaction Kinetics) for modeling biochemical reactions in crowded spaces like in cytoplasm *in vivo*. The DRRK-analysis method enables to represent the fractal dimension of molecular movement in its ODE structure.

Session Dynamic Modeling of Signaling Pathways:

B. Kolodenko (Thomas Jefferson University, Philadelphia). Boris Kholodenko has made pioneering contributions towards the understanding of the spatio-temporal organization of cell signaling and its significance for cell fate determination. A highly combinatorial network generated by phosphorylations and binding forms of a large number of kinases and their substrate effectors at different states of the network can be described by a *domain oriented* macro model of the network.

This approach leads to an important result: the receptor-mediated membrane relocation of cytosolic proteins is very important for the spatial-temporal organization of the GPCR-and RTK- induced signaling (growth factors, RAS signaling).

J. Ferrell (Department of Molecular Pharmacology Department of Biochemistry Stanford). One way to understand the design principles of complex signaling networks is to identify feedback loops, which are involved in the regulatory schemes. In the example presented by James Ferrell a positive feedback loops triggers the *Xenopus* oocyte maturation and determine the function of the mitotic oscillator in *Xenopus* embryos.

P.K. Sorger (MIT, Cambridge). Cytokines and their receptors activate complex signal cascades controlling cell proliferation, cell death and differentiation. In order to understand cell-type variation and differences between normal and

disease cell states, Sorger and colleagues recently developed mechanistic and numerical models that encompass various aspects of cytokines signaling, and focus on pro-apoptotic (Tumor Necrosis Factor) and pro-survival cytokines (EGF and Insulin Growth Factor). Such models are numerical, but they have been formulated on the basis of experimental data and subjected to experimental verification. Systems biology based models, which focus equally on computation and experimentation, are going to play an important role in the development and use of drugs for major Human diseases in the immediate future.

Session Hepatocytes:

H.V. Westerhoff (University of Manchester). Living cells' primary processes are mostly chemical or physical reactions that are carried out by metabolic and other pathways. Each of these pathways has to be regulated in time and tuned according to the functional status of the other. Hans Westerhoff described a new method to dissect such regulation into various subtypes: metabolic regulation, gene expression regulation and regulation by signal transduction.

The quality of most of the conference talks show that significant progress has already been made in systems biology analysis of higher eukaryotes. However, as an increasing number of complex biological processes become amenable to quantitative analysis, this field has the potential and the responsibility to go much further. With new technological advances, both in theoretical and experimental approaches, systems biology can aim at rigorously reshaping various areas of biology, for example, in the field of data integration methodology, the formation of morphogen gradients during developmental processes and, evolutionary systems biology, to name a few. The years to come will hopefully demonstrate how models with increasing and more accurate predictive value can be generated.

Perla Del Conte-Zerial
TU Dresden

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