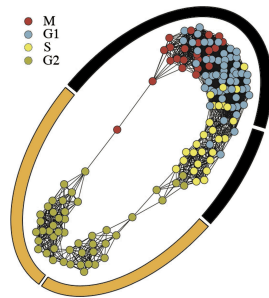


# CECAM Workshop - Report

## “Computational Systems Biology”

CECAM Headquarters – Lausanne, June 23-26 2009



Organizers:

Paolo De Los Rios (EPFL – Lausanne)

Vassily Hatzimanikatis (EPFL – Lausanne)

Felix Naef (EPFL – Lausanne)

### Topic of the Workshop:

The workshop gathered some of the leading scientists in the domain of Systems Biology, a novel research field at the crossroads between several more traditional disciplines: Biology, Chemistry, Physics, Mathematics and Computer Sciences. The ultimate goal of Systems Biology is to integrate the vast amount of molecular/cellular data on biological systems and to provide a comprehensive description of their behavior at the largest scale, developing models that would allow to predict how cells and organisms should react if subject to specific *stimuli*. The potential value of Systems Biology is thus almost self-evident, as both applied research (*e.g.* drug development) and fundamental one would greatly benefit from such holistic understanding of biological systems.

Clearly, and as it has well emerged from the workshop, the field is still in its infancy and it is facing several hurdles. On the one hand, although experiments are becoming more and more precise and quantitative, a definitive assessment of the values of the large number of parameters that are necessary to propose complete models is still unfeasible, although the first high-throughput setups for such purpose are beginning to be designed. On the other hand, even if we could reach a complete quantitative knowledge of the systems' parts and of their relations, the computational schemes and algorithms necessary to turn such knowledge into predictive mathematical models are yet to be developed. Consequently, Computational Systems Biology (which represents the theoretical part of Systems Biology) has come to the fore as a key player in the discipline.

**Scientific content of the program:**

The opening talk by Stolovitsky gave an overview of the manifold challenges of Systems Biology, from data mining to modeling. The rest of the workshop focused on four main Systems Biology topics: metabolic networks, gene regulatory networks, embryo development and, more broadly, bioinformatics. On the first three topics we also had, as planned, invited contributions from experimentalists (Zamboni, Deplanke, Domany and Gonzales-Gaitan respectively), who very clearly laid down the present state-of-the-art in the wet-lab, what has to be expected for the future and what kind of systems (scale-wise) could be reasonably modeled given the present level of experimental characterization (components and parameters), and the present capabilities of testing theoretical/computational predictions using experiments.

Computationally, it has been highlighted that there are a number of hurdles that must be overcome in order to be able to properly define a model. First data, often coming in vast amounts through high-throughput methods, must be mined to extract the relevant relations between the systems' components: novel methods have been discussed by van Dongen,, Molina, Kutalik and Pagnani. Next, the sheer complexity of the ensuing models needs the development of new conceptual schemes and algorithms. Examples in such direction have been introduced by Hatzimanikatis, Sbalzarini, Babu, Timmer, Naef, Leloup and Iber and they mostly focused on a network description of the underlying systems.

Most of the above presentations dealt with systems at the molecular level, whose complexity pertains the number of components and their intricate interactions. Morelli and Bergman have instead shown what kind of computational problems emerge by looking at entire multicellular organisms (*Drosophila Melanogaster* embryo development), where space and time fluctuations must be taken into account, together with molecular details (protein expression levels and gene regulation), thus leading to intrinsically multiscale models.

**Participants:**

The workshop sported nineteen invited speakers and twenty-eight participants (with thirteen out of twenty-five exhibiting posters) for a total of forty-seven attendees (including the organizers). Non-speakers were almost all PhD students and postdocs. The speakers came from eight different countries (six EU, Switzerland, Israel and the USA). Swiss participants were clearly the majority (about half of the invited speakers and the vast majority of the PhD students), which is not surprising since Switzerland has recently emerged as one of the major European powerhouses in Systems Biology thanks

to a consistent and long-lasting financial commitment of the Swiss government that, through the Swiss-wide SystemsX.ch initiative, fosters collaborative projects between the major research institutions in the country. PhD students were mostly local (EPFL), as it could be expected for financial reasons.

**Feedback from the participants:**

The workshop has received an overall enthusiastic appreciation by the participants, who readily asked for a new meeting in two years time, a reasonable timeframe for new developments to mature and new leading researchers to emerge. Moreover, the pedagogical impact has been great, given the high attendance by PhD students. Also, the choice of the topics and the introductory talks by experimentalists has been very much welcome since it has given a better picture of the present theoretical challenges on each specific issue.

**Conclusion and follow-ups:**

Computational Systems Biology is maturing into a discipline in its own right. The complex issues that practitioners in the field must face have been intrinsically recognized as worth studying as stand-alone problems, rather than simple nuisances in the rationalization of specific experiments. This workshop has clearly outlined that the theoretical/computational approach, although it must clearly be inspired by experiments, is increasingly decoupled from the wet-lab, in a way reminiscent of the relation between theoretical physics and chemistry, and their experimental counterparts. In this respect, gathering computational systems biologists in a single venue, such as CECAM, has proven, and for sure will prove in the future, very useful.

Consequently, as already mentioned above, it has been proposed to submit again a CECAM workshop in two years time. Moreover, given the high attendance by PhD students, a tutorial on selected and already mature issues in computational systems biology would be an ideal complement to the workshop.