# Large-scale Simulation of Signal Transduction in Cells using Hybrid Models

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**Abstract:** Biological cell systems show information processing and metabolic networking by interactions between molecules. They process information of stimuli and pass this information e.g. into the nucleus to regulate gene expression by transcription factors, which results in a changed behaviour of cells as the output of information processing. The interaction between different molecules is the fundamental mechanism by which the cell processes information. Due to the high number of possible interactions, signal transduction networks are extremely complex.

The most common simulation techniques are systems of ODEs describing changes in molecule concentrations or stochastic systems. Deterministic approaches are well-established. Unlike stochastic approaches, they do not require vast computing resources. However, these approaches are not sufficient for simulating pathways involving molecules with extremely low particle numbers. On the other hand, stochastic simulations of complex systems using standard algorithms (e.g. Gillespie) still require too much computing time if there are huge differences among the reaction probabilities between the different molecule types. Since this is the typical situation in most signal transduction networks, an algorithm merging both approaches is required. An efficient 'hybrid-solver' will be demonstrated. This solver separates reactions into groups with low and high reaction probabilities. The 'fast' reactions are simulated deterministically whereas stochastic principles apply for all others. The focus will be on the correct handling of interactions between both groups.

Simulations as described above require quantitative information on reaction kinetics and concentrations. This is available for a few simplified pathways only and therefore, quantitative models are very isolated. Usually, interactions with the environment are not taken into account. On the other hand, there are databases, which cover binary information about all known molecule interactions. A possible qualitative approach might be the modelling of signalling behaviour in an agent-based way. The incorporation of quantitative models into such qualitative networks will enable us to make use of all information sources in one model instead of dealing with isolated models. Crosstalk mechanisms or feedback loops might be typical applications. The sensitivity analysis of such hybrid models will be the key for the identification of important system parameters and an efficient planning of new experiments.

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