

Comparing simulation and experimental data in stochastic systems analysis

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Mathematical modeling of intracellular processes dynamics have become an ubiquitous supporting tool in molecular biology research. Among others, it facilitates preliminary testing of hypotheses about regulatory network structures or helps in experiment planning, when data is to be collected for only several time points. An analysis of stationary points provides additional information about possible outcomes of experimental work. When complemented with sensitivity analysis, such modeling may support finding potential drug targets.

However, investigation of intracellular processes is often impeded by heterogeneity of cellular responses to external stimuli, which makes it difficult to both interpret the experimental results and develop mathematical models. Therefore, various approaches to model stochastic systems have been used in this field. While they allowed to take into account individual cells behavior, there is an open question of how to compare experimental and simulation results.

In this work a general procedure of how to deal with that open question is discussed. As an example, a crosstalk between pathways regulating cellular response to heat shock and cytokines will be analyzed. The proposed approach involves choice of a distribution for sampling parameter values, using deterministic and stochastic models to describe the processes under consideration and choice of system response characteristics that is subsequently used to evaluate the quality of fit of simulation data to experimental observations. Additionally, as several hypotheses about the crosstalk mechanisms have been tested with that approach, a relation between the parameters of a distribution, used to sample model parameters, and the strength of conclusions concerning these hypotheses, will be discussed.

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