Jaroslaw Smieja
Institute of Automatic Control, Silesian University of Technology
e-mail: Jaroslaw.Smieja@polsl.pl
Krzysztof Puszynski
Institute of Automatic Control, Silesian University of Technology

Coupled sensitivity and frequency analysis of signalling pathways

Mathematical modeling of signalling pathways has gained large popularity recently. The models that have been developed describe dynamics of NFkB, JAK/STAT, p53/Mdm2 and many other pathways. One of the most important advantages of application of mathematical models in this field is their flexibility and ability to check certain aspects of the dynamics if the investigated systems before committing large resources into experimental work.

Complexity of the models that are under development varies, depending on the particular goals of the modeling. Nevertheless, regardless of model complexity, one of the key issues is proper choice of parameters. As a result, in such work sensitivity analysis is a necessary stages in analysis of simulation results.

Two main categories of sensitivity analysis methods can be distinguished: local and global. Local sensitivity analysis provides information on the effect of a small deviation a single parameter from its nominal value on the system output. Global sensitivities, in turn, describe how the system output changes when multiple parameters change in a relatively wide range.

In this work several sensitivity indices will be applied to find out which parameter subsets have the greatest impact on the dynamical behavior of several signaling pathways. However, instead of using them with reference to steady states, which is the one of the most frequent approaches, they will be coupled with frequency analysis of the models dynamics. That way, it is possible to answer one of the most important questions concerning some signaling pathways. There is an ongoing dispute about oscillations and their importance in cellular responses to external inputs. Analysis of sensitivity of main frequencies in the model outputs will push forward research in this field. If it is the oscillations that are crucial for proper cell behavior, these frequencies should be relatively insensitive to parameter changes. Moreover, sensitivity analysis will indicate the stages of the signaling pathway that are the most prone to disturbances, providing clues for experimental work.

The work was partially supported by The Fundation for Polish Science.