

Computational framework for the analysis of biological oscillators and its application to p53-Mdm2 interaction

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Abstract: Analysis of biological oscillators as well as other biological systems is often based on the establishment of quantitative dynamical models, which however require accurate kinetic data. Since these data are often missing, hard or even impossible to obtain, computer simulations are used in a combination with different optimisation procedures to tune the dynamical response of the model with experimental observations. Herein, we describe a computational framework for efficient analysis of biological oscillators. It applies different characteristics that can be used to describe oscillatory behaviour, such as oscillation amplitudes, periods or spikiness. We perform a global sensitivity analysis to correlate the model's kinetic parameters with their effects on certain dynamical characteristics of oscillatory behaviour. The parameter space, for which the response is optimized, can thus be reduced to a smaller subset, on which the optimisation is performed. Last, but not least, we apply different computational metaheuristics as optimisation methods, e.g., genetic algorithms, to tune the observed oscillatory characteristics with experimental data using a subset of model parameter space. We demonstrate the proposed framework on a computational model of p53-Mdm2 feedback loop oscillator.

Acknowledgements: The research was partially supported by the scientific-research programme Pervasive Computing (P2-0359) financed by the Slovenian Research Agency in the years from 2009 to 2017 and by the basic research and application project Designed cellular logic (J1-6740) financed by the Slovenian Research Agency in the years from 2014 to 2017.