

Model Validation of Biological Pathways Using Petri Nets - Demonstrated for Apoptosis

Monika Heiner¹, Ina Koch², Jürgen Will¹

¹ Brandenburg University of Technology at Cottbus, Department of Computer Science, Postbox 10 13 44, 03013 Cottbus, Germany
{mh, will}@informatik.tu-cottbus.de
<http://www.informatik.tu-cottbus.de/~wwwdssz>

² Technical University of Applied Sciences Berlin, Dept. Bioinformatics, Seestrasse 64, 13347 Berlin-Wedding, Germany
ikoch@tfh-berlin.de
http://www.molgen.mpg.de/~koch_i

Abstract: Biological networks tend to be very dense and large - far beyond human skills. Therefore, a crucial point seems to be their concise and unambiguous representation to handle these highly integrated networks computationally in an efficient manner. Moreover, our knowledge about a particular pathway is generally widely spread over various separate data bases, using a quite large variety of different graphical schemes.

This talk demonstrates the first steps of a new integrating methodology to develop and analyse models of biological pathways in a systematic manner using well established Petri net technologies. Petri nets represent a modelling method, very well-known for its powerful combination of readability and analyzability. They provide a generic description principle, applicable on any abstraction level. At the same time, they have a sound formal semantics, allowing thorough model evaluation. Hence, Petri nets may be used for a concise formal representation, allowing an unifying view on knowledge coming from different sources.

The whole approach comprises step-wise modelling, animation, model validation as well as qualitative and quantitative analysis for behaviour prediction. In this presentation, the first phase is addressed - how to develop and validate a model.

The example used in that talk is devoted to apoptosis, the genetically programmed cell death. Apoptosis is an essential part of normal physiology for most metazoan species. Disturbances in the apoptotic process could lead to several diseases. The pathway of apoptosis includes highly complex mechanisms to control and execute programmed cell death. We have intentionally chosen that example to stress the fact that even incomplete and uncertain knowledge may be subject of our technology. Actually, we are convinced that step-wise incremental modelling accompanied by running repeated analyses are the only chance to get dependable larger models.

The results provide a mathematically unique and valid model, enabling the simulation of known properties as well as to check the model for self-consistency. The next steps are obvious: after being convinced of the model's integrity, we are ready to use the model for questions where the answers are not yet known.