## Model validation and verification

## **David Gilbert**

## Systems Biology Research Group School of Information Science Computing and Mathematics Brunel University, UK

In this tutorial we describe how model checking can be used in the Synthetic Biology development cycle to aid the construction and validation of models of biological systems, as well as to help guide the construction of the synthetic systems.

Model checking in this context is to "Formally check whether a model of a biological system does what we want", and involves the use of a computer programme to check whether a formal model of a biological system exhibits a desired behavioural property.

The things that can be done with model checking in the context of biological systems are:

- Model validation:
  - Show that your model of the pathway matches the lab data
- Model analysis:
  - In a collection of variants of a model (e.g., in silico gene knock-outs), which models show a certain interesting behavior?
- Model development:
  - If the model doesn't do what we want, change the model automatically until it does (parameters, structures,...)
- Model finding:
  - Given database of models, use model checking to query the database and find those models which exhibit a certain behaviour.
- Biosystem verification:
  - Does the constructed system do what we intended?

We illustrate this tutorial by reference to the simulative MC2 Model Checker which operates over properties written in Probabilistic Linear-time Temporal Logic with numerical constraints (PLTLc), and which can handle descriptions ranging from highly qualitative to fully quantitative.

We also introduce the concept of Model Engineering, which is a systematic approach for designing, constructing and analyzing computational models of biological systems, and takes some inspiration from efficient software engineering strategies.

Special thanks to Robin Donaldson, University of Glasgow, who developed the MC2 model checker (<u>www.brc.dcs.gla.ac.uk/software/mc2/</u>) and created the MC2 model checking slides in this presentation.

## **Some References**

David Gilbert, Rainer Breitling, Monika Heiner, Robin Donaldson (2008), An introduction to BioModel Engineering, illustrated for signal transduction pathways, Proc WMC9, LNCS Volume 5391, pp13-28

Robin Donaldson and David Gilbert (2008). A Model Checking Approach to the Parameter Estimation of Biochemical Pathways. In proceedings CMSB 2008 (Computational Methods in Systems Biology). Heiner, Monika; Uhrmacher, Adelinde M. (Eds.) LNCS 5307/2008, pp269-287.

David Gilbert, Monika Heiner, Richard Orton (2008). A structured approach for the engineering of biochemical network models, illustrated for signalling pathways. Briefings in Bioinformatics, 2008 9(5):404-42

Monika Heiner, David Gilbert, and Robin Donaldson (2008), Petri Nets for Systems and Synthetic Biology. In M Bernardo, P Degano, and G Zavattaro (Eds.): Formal Methods for Systems Biology SFM 2008, Springer LNCS 5016, pp. 215-264

Xuan Liu, Jipu Jiang, Oluwafemi Ajayi, Xu Gu, David Gilbert, Richard Sinnott (2008), 'BioNessie(G) - A Grid Enabled Biochemical Networks Simulation Environment'. Stud Health Technol Inform. IOS Press, 2008, 138: 147-157

David Gilbert, Monika Heiner, Susan Rosser, Rachael Fulton, Xu Gu and Maciej Trybilo (2008), A Case Study in Model-driven Synthetic Biology. In Biologically Inspired Cooperative Computing: BICC 2008. IFIP

David Gilbert, Monika Heiner and Sebastian Lehrack (2007). A Unifying Framework for Modelling and Analysing Biochemical Pathways Using Petri Nets In proceedings CMSB 2007 (Computational Methods in Systems Biology), Editors: M.Calder and S.Gilmore, Springer LNCS/LNBI 4695, pp. 200-216.

David Gilbert, Hendrik Fuss, Xu Gu, Richard Orton, Steve Robinson, Vladislav Vyshemirsky, Mary Jo Kurth, C. Stephen Downes and Werner Dubitzky. (2006) Computational methodologies for modelling, analysis and simulation of signalling networks, Briefings in Bioinformatics 2006 7(4):339-353; doi: 10.1093/bib/bbl043 Special Issue: Computational Methodologies for Systems Biology.

(Available from <a href="http://people.brunel.ac.uk/~csstdrg/publications/">http://people.brunel.ac.uk/~csstdrg/publications/</a>)