

Petri Net Based System Analysis

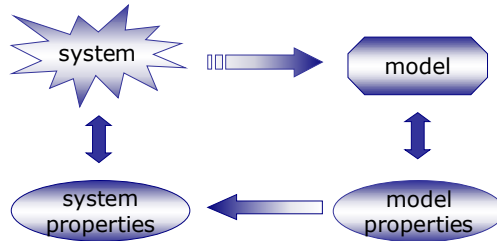


Monika Heiner, Ronny Richter, Alex Tovchigrechko, Sigrid Schenk (secretary)
Brandenburg University of Technology at Cottbus, Computer Science Dept.
= Data Structures and Software Dependability =
<http://www-dssz.informatik.tu-cottbus.de>

Model-based System Analysis

Verification of Technical Systems

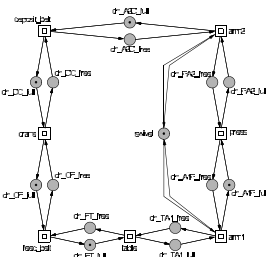
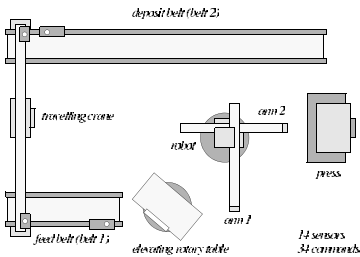
- requirements certification
- quality improvement
- proof engineering



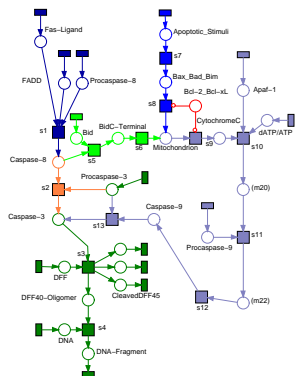
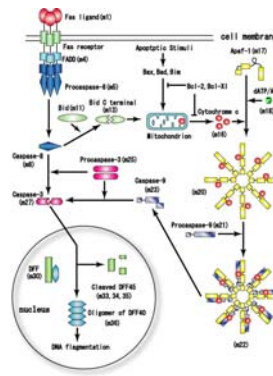
Validation of Natural Systems

- understanding
- experiment design
- behaviour prediction

Production Cell [7]



Apoptosis in Mammalian Cells (signal transduction network) [8]



Typical Net Properties

Technical Systems

- ordinary
- 1-bounded
- live, reversible
- communicating state machines
- exponential, state space growth

Natural Systems

- non-ordinary
- k-bounded / unbounded
- live, reversible, BUT: how to prove?
- apparently unstructured
- over-exponential state space growth

Analysis Tools

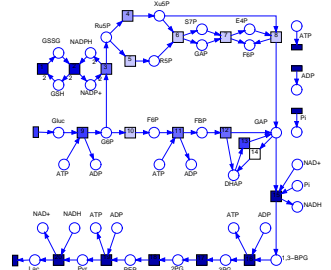
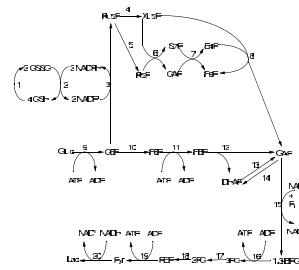
Technical Systems

- many, e.g.
- INA [5]
- PN MC KIT [3]
- BDD-CTL [15]
- BDD-LTL [4]

Natural Systems

- a few, e.g.
- INA (invariants) [5]
- PROD, MARIA [2]
- IDD-CTL [6]
- IDD-LTL [6]

Glycolysis / PPP in Erythrocytes (metabolic network) [12]



Ongoing Case Studies

- packet sort plant
- detailed glycolysis/pentose phosphate pathways in all human cells [16]
- blood clotting in human (hemostasis versus fibrinolysis) [14]
- lipoprotein metabolism (liver) in human [18]
- G1/S - phase in mammalian cells
- detailed central carbon metabolism in potato/tomato tubers
- central carbon metabolism in Escherichia coli
- switch cycle of the Halobacterium salinarum

Outlook

- modular & distributed analysis techniques
- advanced (3D) evaluation of transition/place invariants
- model checking of natural systems
- (discretely treatable) time Petri nets to analyse steady state behaviour
- coloured stochastic Petri nets for detailed kinetic analyses
- continuous Petri nets as structured description of ODEs [1, 17]
- hybrid Petri nets to integrate regulatory and metabolic system aspects

Cooperations

Analysis Methods / Tools

- Bernd Baumgarten, FhG Darmstadt
- Kurt Lautenbach, Univ. Koblenz
- Anastasia Pagnoni, Univ. Milano
- Louchka Popova-Zeugmann, HU Berlin [11]
- Falk Schreiber, IPK Gatersleben

Applications

- David Gilbert, Bioinformatics Research Center, Univ. Glasgow [1]
- Ina Koch, Dept. Bioinformatics, TFH Berlin [8 –12]
- Wolfgang Marwan, MPI, Magdeburg
- Dieter Oesterhelt, MPI for Biochemistry, Martinsried
- Denis Thieffry, Institute of Developmental Biology, Marseille

References

Analysis Methods / Tools

- [1] Gilbert D, Heiner M: Proc. 27th ATPN, LNCS, to appear
- [2] MARIA: <http://www.tcs.hut.fi/Software/maria>, 2004
- [3] MC KIT: Proc. 24th ATPN, LNCS 2697, 463-472, 2003
- [4] Spranger J: Ph.D. Thesis, BTU Cottbus, CS Dept., 12/2001
- [5] Starke PH, Roch S: <http://www.informatik.hu-berlin.de>, 1999
- [6] Tovchigrechko A: Ph.D. Thesis, BTU Cottbus, CS Dept. to appear

Applications

- [7] Heiner M, Deussen P, Spranger S: J. of AMT 15: 139-152, 1999
- [8] Heiner M, Koch I, Will J: J. BioSystems 75/1-3: 15-28, 2004
- [9] Heiner M, Koch I: Proc. 25th ATPN, LNCS 3099: 216-237, 2004
- [10] Koch I, Junker BH, Heiner M: Bioinformatics 21/04: 1219-1226, 2005
- [11] Popova-Zeugmann L, Heiner M, Koch I: FI 67: 149-162, 2005
- [12] Voss K, Heiner M, Koch I: Silico Biol. 3, 0031, 2003

Students' Theses

- [13] Fieber M: Diploma Thesis, Snoopy, 07/2004
- [14] Neumann G: Diploma Thesis, Blood Clotting, 07/2004
- [15] Noack A: Study Project, BDD CTL Model checking, 06/1999
- [16] Runge T: Diploma Thesis, Glycolysis and CPN, 11/2004
- [17] Scheibler D: Diploma Thesis, Continuous Snoopy, 01/2006
- [18] Schröder D: Study Project, Lipoprotein Metabolism, 10/2004