BME Tutorial - Part 6

Summary, Challenges

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SUMMARY
Bio Petri Nets, A Bit of History

- Carl Adam Petri, 1962, PhD University of Technology Darmstadt
  -> basic ideas introduced

- early 1970’s
  -> first papers contributing to Petri net theory

- Petri, 1976
  -> application to chemical networks mentioned

- early 1980’s
  -> first monographs on Petri net theory

- Reddy, 1993
  -> first paper on bio application

- late 1990’s
  -> increasing interest for modelling and analysis of bio networks
A BIT OF HISTORY

C. A. PETRI, NOVEMBER 2006

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PN & Systems Biology

June 2009
A Bit of History

1. TWO kinds of world points:
   - STATES and TRANSITIONS
     - e.g. Substances and Reactions

2. TWO topologies:
   - GIVE and TAKE
     - e.g. Creation and Annihilation

3. TWO kinds of continuity expressible:
   - Mathematical continuity ("connected and compact")
   - Experienced continuity ("connected")
representation of bio networks by Petri nets

- partial order representation  ->  better comprehension
- formal semantics    ->  sound analysis techniques
- unifying view       ->  various abstraction levels
representation of bio networks by Petri nets

- partial order representation  -> better comprehension
- formal semantics           -> sound analysis techniques
- unifying view              -> various abstraction levels

purposes

- animation                   -> to experience the model
- model validation against consistency criteria -> to increase confidence
- qualitative / quantitative behaviour prediction -> experiment design, new insights
SUMMARY

- representation of bio networks by Petri nets
  -> partial order representation
  -> formal semantics
  -> unifying view
  -> better comprehension
  -> sound analysis techniques
  -> various abstraction levels

- purposes
  -> animation
  -> model validation against consistency criteria
  -> qualitative / quantitative behaviour prediction
  -> to experience the model
  -> to increase confidence
  -> experiment design, new insights

- step-wise model development
  -> qualitative model
  -> discrete quantitative model
  -> continuous quantitative model
  -> discrete Petri nets
  -> stochastic Petri nets
  -> continuous Petri nets = ODEs
CHALLENGES
- **discrete models:** increasing level number = increasing accuracy
**CHALLENGE 1**

**BUT**, monotonous liveness holds for substructures only!

---

[STARKE 1990]
sharing structure = sharing properties

BUT, that’s not always the case! to which extend?

- stochastic and continuous behaviour may differ; why? when?

- relation: discrete & continuous behaviour?
CHALLENGE 2

- sharing structure = sharing properties
  
  **BUT**, that’s not always the case! to which extend?  
  -> stochastic and continuous behaviour may differ; why? when?  
  -> relation: discrete & continuous behaviour?

- two continuous Petri nets, generating the same ODEs,  
  but having different qualitative behaviour

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Challenge 2

- sharing structure = sharing properties
  
  **BUT**, that’s not always the case! to which extend?
  
  -> stochastic and continuous behaviour may differ; why? when?
  
  -> relation: discrete & continuous behaviour?

- two continuous Petri nets, generating the same ODEs, but having different qualitative behaviour
CHALLENGE 3

- unbounded qualitative model + time = bounded model
  - $\rightarrow$ stochastic models
  - $\rightarrow$ continuous models / ODEs

$\{ \text{simulation} \}$
**Challenge 3**

- **unbounded qualitative model + time = bounded model**
  - -> *stochastic models*
  - -> *continuous models / ODEs* 

  \(\{\text{simulation}\}\)

- **Should also work for timed Petri nets!**
  - -> *steady state behaviour*

- **What are timed Petri nets?**
  - -> *qualitative --- time --- stochastic - continuous - hybrid Petri nets*
  - -> *modelling power: TURING*
  - -> *analysis power: discrete state space construction (if bounded)*

- **How to derive time parameters?**
  - -> *T-invariants give steady state behaviour*
**T-invariants**

- **T-invariants**
  - integer solutions $x$ of $Cx = 0$, $x \neq 0$, $x \geq 0$ -> multisets of transitions
  - Parikh vector

- **T-invariants = (multi-) sets of transitions = Parikh vector**
  - zero effect on marking
  - reproducing a marking / system state

- **two interpretations**
  1. partially ordered transition sequence
     - of transitions occurring one after the other
     - substance / signal flow
     -> behaviour understanding
  2. relative transition firing rates
     - of transitions occurring permanently & concurrently
     -> steady state behaviour
TRANSFORMATION, Ex1

A + 2 B -> C + 3 D

-> properties as time-free net

INA
ORD HOM NBM PUR CSV SCF CON SC Ft0 tF0 Fp0 pF0 MG SM FC EFC ES
N Y N Y N Y Y Y N N Y Y Y Y
CPI CTI B SB REV DSt BSt DTr DCF L LV L&S
N Y Y N N N ? N Y N Y N
**TRANSFORMATION, Ex1**

\[ A + 2 \, B \rightarrow C + 3 \, D \]

-> properties as time-free net

- **INA**
  - ORD HOM NBM PUR CSV SCF CON SC Ft0 tF0 Fp0 pF0 MG SM FC EFC ES
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  - CPI CTI B SB REV DSt BSt DTr DCF L LV L&S
  - N Y N N Y N ? N Y Y Y Y N
TRANSFORMATION, Ex1

\[ A + 2B \rightarrow C + 3D \]

1 prod_A

2 prod_B

T-INARIANT

\[ \rightarrow \text{properties as time-free net} \]

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CPI CTI B SB REV DSt BSt DTr DCF L LV L&S
N Y N N Y N ? N Y Y Y N

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TRANSFORMATION, Ex1

\[ A + 2B \rightarrow C + 3D \]

\[
\begin{array}{c}
\text{prod}_A \\
<6>
\end{array}
\quad
\begin{array}{c}
\text{prod}_B \\
<3>
\end{array}
\]

\[
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\text{r1} \\
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\end{array}
\quad
\begin{array}{c}
\text{cons}_C \\
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\quad
\begin{array}{c}
\text{cons}_D \\
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\]

T-IN Variant

-> properties as time net

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TRANSFORMATION, Ex2

A -> 2 B, A -> 3 C

-> properties as time-free net

INA
ORD HOM NBM PUR CSV SCF CON SC Ft0 tf0 Fp0 pF0 MG SM FC EFC ES
N Y N Y N Y N Y N N Y N Y Y Y
CPI CTI B SB REV DSt BSt DTr DCF L LV L&S
N Y Y N N N ? N N N Y N

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TRANSFORMATION, Ex2

\[ A \rightarrow 2 \text{B}, A \rightarrow 3 \text{C} \]

\[ \text{prod}_A \]

\[ r1 \rightarrow A \]

\[ \text{cons}_B \]

\[ r2 \rightarrow A \]

\[ \text{cons}_C \]

\[ \rightarrow \text{properties as time-free net} \]

\[ \begin{array}{cccccccccccccccc}
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\end{array} \]
**TRANSFORMATION, Ex2**

A -> 2 B, A -> 3 C

- **T-INARIANT1**
- **T-INARIANT2**

-> properties as time-free net

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ORD HOM NBM PUR CSV SCF CON SC Ft0 tF0 Fp0 pF0 MG SM FC EFC ES
N Y N Y N Y Y N Y Y N N Y N Y Y Y
CPI CTI B SB REV DSt BSt DTr DCF L LV L&S
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TRANSFORMATION, Ex2

A -> 2 B, A -> 3 C

-> properties as time net

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CPI CTI B SB REV DSt BSt DTr DCF L LV L&S
N Y Y N N N ? N Y Y Y N

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transient state
steady state

s6 (A,2B,C)
\[ t(r2)=3 \]
\[ t(cons_C)=1 \]

prod_A start
r1 start
cons_B start, cons_C end

s7 (0,B,C)
\[ t(prod_A)=2 \]
\[ t(r1)=5 \]
\[ t(r2)=2 \]
\[ t(cons_B)=2 \]

prod_A end
r1 end
cons_B end, cons_C

s8 (A,B,3C)
\[ t(r1)=3 \]

prod_A start
r2 start
cons_B start, cons_C

s9 (0,0,2C)
\[ t(prod_A)=1 \]
\[ t(r1)=1 \]
\[ t(r2)=4 \]
\[ t(cons_B)=1 \]

terminal SCC
RG(Ex2), TERMINAL SCC

- contains all transitions
  -> always running
  -> start / end
    at different time points

- contains all minimal T-invariants

- timing diagram

- relative transition firing rates

  prod_A : 1 + 1
  r1 : 1 r2 : 1
  cons_B : 2 cons_C : 3

6 time units
CTI, but not CPI

**transient state**
- initial behaviour to reach steady state
- not REV
- generally, not DCF

**steady state behaviour**
- terminal scc
- here, BND
- here, DCF
However, this does not always work!
COUNTEREXAMPLE 1

1-working time for all transitions;
FC, there are no deadlocks, traps, p-invariants, besides the pseudo-P-invariant \((A, co_A)\);

wBND & LIVE for the given initial marking
COUNTEREXAMPLE 2

producer

consumer

weakly bounded

producer

consumer

not weakly bounded

[DESEL 2006], weakly bounded Petri nets; awpn ’06
**CHALLENGE 3 - TIME-DEPENDENT BOUNDEDNESS**

- **given:** time-free Petri net
  - $\Rightarrow$ unbounded
  - $\Rightarrow$ live (supposed to be)

- **wanted:** corresponding time-dependent Petri net
  - $\Rightarrow$ (weakly) bounded
  - $\Rightarrow$ (still) live
CHALLENGE 3 - TIME-DEPENDENT BOUNDEDNESS

- **given:** time-free Petri net
  - $\rightarrow$ unbounded
  - $\rightarrow$ live (supposed to be)

- **wanted:** corresponding time-dependent Petri net
  - $\rightarrow$ (weakly) bounded
  - $\rightarrow$ (still) live

- **questions**
  - $\rightarrow$ for which structures does it work / does it not work ?
  - $\rightarrow$ are there sufficient / necessary conditions ?
  - $\rightarrow$ which time intervals make the net bounded ?
  - $\rightarrow$ which time intervals preserve a transition sequence's realizability ?

- **consistency criterion for (steady state) bio networks !?**
live under certain timing constraints
Challenge 4 - Time-dependent Liveness

The red transition brings liveness under any timing
**CHALLENGE 4 - TIME-DEPENDENT LIVENESS**

- **given:** time-free Petri net
  - -> non-live

- **question**
  - -> under which conditions are there time restrictions, making this Petri net live?
CHALLENGES, SUMMARY

- increasing level number = increasing accuracy
  \textit{BUT, monotonous liveness holds for substructures only!}

- sharing structure = sharing properties
  \textit{BUT, that's not always the case!} to which extend?
  -> stochastic and continuous behaviour may differ; why? when?
  -> relation: qualitative & continuous behaviour?

- unbounded qualitative model + time = bounded model
  \textit{BUT, that's not always the case!}
  -> (structural) criteria for time-dependent boundedness?

- non-live qualitative model + time = live model
  \textit{BUT, how to do it in general the case?}
  -> (structural) criteria for time-dependent liveness?
**FURTHER READING**


- **Your paper to one or the other of the challenges ?**
THANKS!

HTTP://WWW-DSSZ.INFORMATIK.TU-COTTBUS.DE/BME/PETRINETS2009