Hybrid Modelling using Generalised Hybrid Petri Nets

Mostafa Herajy and Monika Heiner

Chair of Data Structures and Software Dependability,
Computer Science Department,
Brandenburg University of Technology,
Cottbus, Germany

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Motivations

- Some biological models require to be represented in hybrid way (Cells/Molecular interactions in one model).
- Continuous deterministic simulation does not consider the fluctuation of molecules, specially when there is a low number of them.
- Stochastic Simulation is computational expensive (fast reactions, large number of molecules).
CPN and GSPN

- **Continuous Petri Nets:**
  - Continuous places
  - Continuous transitions

- **Generalized Stochastic Petri Nets**
  - Discrete places
  - Stochastic transitions
  - Immediate transitions
  - Deterministic transitions
  - Scheduled transitions
Features of GHPN

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Elements

Places

- Discrete
- Continuous

Transitions

- Stochastic
- Continuous Immediate
- Deterministic
- Scheduled

Edges

- Standard
- Read
- Inhibitor
- Equal
- Reset
- Modifier

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Generalised Hybrid Petri Nets
Connectivity

Continuous Transition

Discrete Transition

Continuous Transition
Simulation Methods

- Stochastic
- Hybrid
- Deterministic

- Much Faster
- Much Accurate
Simulation of GHPN

- Static partitioning: partitioning is done off-line before the simulation starts.

- Dynamic partitioning: partitioning is done on-line during the simulation.
Static Partitioning:

- The user has to provide the partitioning.
- There is no additional computational overhead due to partitioning.
- It is not user friendly.
- It is not suitable for all applications.
Dynamic Partitioning:

- The partitioning is done automatically without user intervention.
- There is additional computational overhead due to partitioning.
- The simulation is independent from the Petri net representation.
- It is suited for models where the time saving due to on-line partitioning is greater than the partitioning time overhead.
Examples

- Water Tank
- T7 Phage
- Goutsias Model
- Circadian Oscillator
The Water Tank Model

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The Water Tank Model

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Generalised Hybrid Petri Nets
### T7 Phage

<table>
<thead>
<tr>
<th>No.</th>
<th>Reaction</th>
<th>Propensity</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1</td>
<td>$gen \rightarrow temp$</td>
<td>$c_1 \cdot gen$</td>
<td>$c_1 = 0.0025$</td>
</tr>
<tr>
<td>R2</td>
<td>$temp \rightarrow \phi$</td>
<td>$c_2 \cdot temp$</td>
<td>$c_2 = 0.25$</td>
</tr>
<tr>
<td>R3</td>
<td>$temp \rightarrow temp + gen$</td>
<td>$c_3 \cdot temp$</td>
<td>$c_3 = 1.0$</td>
</tr>
<tr>
<td>R4</td>
<td>$gen + struct \rightarrow &quot;virus&quot;$</td>
<td>$c_4 \cdot gen \cdot struct$</td>
<td>$c_4 = 7.5 \times 10^{-6}$</td>
</tr>
<tr>
<td>R5</td>
<td>$temp \rightarrow temp + struct$</td>
<td>$c_5 \cdot temp$</td>
<td>$c_5 = 1000$</td>
</tr>
<tr>
<td>R6</td>
<td>$struct \rightarrow \phi$</td>
<td>$c_6 \cdot struct$</td>
<td>$c_6 = 1.99$</td>
</tr>
</tbody>
</table>

Srivastava et al 2002
T7 Phage (GHPN)

- $R_5$ and $R_6$ are represented as continuous reactions

- $R_1$, $R_2$, $R_3$, and $R_4$ are represented as continuous reactions
T7 Phage Simulation Results

![Graph showing simulation results with three curves: Hybrid (red solid line), Continuous (green dashed line), and Stochastic (blue dotted line). The x-axis represents time, and the y-axis represents the amount of water. The graph illustrates the comparison between different simulation approaches.]

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Generalised Hybrid Petri Nets
Goutsiàs Model (GHPN)
Goutsias Model (Simulation Results)
Circadian Oscillator

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Generalised Hybrid Petri Nets
Circadian Oscillator (Cont.)

Continuous ($k_{17}=0.2$)

![Continuous ($k_{17}=0.2$) Graph]

Continuous ($k_{17}=0.08$)

![Continuous ($k_{17}=0.08$) Graph]

Stochastic ($k_{17}=0.08$)

![Stochastic ($k_{17}=0.08$) Graph]

Hybrid ($k_{17}=0.08$)

![Hybrid ($k_{17}=0.08$) Graph]
## Simulation Time

<table>
<thead>
<tr>
<th>Model</th>
<th>Continuous</th>
<th>Stochastic</th>
<th>hybrid (static)</th>
<th>hybrid (dynamic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goutsias</td>
<td>0.01</td>
<td>0.972</td>
<td>0.014</td>
<td>0.138</td>
</tr>
<tr>
<td>Oscillator</td>
<td>0.258</td>
<td>5.995</td>
<td>4.21</td>
<td>1.991</td>
</tr>
<tr>
<td>T7 Phage</td>
<td>0.007</td>
<td>12.36</td>
<td>0.210</td>
<td>0.107</td>
</tr>
</tbody>
</table>
Live Demo using Snoopy
Thank You