Generalized Hybrid Petri Nets

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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

- Combines both CPN and GSPN into one class
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- Different transition types $\rightarrow$ different reaction types can be modelled using GHPN

Stiff biochemical networks can be easily modelled and simulated using GHPN.
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Elements

Discrete  Continuous

stochastic  continuous  immediate  deterministic

<1>  [_SimStart,1,_SimEnd]

Places

stochastic  continuous  immediate  deterministic  scheduled

Transitions

standard  read  inhibitor  equal  reset  modifier

Edges
Connectivity

Continuous transition
Stochastic transition

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Examples

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

Introduction

- Elements
- Connectivity
- Examples

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Generalized Hybrid Petri Nets
The Water Tank Model

Elements Connectivity Examples

On
Off
Water_tank
Water_increase
Water_decrease
On_to_Off
Off_to_ON
2
0.1
[50,1,51]

Amount of Water
time
water tank
On
Off

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# 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><code>gen</code> $\rightarrow$ <code>temp</code></td>
<td>$c_1 \cdot gen$</td>
<td>$c_1 = 0.0025$</td>
</tr>
<tr>
<td>R2</td>
<td><code>temp</code> $\rightarrow$ <code>\phi</code></td>
<td>$c_2 \cdot temp$</td>
<td>$c_2 = 0.25$</td>
</tr>
<tr>
<td>R3</td>
<td><code>temp</code> $\rightarrow$ <code>temp + gen</code></td>
<td>$c_3 \cdot temp$</td>
<td>$c_3 = 1.0$</td>
</tr>
<tr>
<td>R4</td>
<td><code>gen + struct</code> $\rightarrow$ ”virus”</td>
<td>$c_4 \cdot gen \cdot struct$</td>
<td>$c_4 = 7.5 \times 10^{-6}$</td>
</tr>
<tr>
<td>R5</td>
<td><code>temp</code> $\rightarrow$ <code>temp + struct</code></td>
<td>$c_5 \cdot temp$</td>
<td>$c_5 = 1000$</td>
</tr>
<tr>
<td>R6</td>
<td><code>struct</code> $\rightarrow$ <code>\phi</code></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
Goutsias Model (GHPN)

DNA
DNA_2D
DNA_D
M 10
D
10
RNA
10
R2
R4
R5
R6
R7
R8
R9
R10
R1
R3

k1
0.043
k2
0.0007
k3
71.5
k4
3.9e−06
k5
0.02
k6
0.48
k7
0.0002
k8
9e−12
k9
0.08
k10
0.5

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Goutsias Model (Simulation Results)
## Simulation Time

<table>
<thead>
<tr>
<th></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>T7 Phage</td>
<td>0.007</td>
<td>12.36</td>
<td>0.210</td>
<td>0.107</td>
</tr>
</tbody>
</table>
Try It Now

- Get your copy at: http://www-dssz.informatik.tu-cottbus.de/DSSZ/Software/Snoopy
- The implementation is freely available as part of Snoopy
- GHPN enjoys all of Snoopy features
Thank You