

NetBuilder' (Apostrophe)

Katja Wegner and Maria Schilstra

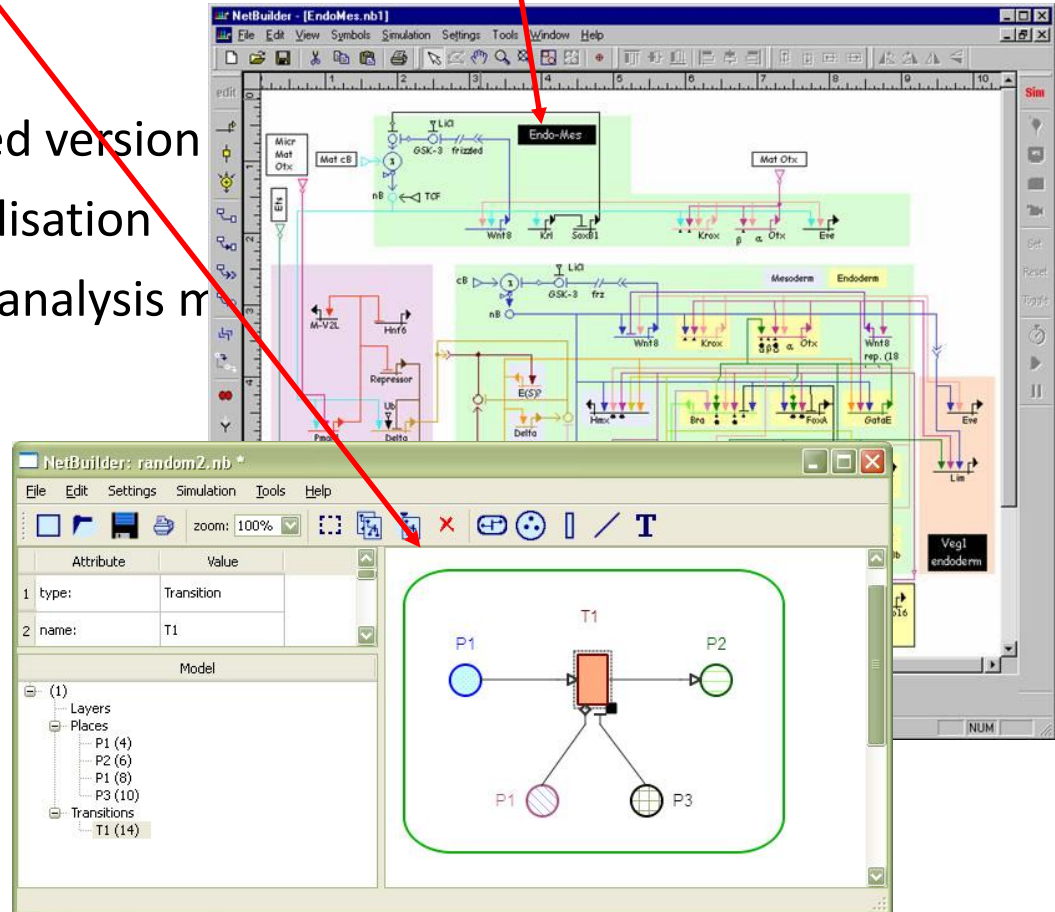
<http://strc.herts.ac.uk/bio/maria/Apostrophe/>

NetBuilder' (Project Apostrophe)

- A tool for biological networks
 - To construct, model, simulate (stochastic, deterministic, hybrid) quantitative **GRNs** and more
 - For researchers with little experience of mathematical modelling
 - OPEN SOURCE
- Further information and download:
 - <http://strc.herts.ac.uk/bio/maria/Apostrophe/>
 - <http://sourceforge.net/projects/apostrophe/>

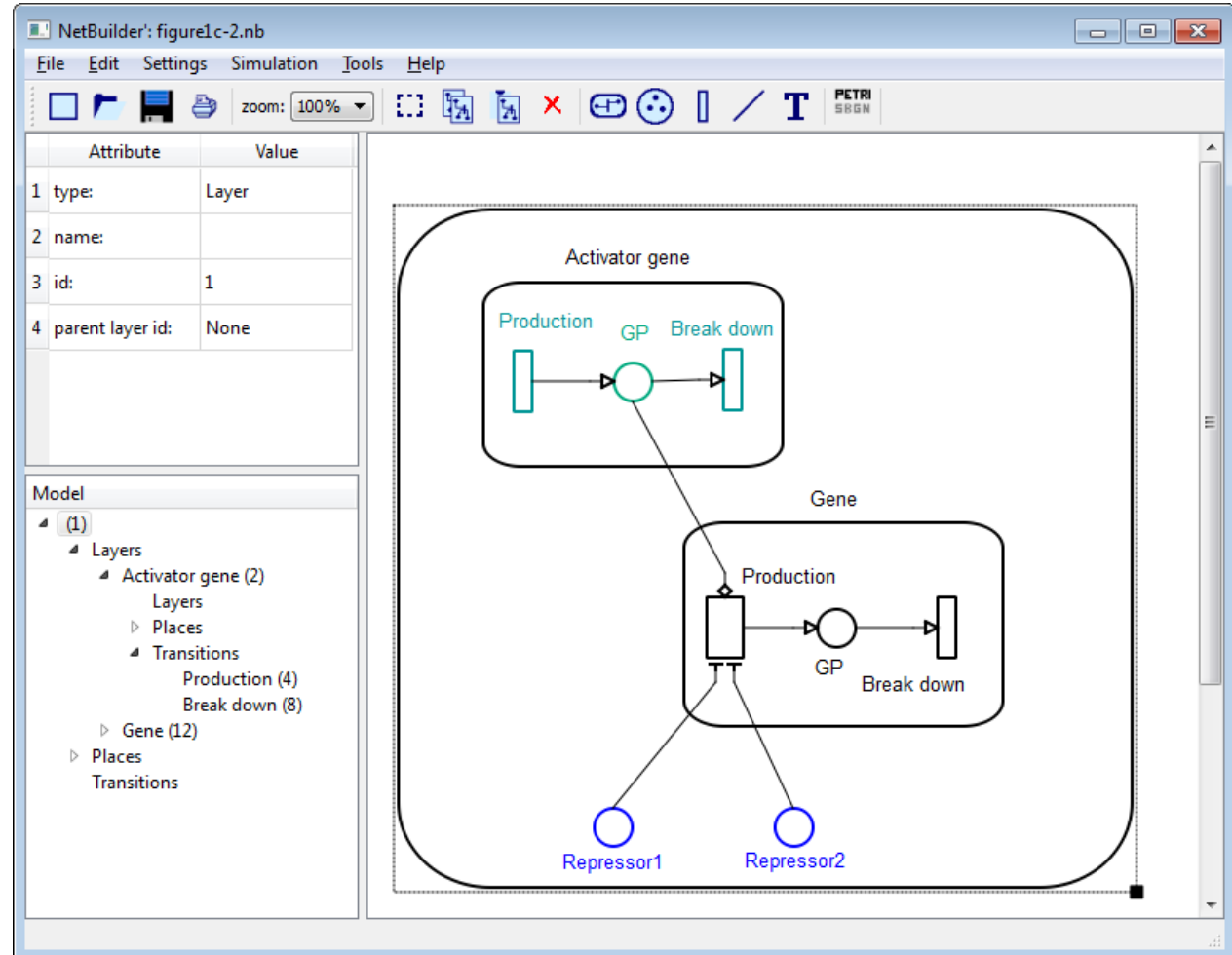
NetBuilder' ≠ NetBuilder

- NetBuilder':
 - completely overhauled version
 - different model visualisation
 - more simulation and analysis m



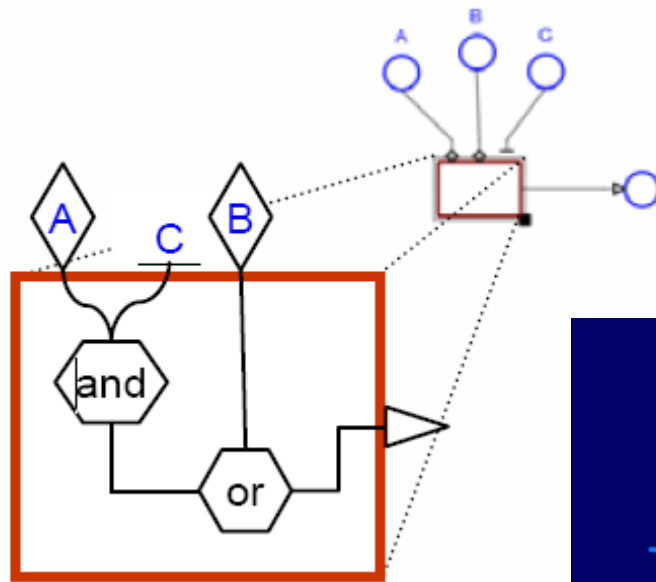
NetBuilder' - Features

- Graphical editor
- Using the **Petri Net** formalism as representation

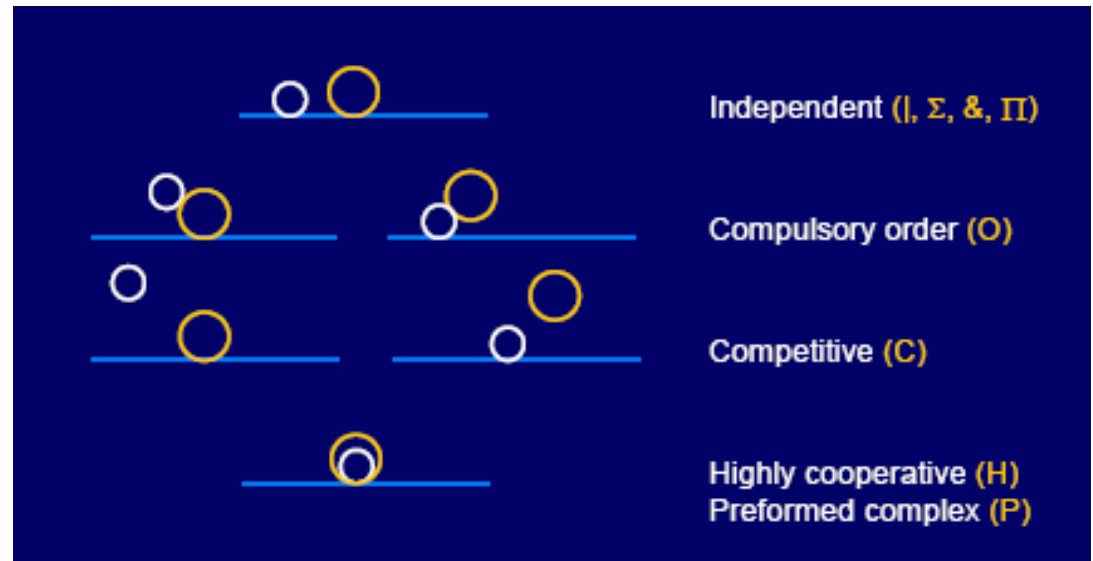


NetBuilder - Features

- Rules for (combined) effects of regulatory interactions

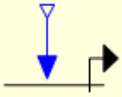
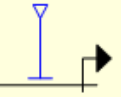
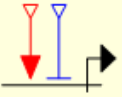
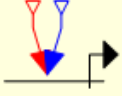
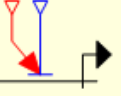
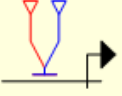
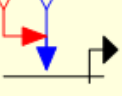
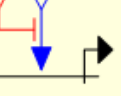
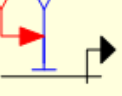
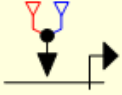
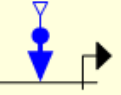
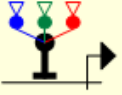


Bio-logic: Gene Expression and the
Laws of Combinatorial Logic
Artificial Life 14: 1–13 (2008)



NetBuilder - Features

- Rules for (combined) effects of regulatory interactions

<p>A binds independently from other TFs</p>	<p>A activates</p>  <p>$\alpha = a/(1+a)$</p>	<p>A represses</p>  <p>$\alpha = 1/(1+a)$</p>	<p>A represses, B activates</p>  <p>$\alpha\beta = b/(1+a+b+ab)$</p>
<p>A and B compete for the same site</p>	<p>A and B activate</p>  <p>$\alpha = (a+b)/(1+a+b)$</p>	<p>A represses, B activates</p>  <p>$\alpha = b/(1+a+b)$</p>	<p>A and B repress</p>  <p>$\alpha = 1/(1+a+b)$</p>
<p>B binds to bound A (compulsory order binding)</p>	<p>B activates activator A</p>  <p>$\alpha = ab/(1+a+ab)$</p>	<p>B represses activator A</p>  <p>$\alpha = a/(1+a+ab)$</p>	<p>B activates repressor A</p>  <p>$\alpha = (1+a)/(1+a+ab)$</p>
<p>A and B bind as a complex</p>	<p>A and B form a hetero-oligomeric activator</p>  <p>$\alpha = ab/(1+ab)$</p>	<p>A forms a homo-oligomeric activator</p>  <p>$\alpha = a^n/(1+a^n)$</p>	<p>A, B, and C, form a complex repressor</p>  <p>$\alpha = 1/(1+a^n b^m c^d)$</p>

Specify interaction in settings

Equations are automatically generated

NetBuilder' - Features

Initial state [?] [X]

Places:

Place:	Value:	
lc (3)	<input type="text" value="0.0"/>	<input type="checkbox"/> fixed
mRNA TetR (5)	<input type="text" value="0.0"/>	<input type="checkbox"/> fixed
TetR (7)	<input type="text" value="0.0"/>	<input type="checkbox"/> fixed
mRNA LacI (9)	<input type="text" value="0.0"/>	<input type="checkbox"/> fixed
LacI (11)	<input type="text" value="5.0"/>	<input type="checkbox"/> fixed
mRNA lc (13)	<input type="text" value="1.0"/>	<input type="checkbox"/> fixed

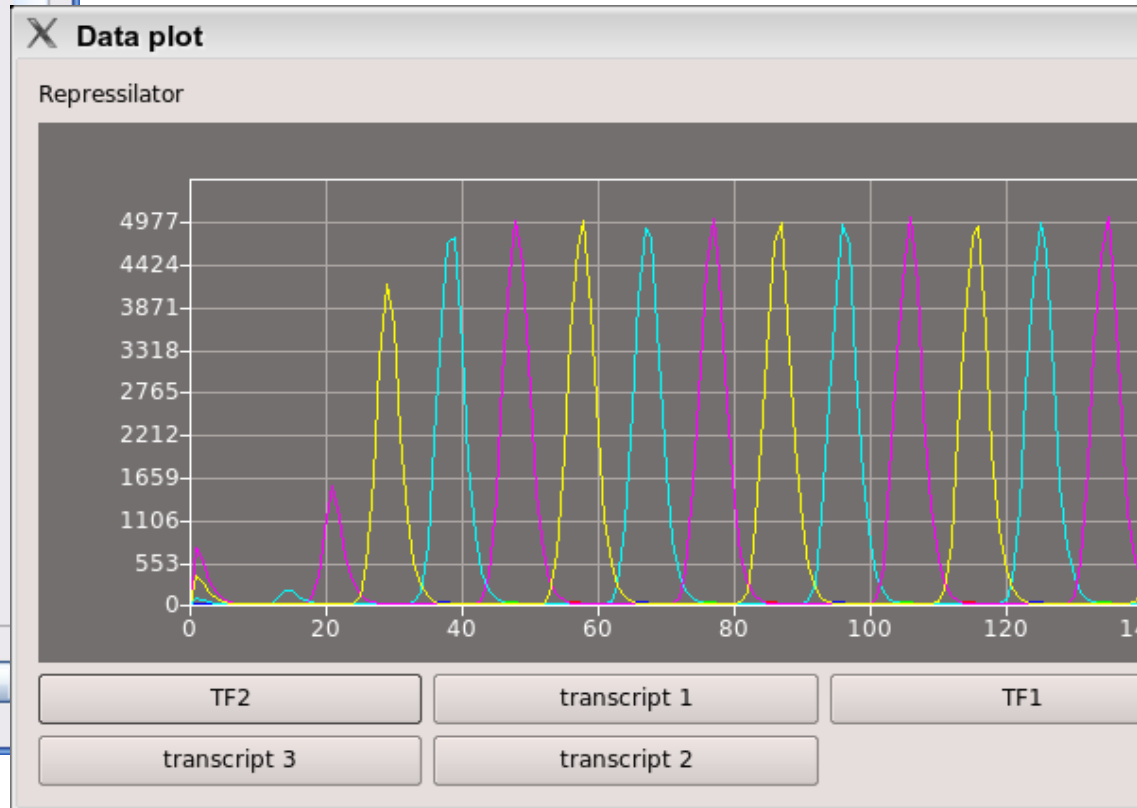
Transitions:

Gen TetR (15)

rate:	<input type="text" value="30.0"/>
Arc:	Attributes:
-> mRNA TetR (5) weight:	<input type="text" value="0.0"/>
mRNA LacI (9) -> exponent:	<input type="text" value="2.0"/>
multiplier:	<input type="text" value="40.0"/>

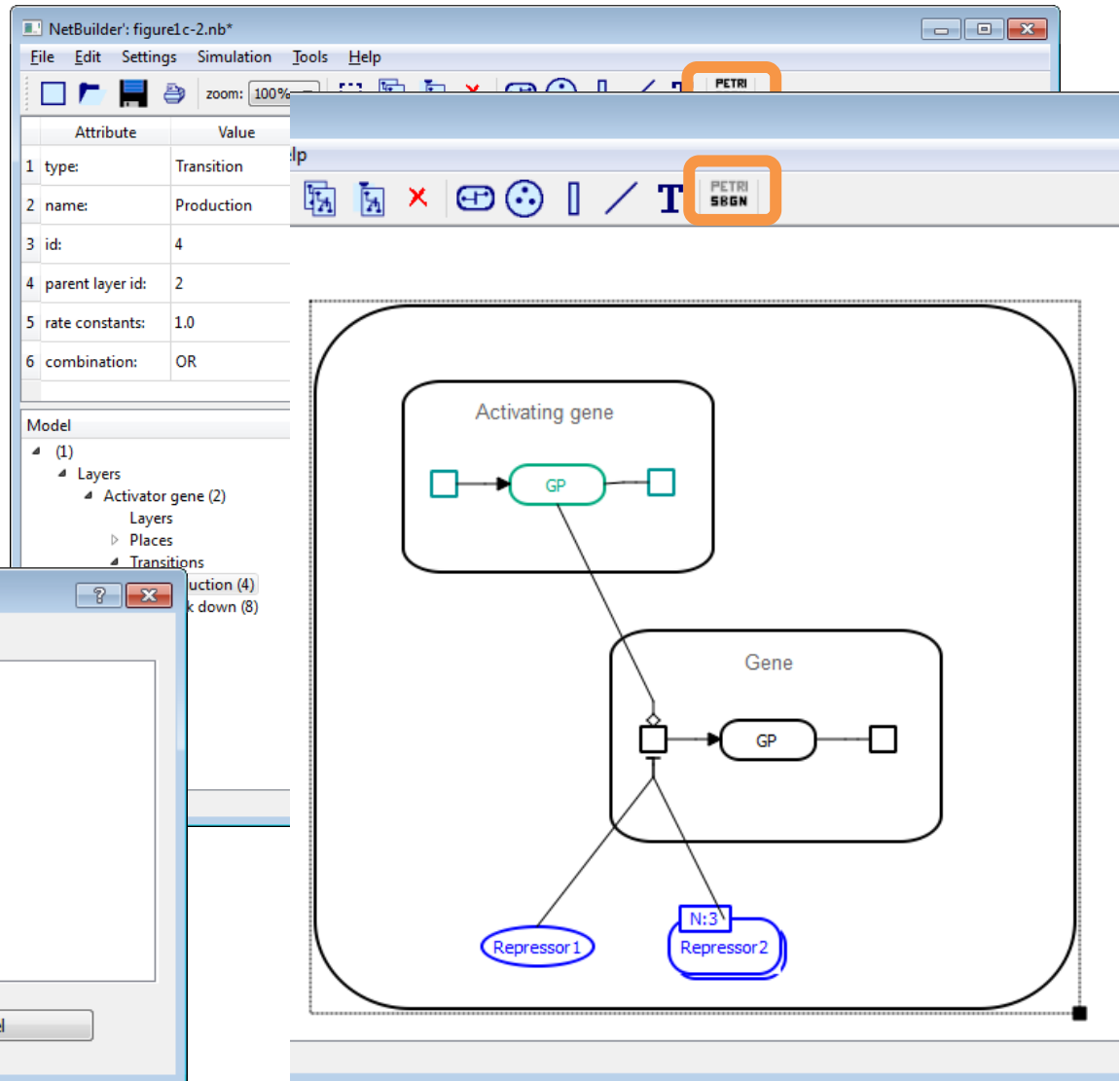
OK Cancel

- **Evaluation methods:**
 - Stochastic (based on Gibson & Bruck)
 - Deterministic (LSODA and Euler)
 - **Hybrid**



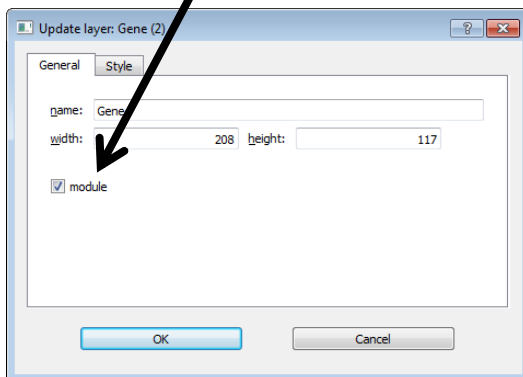
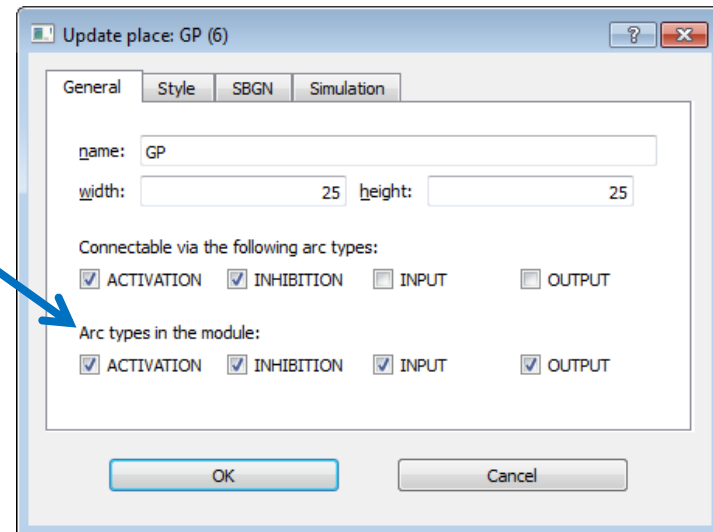
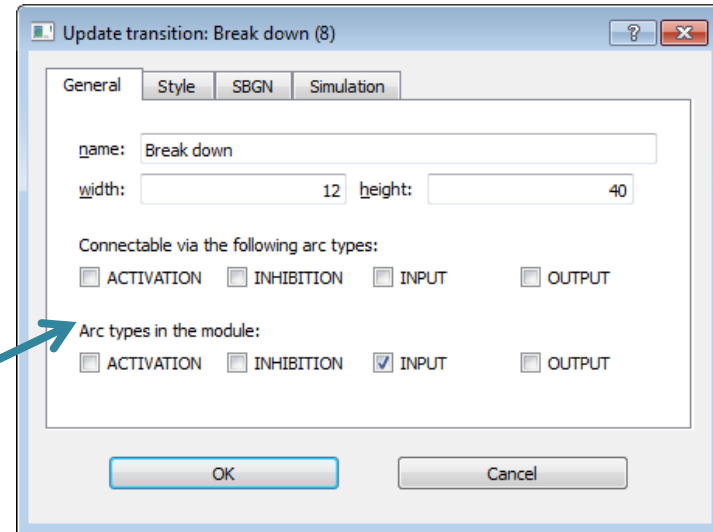
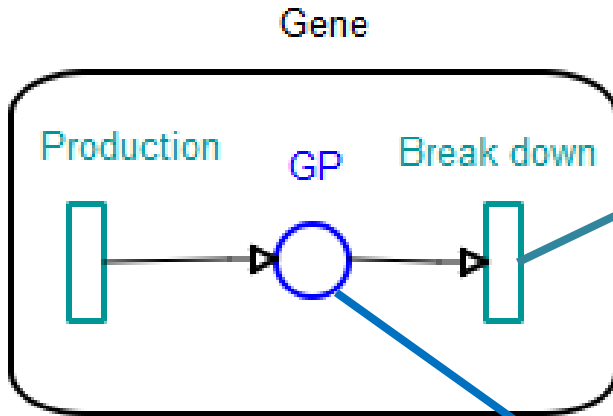
NetBuilder' – Latest features

- Graphical editor
- Using the Petri Net formalism as representation as well as the **SBGN process description language**





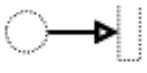
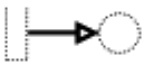
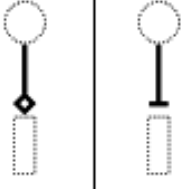

NetBuilder' – Latest features

- Modules



NetBuilder – Exchange

- **Data exchange:**
SBML, PNML
- **Representation:**
Petri net and SBGN
process description
language

Component name	Symbol	Role
Place		Container for tokens (SBML: species) (SBGN: entity pool node)
Transition		Represents a process (SBML: reaction) (SBGN: process node)
Input arc		Associated place is a reactant (SBML: SpeciesReference for reactant) (SBGN: consumption)
Output arc		Associated place is a reaction product (SBML: SpeciesReference for product) (SBGN: production)
Modifier arcs: Activator Inhibitor		Stimulatory (right) or inhibitory (left) effect on reaction rate (SBML: ModifierSpeciesReference) (SBGN: stimulation, inhibition)
Layer		(Sub)model (SBML: model) (SBGN: container node)

NetBuilder' – technical details

- The latest version (0.5) is based on:
 - Python 2.7
 - PyQt 4.8.5 (GUI)
 - NumPy (1.6.1) and SciPy (0.9.0)
 - libSBML 4.3.1 with the layout extension
 - SBGN support but without libSBGN, yet

NetBuilder' – Summary

- Graphical editor
- Rules for (combined) effects of regulatory interactions
- Equations describing process dynamics
 - Mass-action type rate equations
 - Define kinetics
 - Finally equations are automatically generated
- Numerical representation of component values
 - Continuous and/or discrete places
- Evaluation methods:
 - Stochastic (based on Gibson & Bruck)
 - Deterministic (LSODA and Euler)
 - Hybrid
- **Further contributors:**
 - Marcel Block, Attila Egri-Nagy, Mark Robinson, Johannes Knabe