

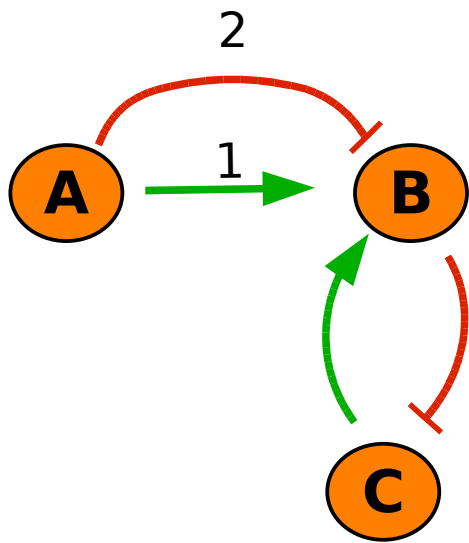
Extended Logical Formalism, GINsim, GINML, SBML

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<http://tagc.univ-mrs.fr>

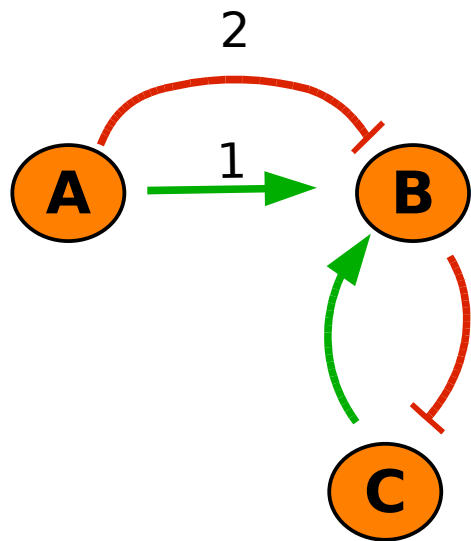
Logical Formalism



Regulatory graph

- Genes (A, B, C)
 - Discrete expression levels (Boolean or multivalued)
- Interactions
 - Activity threshold
 - Activations, inhibitions
- Dynamical rules
 - Target expression level depending on regulator levels

Dynamical Rules



- B expressed in presence of:
A at medium level or C (or both)

- C expressed in absence of B

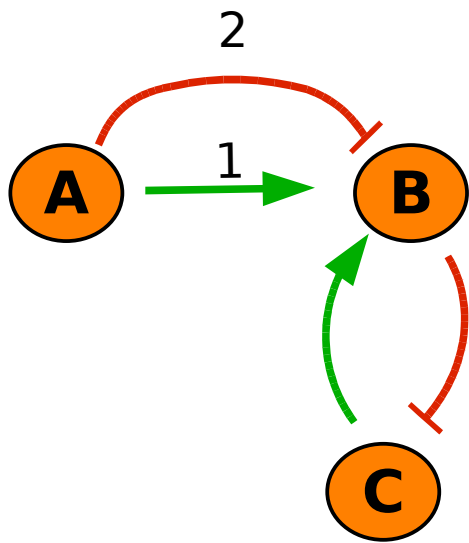
Dynamics of B as **logical parameters** $K_B(\mathbf{I})$

$K_B(\mathbf{I}) = \mathbf{x} \longrightarrow \mathbf{B}$ tends toward \mathbf{x} when interactions in \mathbf{I} are active (and other are not)

$$K_B(A_1) = K_B(C) = K_B(A_1, C) = K_B(A_2, C) = 1$$

$$K_B(A_2) = K_B() = 0$$

Dynamical Rules



- B expressed in presence of:
A at medium level or C (or both)
- C expressed in absence of B

Dynamics of B given by the **logical function** K_B

$$K_B = \begin{cases} 1 & \text{if } (A_1 \vee C) \\ 0 & \text{otherwise} \end{cases}$$

GINML: the Format

XML format, based on GXL (graph exchange format)

gxl

graph

node. Attributes: id, maxvalue

parameter. Attributes: idActiveInteractions, value

Coming soon: logical functions

...

edge. Attributes: id, from, to, minvalue, maxvalue, sign

...

...

GINML: Example

```
<gxl>
  <graph id="default_name" class="regulatory" nodeorder="A B C">

    <node id="A" maxvalue="2" />
    <node id="B" maxvalue="1">
      <parameter idActiveInteractions=" A:B:1" val="1"/>
      <parameter idActiveInteractions=" C:B" val="1"/>
      <parameter idActiveInteractions=" A:B:1 C:B" val="1"/>
      <parameter idActiveInteractions=" A:B:2 C:B" val="1"/>
    </node>
    <node id="C" maxvalue="1">
      <parameter val="1"/>
    </node>

    <edge id="A:B:1" from="A" to="B" minvalue="1" maxvalue="1"
sign="positive" />
    <edge id="A:B:2" from="A" to="B" minvalue="2" sign="negative" />
    <edge id="B:C" from="B" to="C" minvalue="1" sign="negative" />
    <edge id="C:B" from="C" to="B" minvalue="1" sign="positive" />

  </graph>
</gxl>
```

GINsim: the Software

The screenshot displays the GINsim software interface for editing a Petri net. The main workspace shows a Petri net with three places: A, B, and C. Place A is connected to place B by a transition (indicated by a thick arrow). Place C is connected to place B by two arcs: a red arc from C to B and a green arc from B to C. Place B is currently selected, as indicated by a dashed blue border.

The bottom panel shows the 'Modelling Attributes' for the selected place B:

- Id:** B
- Name:** (empty)
- Max:** 1

Value	Active Interactions
1	A
1	C
1	A C
1	A:2 C

On the right side of the bottom panel, the following text is displayed:

```
C [1,max]; positive  
A [1,1]; positive  
A:2 [2,max]; negative
```

GINsim: Some Features

- Regulatory graph edition
- Simulation
- Analysis
- Export
 - Petri Net (PNML, INA, APNN)
 - Cytoscape
 - x Cytoscape plugin: export to GINML
- Import
 - From SBML, relying on libSBML ?

Logical Models in SBML: history

Long standing question

Early proposal at ICSB2006

- Attempt to fit it in SBML L2
 - Involved ambiguous use of existing tags
- Preliminary extension proposal
 - Add initialActivity attribute to species
 - Add a regulation element
 - ✗ Target
 - ✗ ListOfRegulators
 - ✗ Logical function giving the focal point

Extension mechanism in L3: a better approach