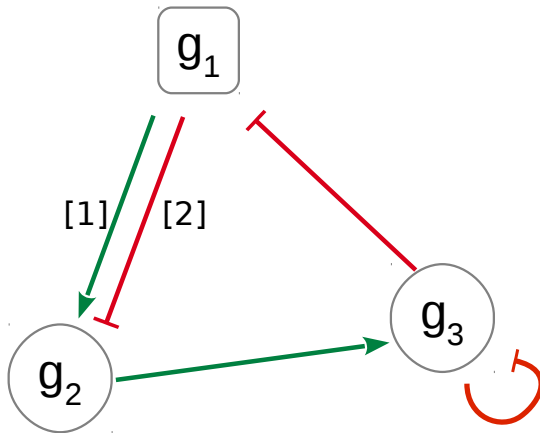


SBML qual and LogicalModel: building bridges for qualitative models

Logical modeling

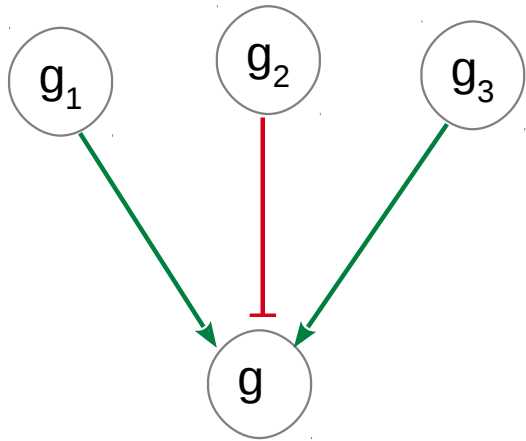
- Nodes: genes, proteins...
Activity level (Boolean, MV)



- Edges: interactions
Threshold for MV source

- Logical rules
 $\text{next}(G3) = G2$ and not $G3$

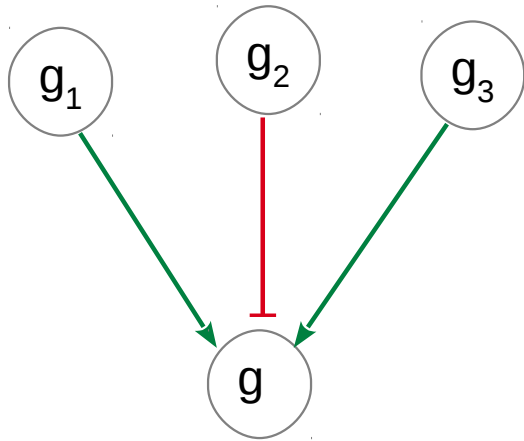
Discrete modelling methods



$$(g_1 \mid g_3) \& !g_2$$

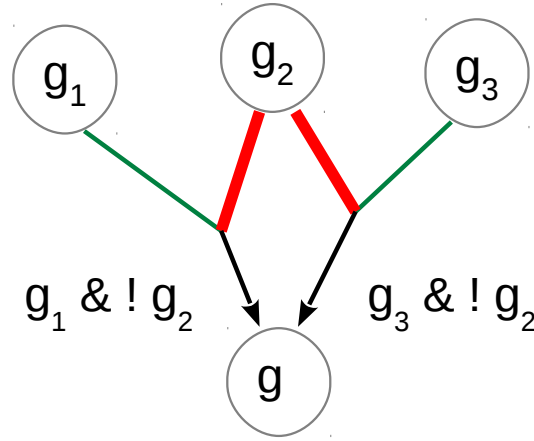
g1	g2	g3	g
0	0	0	0
0	0	1	1
0	1	0	0
0	1	1	0
1	0	0	1
1	0	1	1
1	1	0	0
1	1	1	0

Discrete modelling methods



$$(g_1 \mid g_3) \& !g_2$$

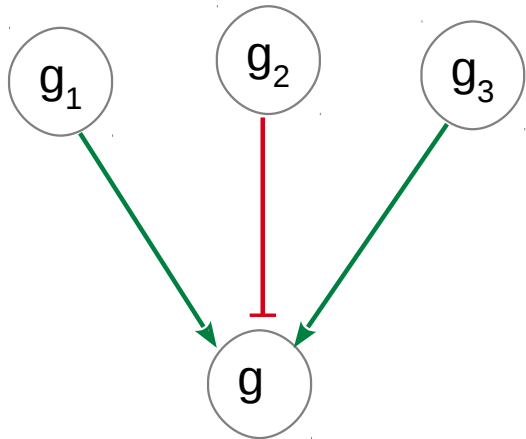
g1	g2	g3	g
0	0	0	0
0	0	1	1
0	1	0	0
0	1	1	0
1	0	0	1
1	0	1	1
1	1	0	0
1	1	1	0



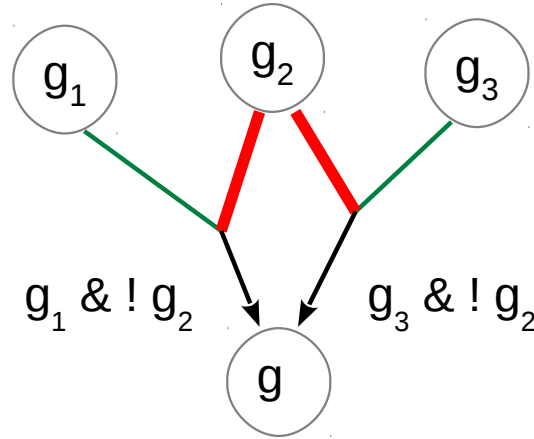
$$g_1 \& !g_2$$

$$g_3 \& !g_2$$

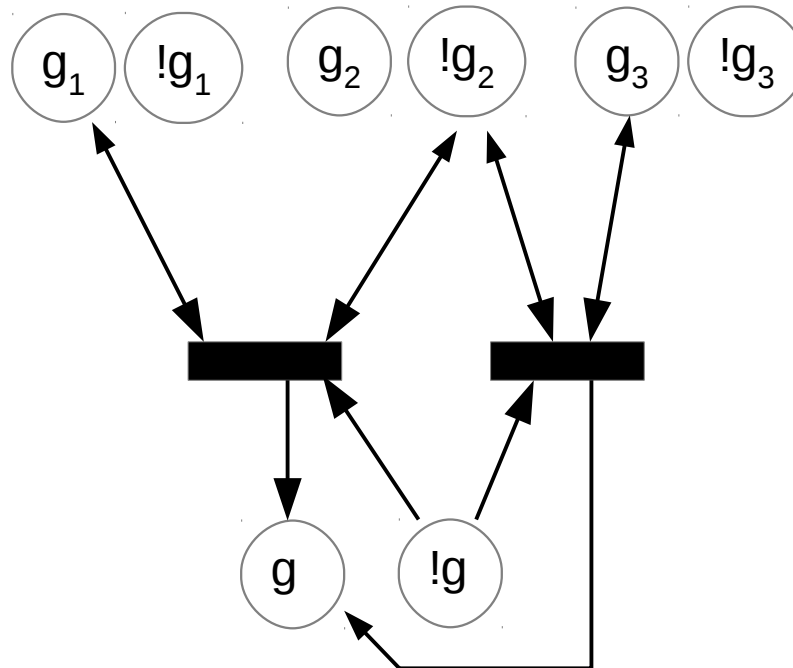
Discrete modelling methods



$$(g_1 \mid g_3) \& !g_2$$



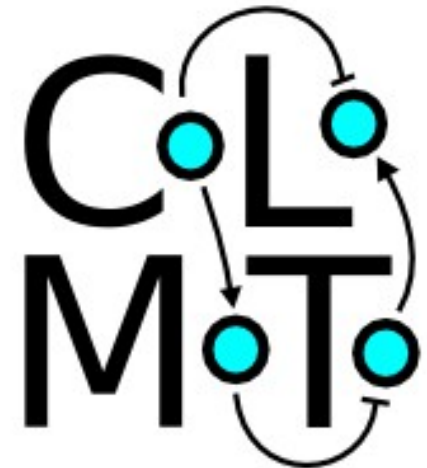
g1	g2	g3	g
0	0	0	0
0	0	1	1
0	1	0	0
0	1	1	0
1	0	0	1
1	0	1	1
1	1	0	0
1	1	1	0

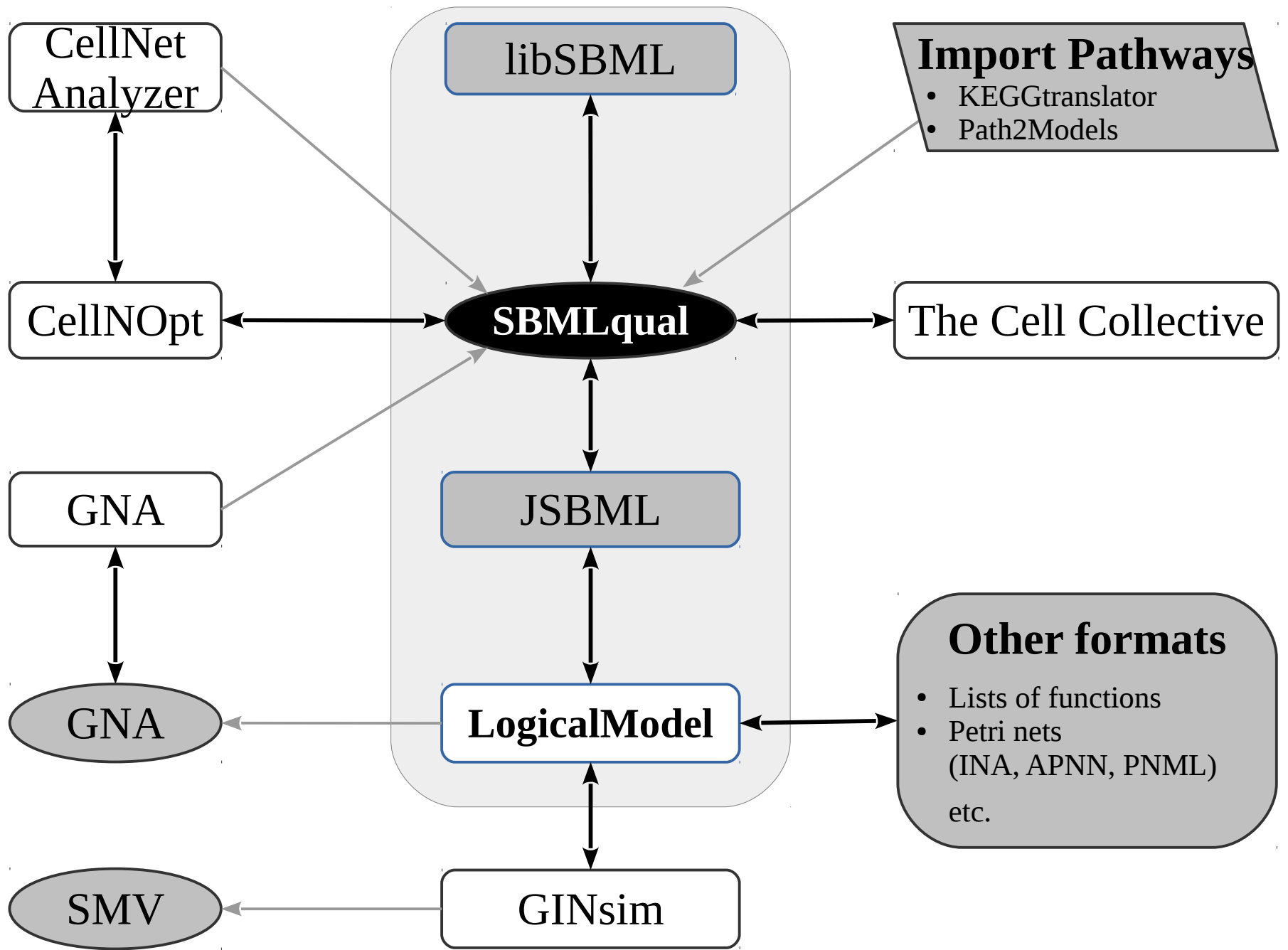


Petri net

CoLoMoTo: exchanging models

- SBML qual extension: common exchange format
- Conversion tool
 - Read/write SBML qual and a few simple formats
 - Write several other formats
 - Can be extended
- Existing tools
 - Write SBML qual



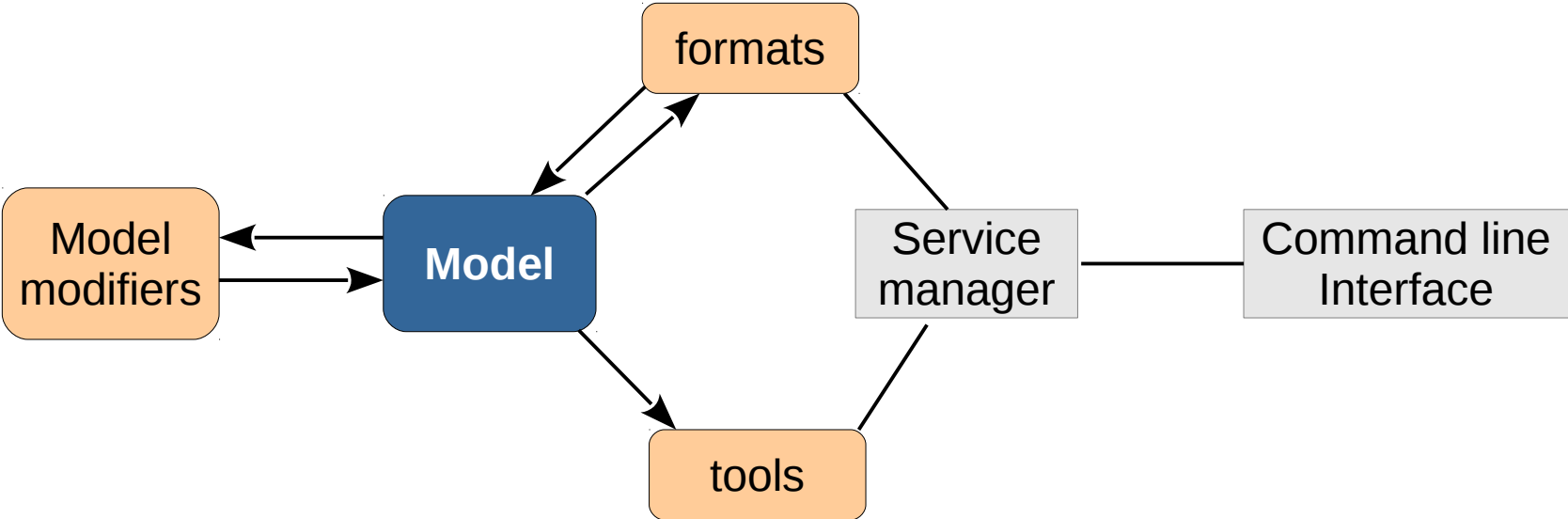


□ Tool

▭ Lib

○ Format

Organisation



Implemented

Model

Core and extra components
Multivalued Decision Diagrams

Model modifiers

Perturbations

Reduction
Output stripping

Formats

B <> boolsim
B <> Raw functions

M <> SBML qual

M > GINML

M > GNA

M > Petri net

M < Truth table

Tools

Stable state search

How to use?

As command-line tool

```
java -jar LogicalModel.jar model.sbml model.pnt  
-r stable model.sbml
```

- Search stable states
- Format conversion

As (Java) library

- GINsim (general qualitative modelling tool)
 - Data structure for simulation
 - Import/export backend (adds SBML layout markup)
 - Some tools backend (stable search, reduction)
- EpiLog (specialised for networks of epithelial cells)

Adding a format: minimal boilerplate

```
@ProviderFor(LogicalModelFormat.class)
public class YourFormat extends AbstractFormat {

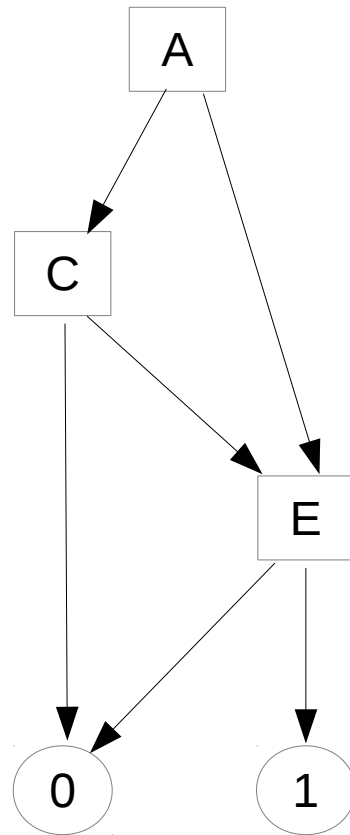
    public YourFormat() {
        super("extension", "your description", true);
    }

    @Override
    public void export(LogicalModel model, OutputStream out) throws IOException {
        new YourFormatWriter(model).export(out);
    }

    @Override
    public LogicalModel importFile(File f) throws IOException {
        Return new YourFormatImporter.import(f);
    }
}
```

Decision Diagrams (MDD)

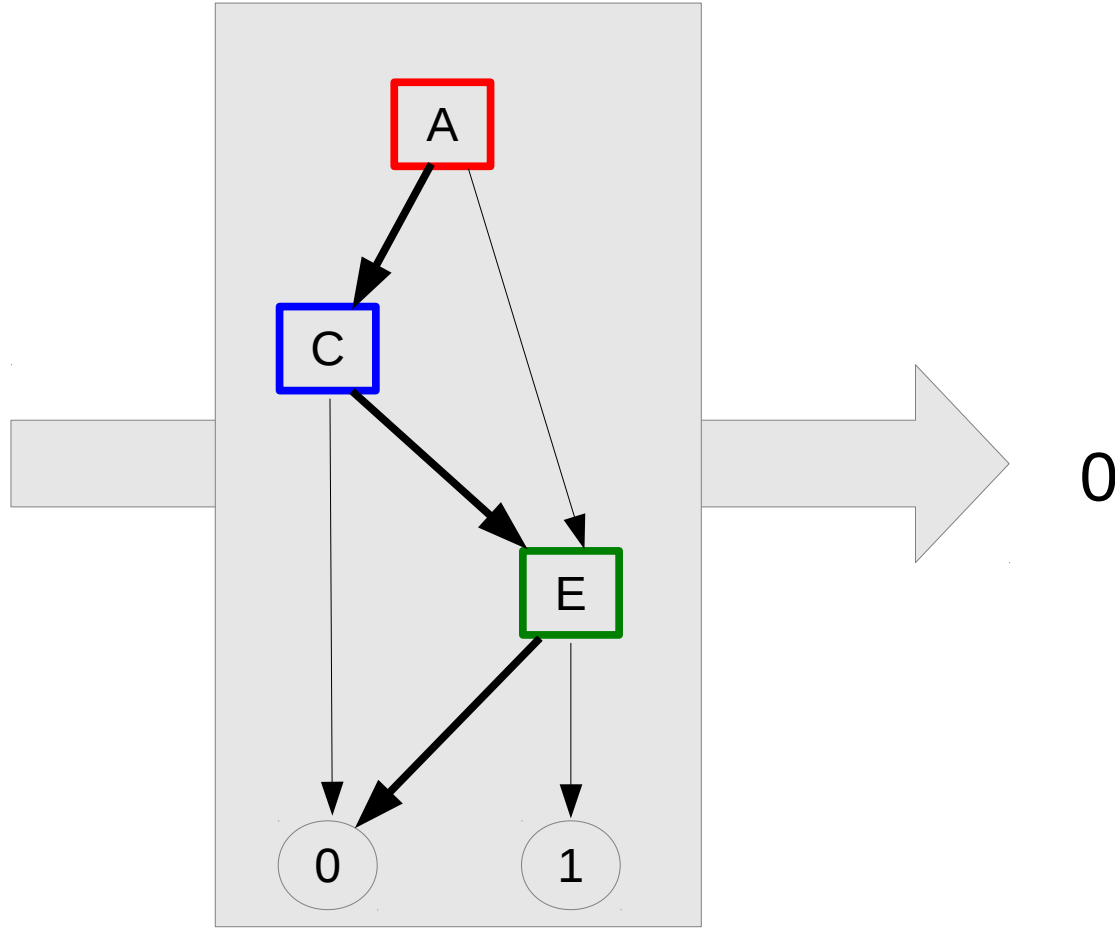
(A or C) and E



- A,B,C,D,E,F: ordered
- Fast (at most 6 tests, here 3)
- Predictable
- Picking order is hard

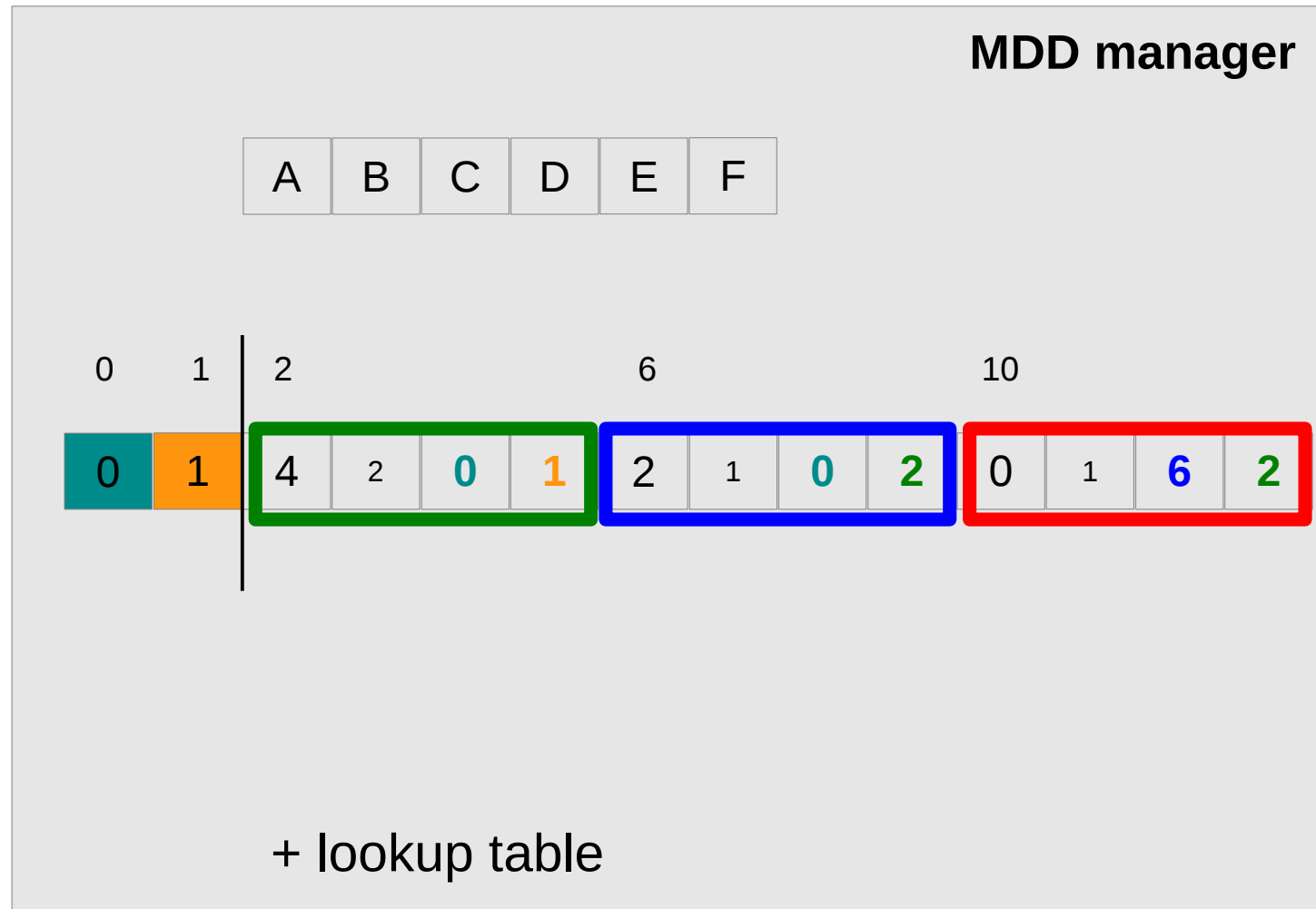
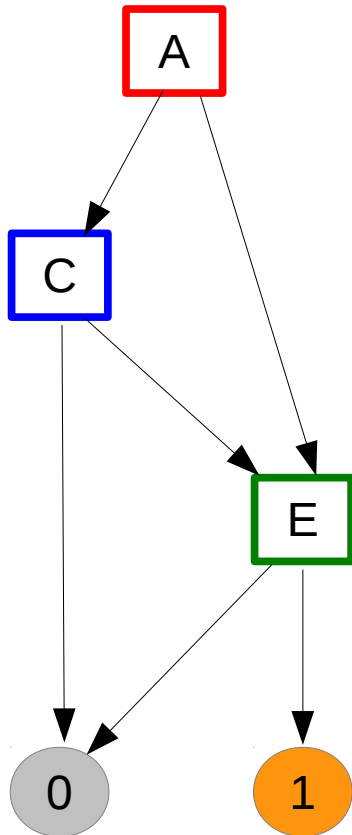
MDD query

A	0
B	1
C	1
D	1
E	0
F	0



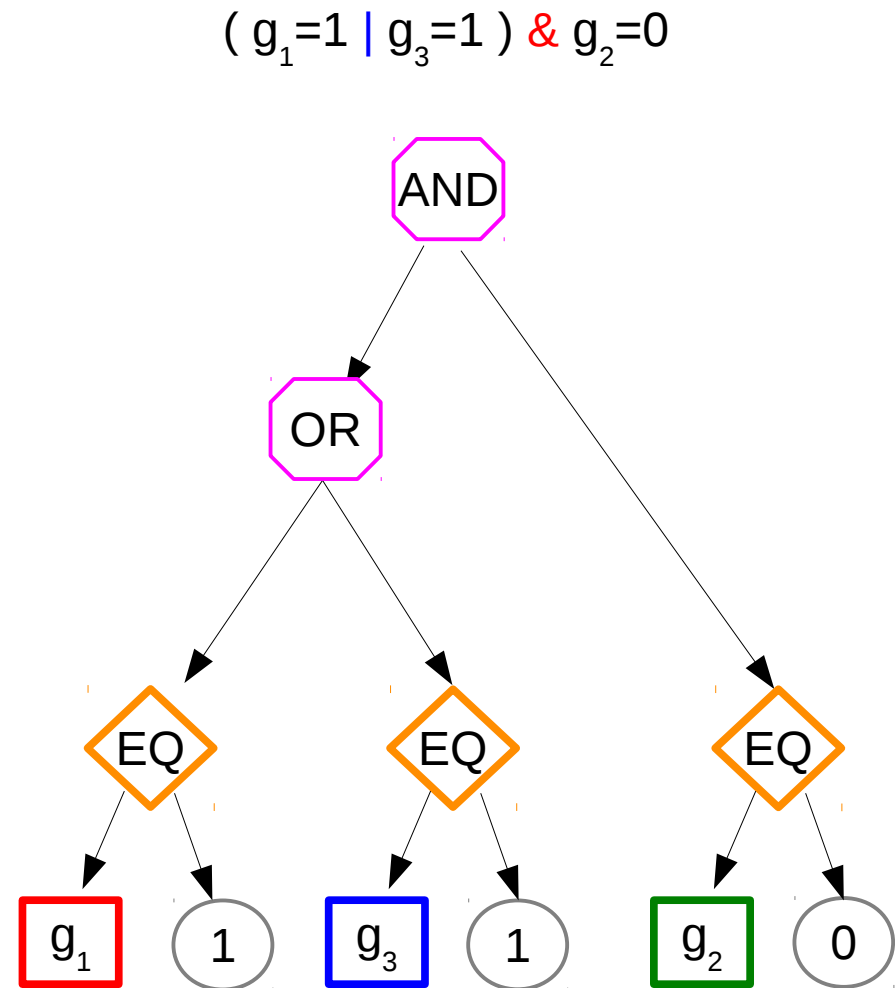
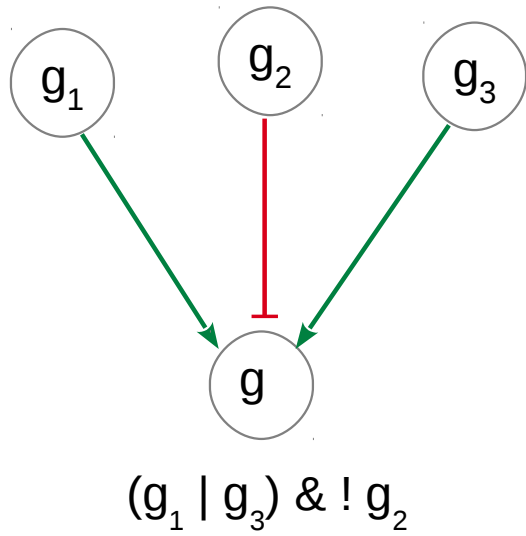
Decision Diagrams (MDD)

(A or C) and E

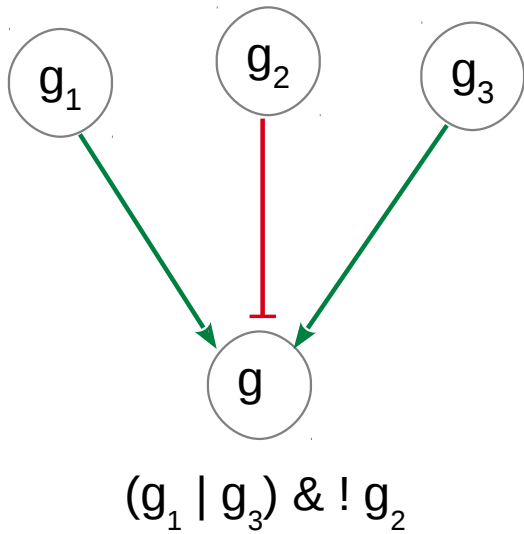


Multi-valued: some variables have more than two children

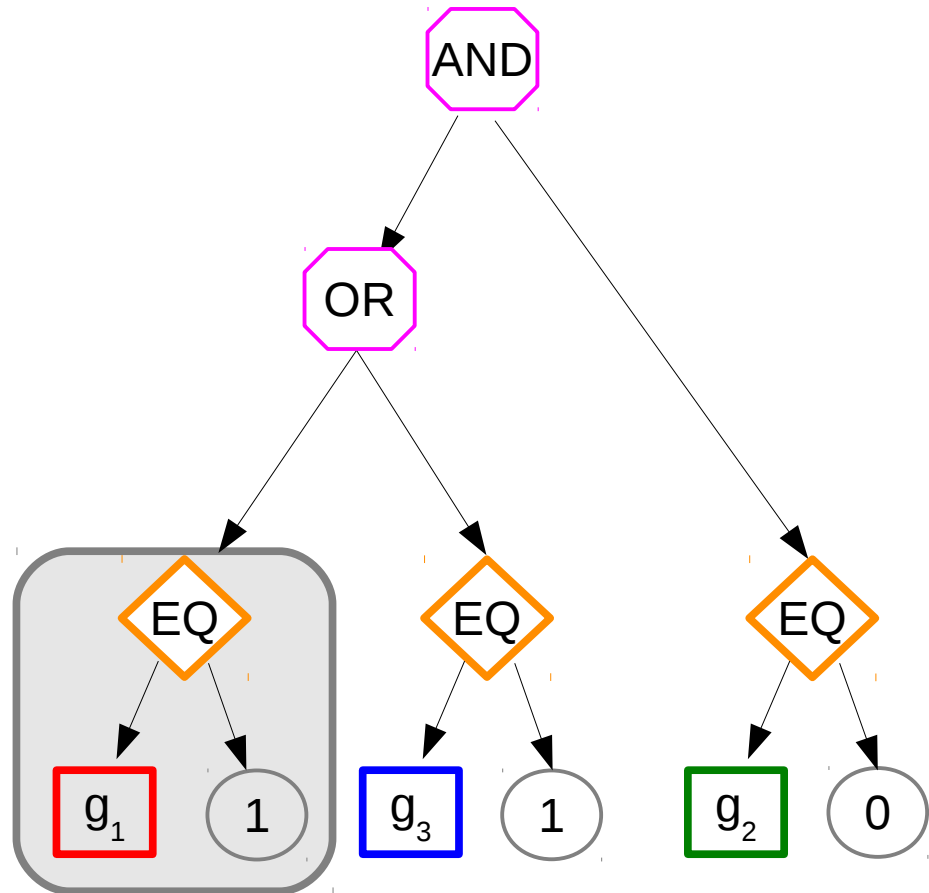
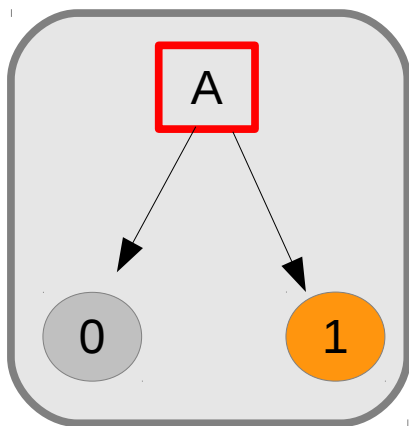
Functions in SBML-qual (and other)



Functions in SBML-qual (and other)



$$(g_1=1 | g_3=1) \& g_2=0$$



MDD manipulation for “OR”, “AND” operators

Helpers

Little MDDs knowledge required

- Extract list of regulators from function
- Iterate paths in the MDD
- Construct a function?

Iterate paths in a MDD

```
// input: LogicalModel model
MDDManager ddmanager = model.getMDDManager();
PathSearcher searcher = new PathSearcher(ddmanager);

for (int function: model.getLogicalFunctions()) {

    int[] path = searcher.setNode(functions[idx]);
    for (int leaf: searcher) {
        // leaf gives the value of the function
        // path gives the value of the components
    }
}
```

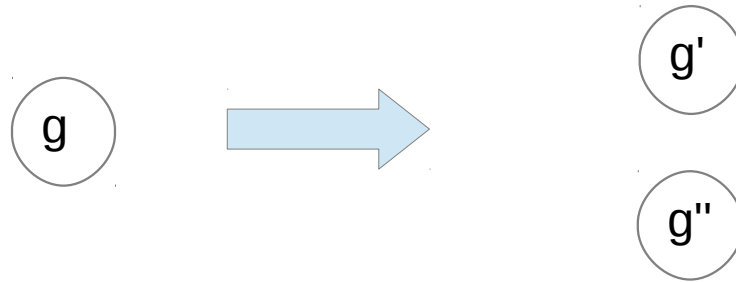
Future extensions

- Model modifiers
 - Transform multi-valued to Boolean
 - Perturbations
- Data
 - Documentation (SBML, GINML, JSON file)
 - Visual information (positions, styles?)
- Tools
 - state → successors: (a)synchronous, sequential

From multivalued to Boolean

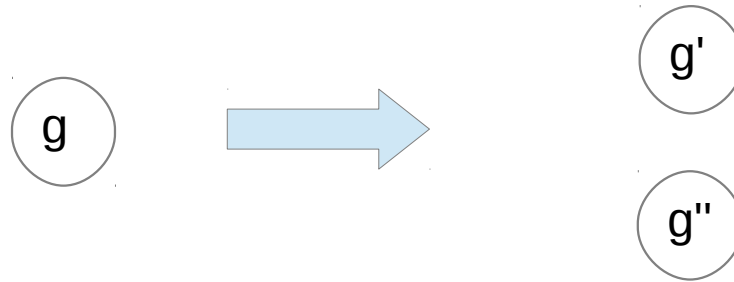
- Some tools support only Boolean models
- Multivalued models getting more common
- “Booleanize” a multivalued model when needed:
 - Multiply components
 - Rewrite functions

From multivalued to Boolean



g'	g''	g'''	g
0			0
1			1
0	1		2
1	1		3
0	0	1	4
1	0	1	5
0	1	1	6
1	1	1	7

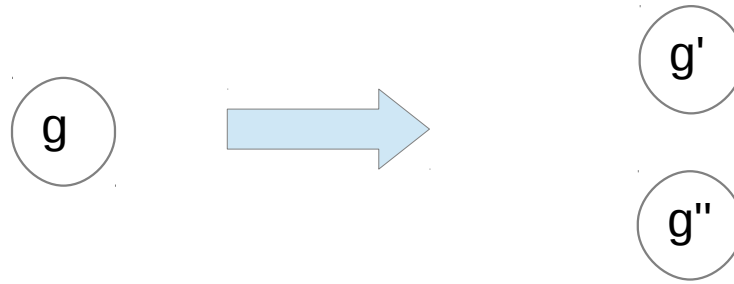
From multivalued to Boolean



g'	g''	g'''	g
0			0
1			1
0	1		2
1	1		3
0	0	1	4
1	0	1	5
0	1	1	6
1	1	1	7

g'	g''	g'''	g
0			0
1			1
1	1		2
0	1		3
0	1	1	4
1	1	1	5
1	0	1	6
0	0	1	7

From multivalued to Boolean



g'	g''	g'''	g
0			0
1			1
0	1		2
1	1		3
0	0	1	4
1	0	1	5
0	1	1	6
1	1	1	7

g'	g''	g'''	g
0			0
1			1
1	1		2
0	1		3
0	1	1	4
1	1	1	5
1	0	1	6
0	0	1	7

g'	g''	g'''	g''''	g
0				0
1				1
1	1			2
1	1	1		3
1	1	1	1	4

Perturbations

- Set the value: Knockout, Ectopic expression
- Restrict the function to a range
- Change the function
 - Explicitly: provide a new function
 - Semantic: Loss of a regulator
- Anything else?

Acknowledgements



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github.com/colomoto

