Model conversion, modification, and analysis with bioLQM

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History and Objectives

LogicalModel library started in 2013

- Format conversion to facilitate model exchange
- Motivated by the first CoLoMoTo meetings
- Some algorithmic code from **GINsim**

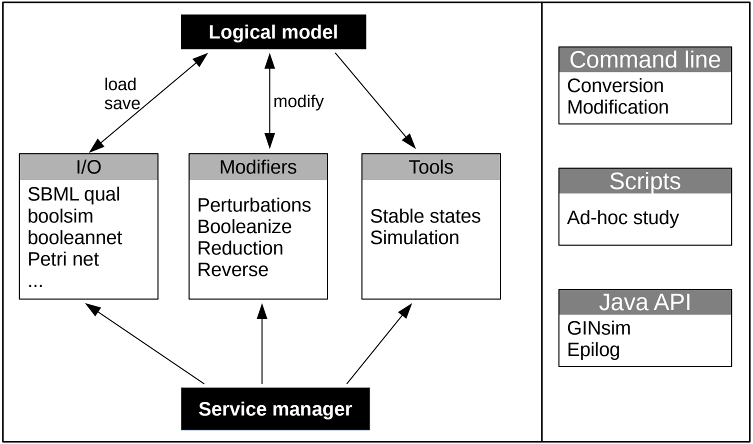
Current bioLQM status

- Multivalued logical models
- Import/Export filters
- Model modifications
- Model analysis

Facilitate novel developments and collaboration

Software Architecture

Use API interfaces and service discovery



Data Structure

- List of components (ID, max level)
- List of functions (currently as decision diagrams)

- Core vs extra components
- Infer signed interactions

Supported formats

MV	Import	Description		
x	x	SBML qual		C Chaouiya* et al. *BMC Syst Biol* (2013)
x	x	Truth table		
x		Pint		L. Paulevé et al. *Math Structures Comput Sci* (2012)
x		GINML		A Naldi et al. *Bio Systems* (2009)
x		GNA	✓	G. Batt et al. *Methods Mol. Biol.* (2012)
x		Petri Net		C Chaouiya et al. *Natural Computing* (2011)
	x	booleannet		I. Albert et al. *Source Code Biol Med* (2008)
	x	(Py)BoolNet	✓	C. Müssel et al. *Bioinformatics* (2010)
	x	BNS		E. Dubrova and M. Teslenko. *TCBB* (2011)
	x	BoolSim	✓	A. Garg et al. *Bioinformatics* (2008)
		MaBoSS		G. Stoll et al. *BMC Syst Biol* (2012)

✓Direct SBML qual support

Some other tools

See http://colomoto.org/software/

- The Cell Collective
  Web-based plateform for the construction and simulation of Boolean models

- CellNOpt
  Model optimisation and training

- CellNetAnalyzer
  MATLAB GUI, cut sets, intervention sets

Model modifiers

Model + settings → modified model

Perturbation

- Fixed value (KO, ectopic) G1%0
- Range restriction (Multivalued) G1%1:2
- Regulator perturbation (remove or enforce) G1:G2%1

Model Reduction

Reduce selected components, propagate fixed, eliminate duplicates

A Naldi et al. *Theor Comput Sci* (2011)

Booleanization

Map multivalued components on multiple Boolean ones

G. Didier et al. *Journal of Theoretical Biology* (2011)

Model analysis

Simulation

Deterministic (synchronous), non-deterministic (asynchronous), stochastic updaters

Stable states

Constraint solving: all components are stable

A Naldi et al. *CMSB (2007)*

Trap spaces

Identify stable sets of prime implicants using ASP

H Klarner et al. *Cellular Automata (2014)*

Command line use

- Load a model
- Apply modifier(s)
- Save (convert) or run analysis

```
java -jar bioLQM.jar model.sbml model.boolsim
```

```
java -jar bioLQM.jar model.sbml -p MAPK%1 -r stable
```

Scripting

```
bioLQM.jar -s generate_perturbations.js model.sbml
```

```
name  = lqm.args[0]
model = lqm.load(name)
nodes = model.getComponents()
for (i in nodes) {
  node = nodes[i]
  perturbed = lqm.modify(model, ’perturbation’, node+’%0’)
  lqm.save(perturbed, name+’_’+node+’.net’, ’boolsim’)
}
```

Embding

- Java library, available through Maven
- Currently used by GINsim and Epilog

```
<repository>
   <id>ginsim_snapshot</id>
   <snapshots><enabled>true</enabled></snapshots>
   <releases><enabled>false</enabled></releases>
   <name>GINsim snapshot repository</name>
   <url>http://ginsim.org/maven/snapshot</url>
</repository>
[...]
<dependency>
  <groupId>org.colomoto</groupId>
  <artifactId>bioLQM</artifactId>
  <version>0.4-SNAPSHOT</version>
</dependency>
```

Perspectives

- Manipulate functions explicitely instead of decision diagrams
  - Closer to the original model
  - Associate different rates to sub-functions
- Do something with SBML annotations
  - JSON representation useful?
- Better integrate native tools: clingo, NuSMV, boolsim
- Part of a future "CoLoMoTo" distribution (docker, conda env) ?
- Interactive use: jupyter notebook
  - Java notebook, separate calls, custom IPC?