Standards for logical models: current status of SBML qual & SED-ML

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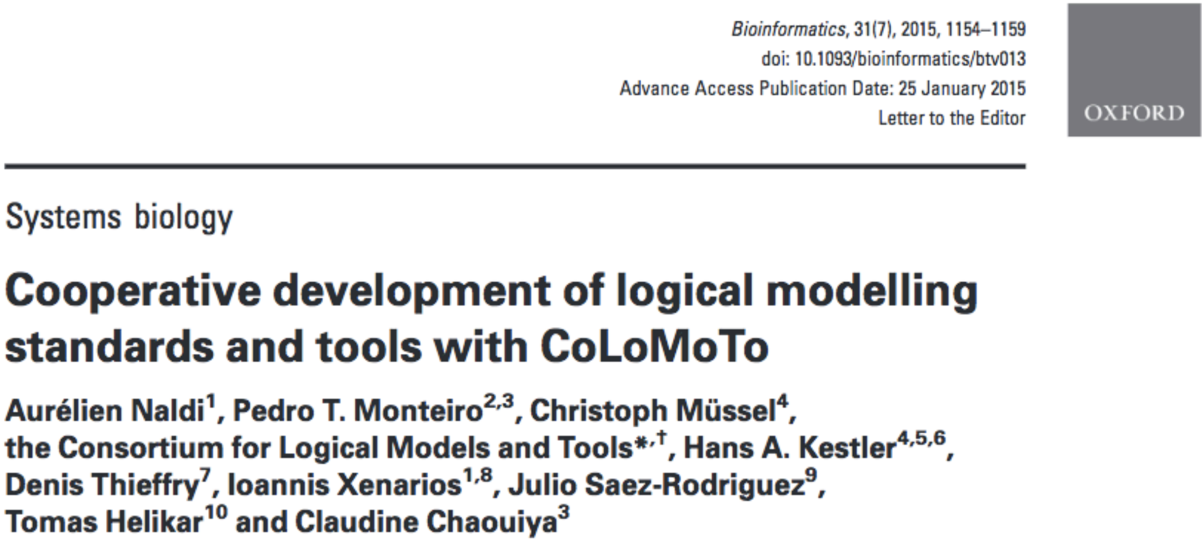
Network
Modelling

Standard formats for logical models

Motivation

- Ease model storing, exchange, maintenance, extension, etc.
- Ensure result reproducibility
- Strengthen the community, increase awareness



Bioinformatics, 31(7), 2015, 1154–1159
doi: 10.1093/bioinformatics/btv013
Advance Access Publication Date: 25 January 2015
Letter to the Editor

OXFORD

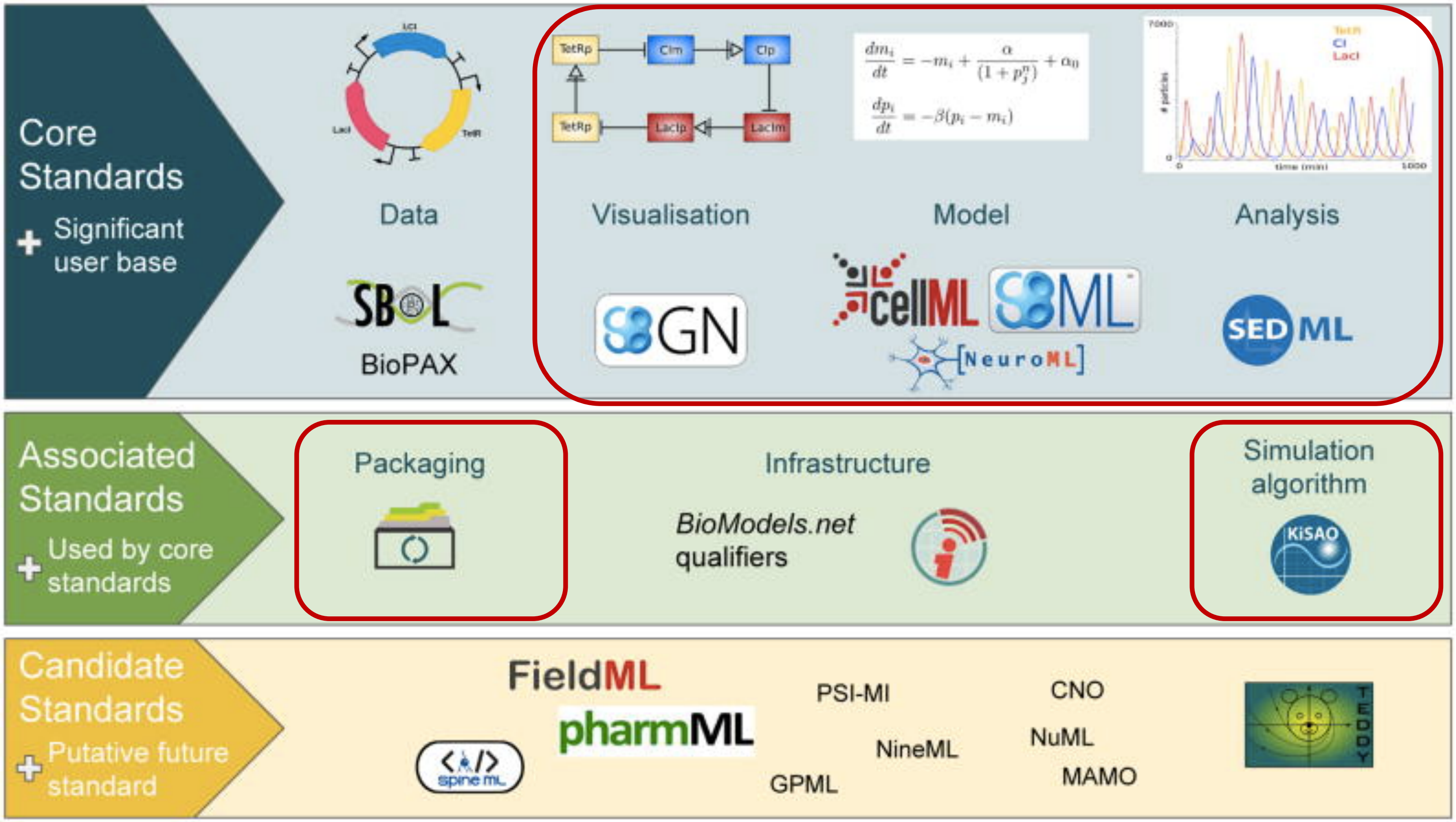
Systems biology

Cooperative development of logical modelling standards and tools with CoLoMoTo

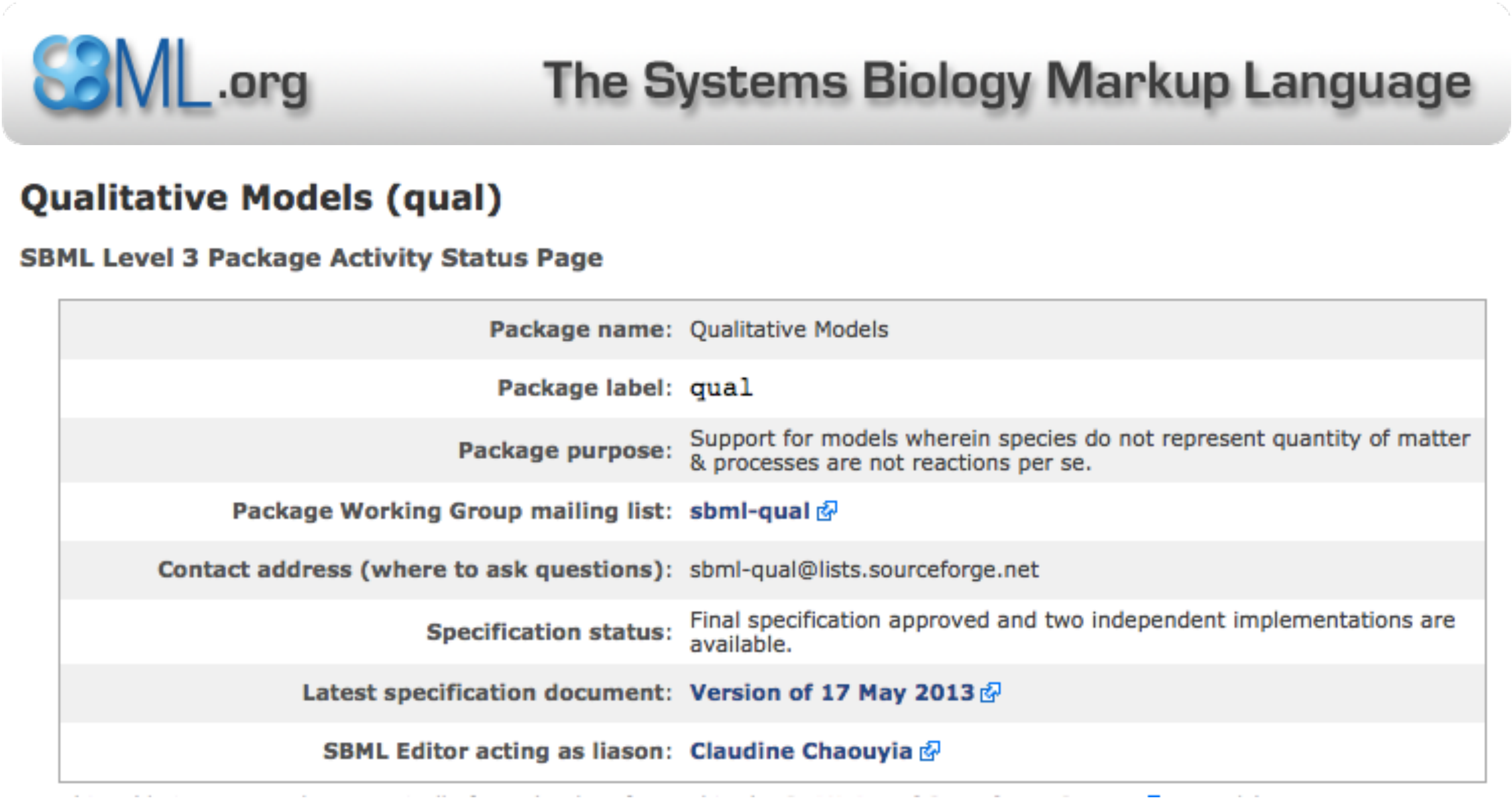
Aurélien Naldi[1], Pedro T. Monteiro[2,3], Christoph Müssel[4], the Consortium for Logical Models and Tools[*,†], Hans A. Kestler[4,5,6], Denis Thieffry[7], Ioannis Xenarios[1,8], Julio Saez-Rodriguez[9], Tomas Helikar[10] and Claudine Chaouiya[3]

COMBINE standards and associated standardisation efforts

From Schreiber F et al. (2016) J Integr Bioinform. 13(3):289.



SBML qual, standard for model exchange

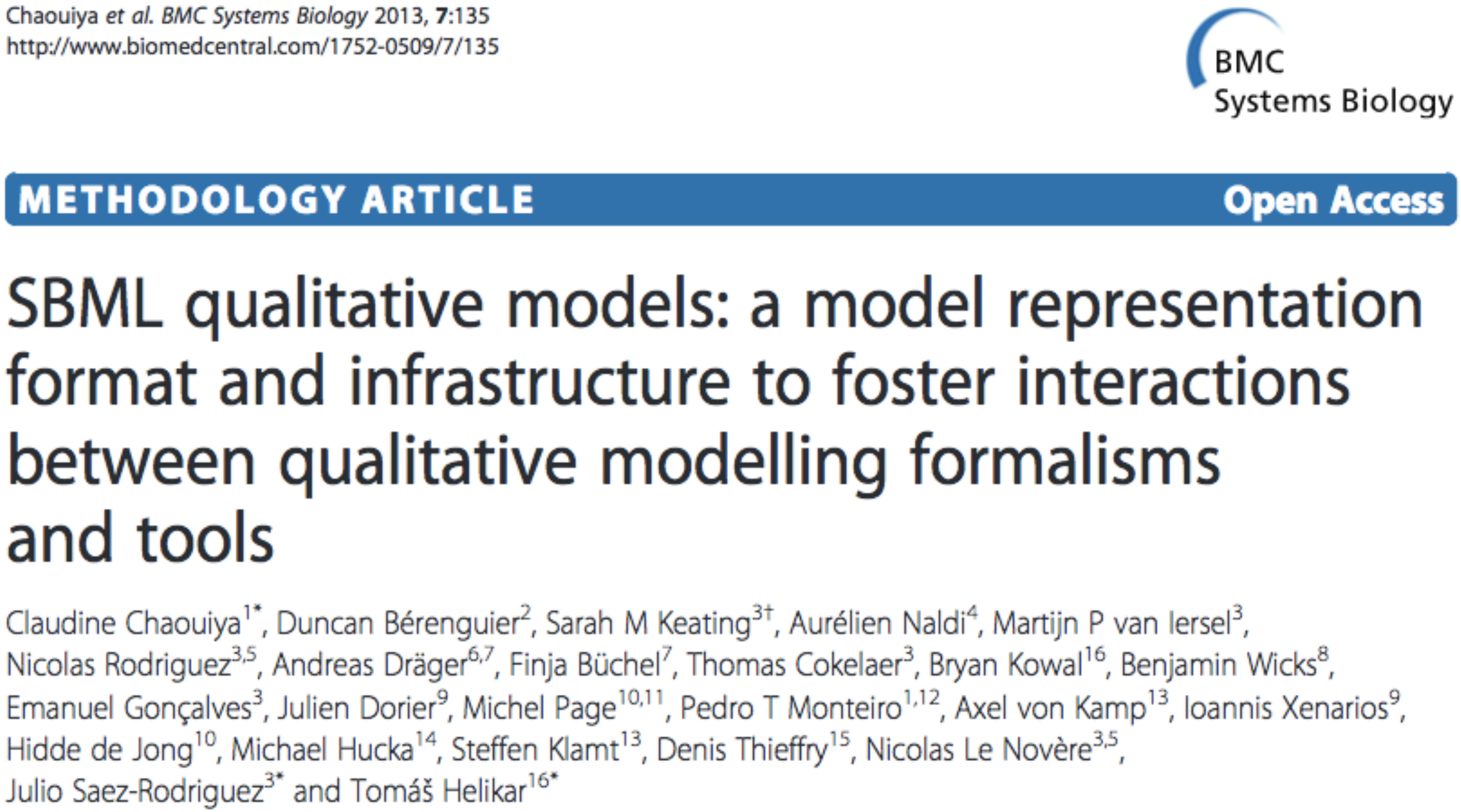


SBML.org The Systems Biology Markup Language

Qualitative Models (qual)

SBML Level 3 Package Activity Status Page

Package name:	Qualitative Models
Package label:	`qual`
Package purpose:	Support for models wherein species do not represent quantity of matter & processes are not reactions per se.
Package Working Group mailing list:	**sbml-qual**
Contact address (where to ask questions):	sbml-qual@lists.sourceforge.net
Specification status:	Final specification approved and two independent implementations are available.
Latest specification document:	**Version of 17 May 2013**
SBML Editor acting as liason:	**Claudine Chaouyia**



Chaouiya *et al. BMC Systems Biology* 2013, **7**:135
http://www.biomedcentral.com/1752-0509/7/135

METHODOLOGY ARTICLE **Open Access**

SBML qualitative models: a model representation format and infrastructure to foster interactions between qualitative modelling formalisms and tools

Claudine Chaouiya[1*], Duncan Bérenguier[2], Sarah M Keating[3†], Aurélien Naldi[4], Martijn P van Iersel[3], Nicolas Rodriguez[3,5], Andreas Dräger[6,7], Finja Büchel[7], Thomas Cokelaer[3], Bryan Kowal[16], Benjamin Wicks[8], Emanuel Gonçalves[3], Julien Dorier[9], Michel Page[10,11], Pedro T Monteiro[1,12], Axel von Kamp[13], Ioannis Xenarios[9], Hidde de Jong[10], Michael Hucka[14], Steffen Klamt[13], Denis Thieffry[15], Nicolas Le Novère[3,5], Julio Saez-Rodriguez[3*] and Tomáš Helikar[16*]

SBML qual, standard for model exchange

Supports the definition of

- Boolean & multi-valued models
- Input components (constant values?)
- One initial state

Supported by

- JSBML, Java API library for parsing and writing SBML files and for in-memory manipulation of SBML data structures
- **bioLQM**, interoperability between logical modeling tools
- BoolNet, BoolSim, GINsim, the Cell Collective, EpiLog
- Model repositories: BioModels, Cell Collective, GINsim

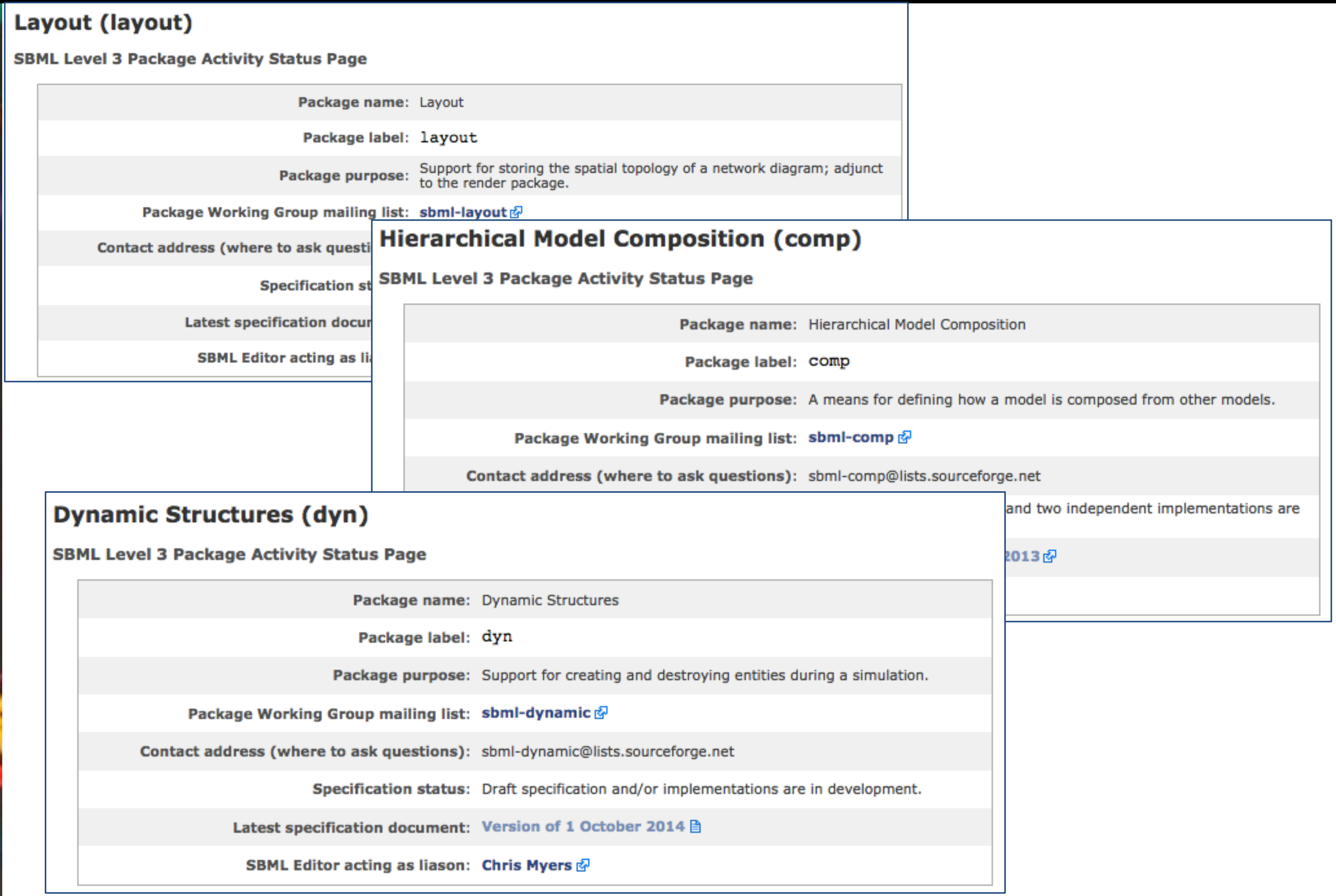
Need f/ update

Future extensions

- Incomplete models (rules not (all) instantiated),
- Timing constraints (priorities or rates) → see SED-ML?
- Probabilistic models (≠ variants)

Consideration of other SBML packages (e.g. layout, comp & dyn)

SBML qual, standard for model exchange



Layout (layout)

SBML Level 3 Package Activity Status Page

Package name:	Layout
Package label:	`layout`
Package purpose:	Support for storing the spatial topology of a network diagram; adjunct to the render package.
Package Working Group mailing list:	**sbml-layout**
Contact address (where to ask questi	
Specification st	
Latest specification docur	
SBML Editor acting as lia	

Hierarchical Model Composition (comp)

SBML Level 3 Package Activity Status Page

Package name:	Hierarchical Model Composition
Package label:	`comp`
Package purpose:	A means for defining how a model is composed from other models.
Package Working Group mailing list:	**sbml-comp**
Contact address (where to ask questions):	sbml-comp@lists.sourceforge.net
	and two independent implementations are
	2013

Dynamic Structures (dyn)

SBML Level 3 Package Activity Status Page

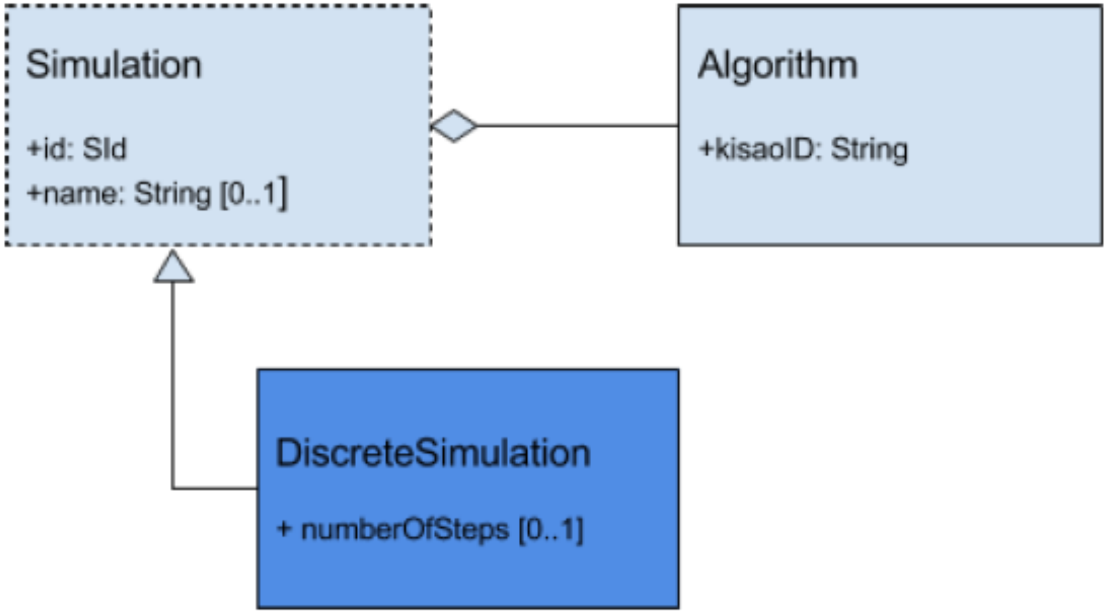
Package name:	Dynamic Structures
Package label:	`dyn`
Package purpose:	Support for creating and destroying entities during a simulation.
Package Working Group mailing list:	**sbml-dynamic**
Contact address (where to ask questions):	sbml-dynamic@lists.sourceforge.net
Specification status:	Draft specification and/or implementations are in development.
Latest specification document:	**Version of 1 October 2014**
SBML Editor acting as liason:	**Chris Myers**

Proposal for an extension of SED-ML

SED ML Simulation Experiment Description Markup Language

→ Draft version 2 (June 2016)

- Definition of simulation settings for logical models, using the SED-ML
- Adoption of the kinetic simulation algorithm ontology (KiSAO) to describe the algorithms, their parameters and relationships


Simulation

+id: SId

+name: String [0..1]

Algorithm

+kisaoID: String

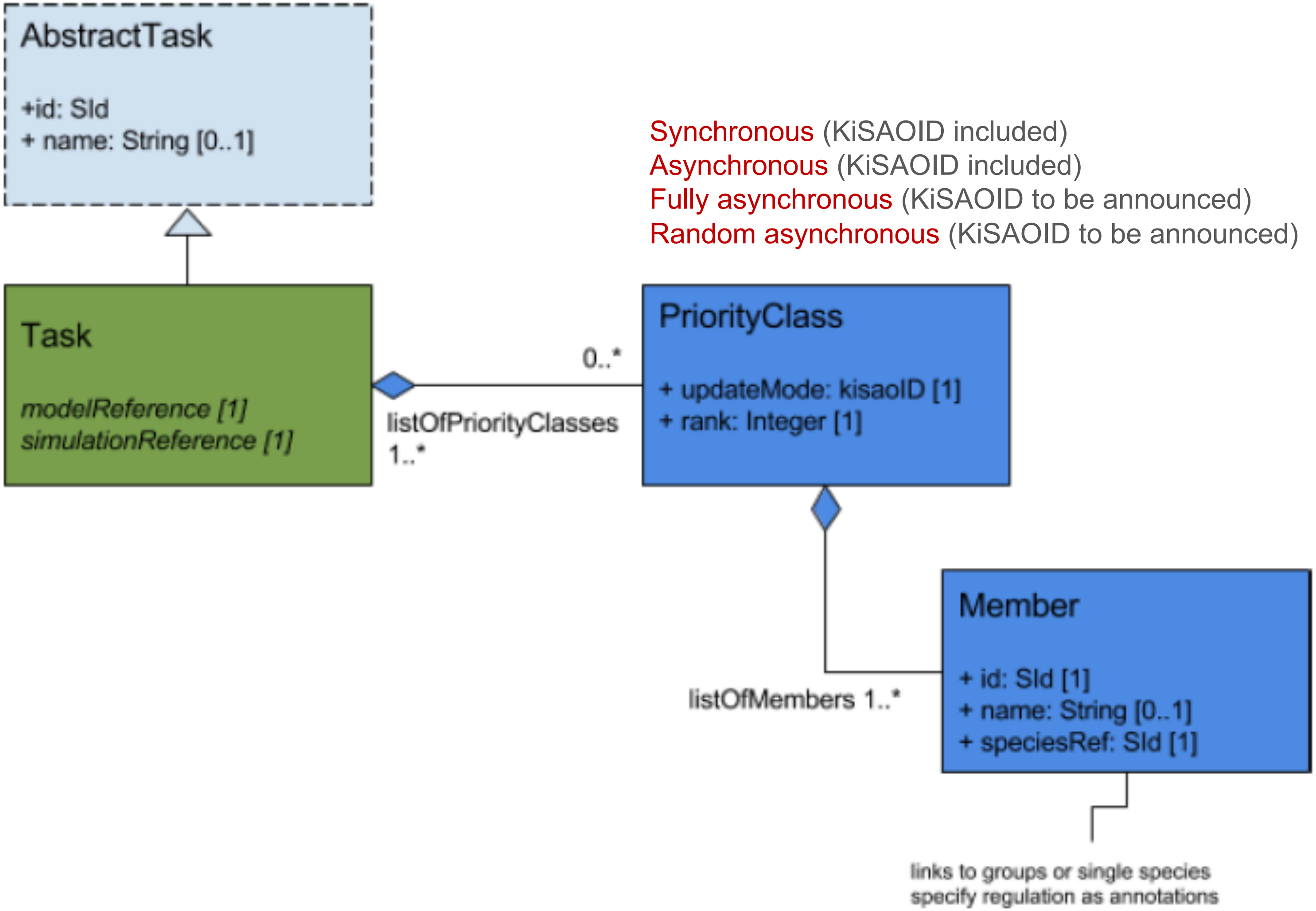
DiscreteSimulation

+ numberOfSteps [0..1]

Figure 1: DiscreteSimulation as a specialisation of the abstract Simulation class.

Proposal for an extension of SED-ML

→ Draft version 2 (June 2016)



AbstractTask

+id: SId
+ name: String [0..1]

Task

modelReference [1]
simulationReference [1]

PriorityClass

+ updateMode: kisaoID [1]
+ rank: Integer [1]

Member

+ id: SId [1]
+ name: String [0..1]
+ speciesRef: SId [1]

Synchronous (KiSAOID included)
Asynchronous (KiSAOID included)
Fully asynchronous (KiSAOID to be announced)
Random asynchronous (KiSAOID to be announced)

links to groups or single species
specify regulation as annotations

Figure 2: PriorityClass class and Member class

Proposal for an extension of SED-ML

→ Draft version 2 (June 2016)

Production of the results in terms of STG

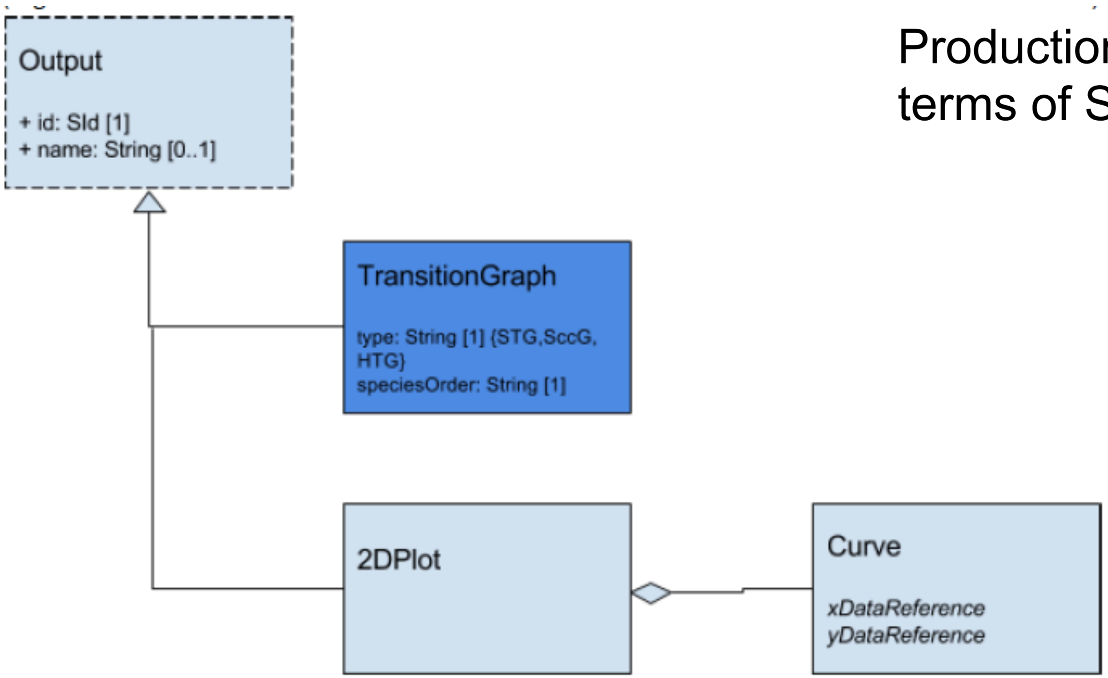


Figure 3: DynamicProfile and TransitionGraph classes

Proposal for an extension of SED-ML

→ Draft version 2 (June 2016)

Use of existing SEDML concepts for

1. Changes to the model (preprocessing)
    - Initial state(s)
    - Mutants

2. Output types
    - Dynamic profiles (tabular displays of species behaviours, e.g lists of values of the (selected) species over time)
    - Curves (2D plots)

Proposal for an extension of SED-ML

Kinetic Simulation Algorithm Ontology

- modelling and simulation algorithm
  - Bayesian inference algorithm
  - CVODE-like method
  - discrete event simulation algorithm
  - hard-particle molecular dynamics
  - hybrid method
  - iterative method for linear system
  - KLU
  - Lagrangian sliding fluid element algorithm
  - Livermore solver
  - **logical model simulation method**
    - asynchronous logical model simulation method
    - synchronous logical model simulation method
  - metamodelling method
  - Monte Carlo method
    - first-passage Monte Carlo algorithm
    - Gillespie-like method
    - Metropolis Monte Carlo algorithm
  - multistep method
  - Newton-type method

Preferred Name	logical model simulation method
Definitions	Qualitative (logical) models specify the evolution rules of their components. In each state a number of transitions are enabled. A 'logical model simulation method' guides the choice of the transitions processed at each step.
ID	http://www.biomodels.net/kisao/KISAO#KISAO_0000448
created	2013-01-28
creator	AZ
definition	Qualitative (logical) models specify the evolution rules of their components. In each state a number of transitions are enabled. A 'logical model simulation method' guides the choice of the transitions processed at each step.
label	logical model simulation method

→ Inclusion of new terms in KiSAO

Proposal for an extension of SED-ML

Points to be discussed, e.g.

Status of time (SBML?)

- Iterations / discrete time / continuous time

Scope of the simulation(SED-ML)

- Number of steps, of visited states?
- Exploration breadth / depth?

Update modes (SED-ML)

- Synchronous / asynchronous and its variants
- Priorities (SBML?)
- Rates or probabilities (SBML?)
- Variations of input components (*à la* Cell Collective)

Outputs and reports

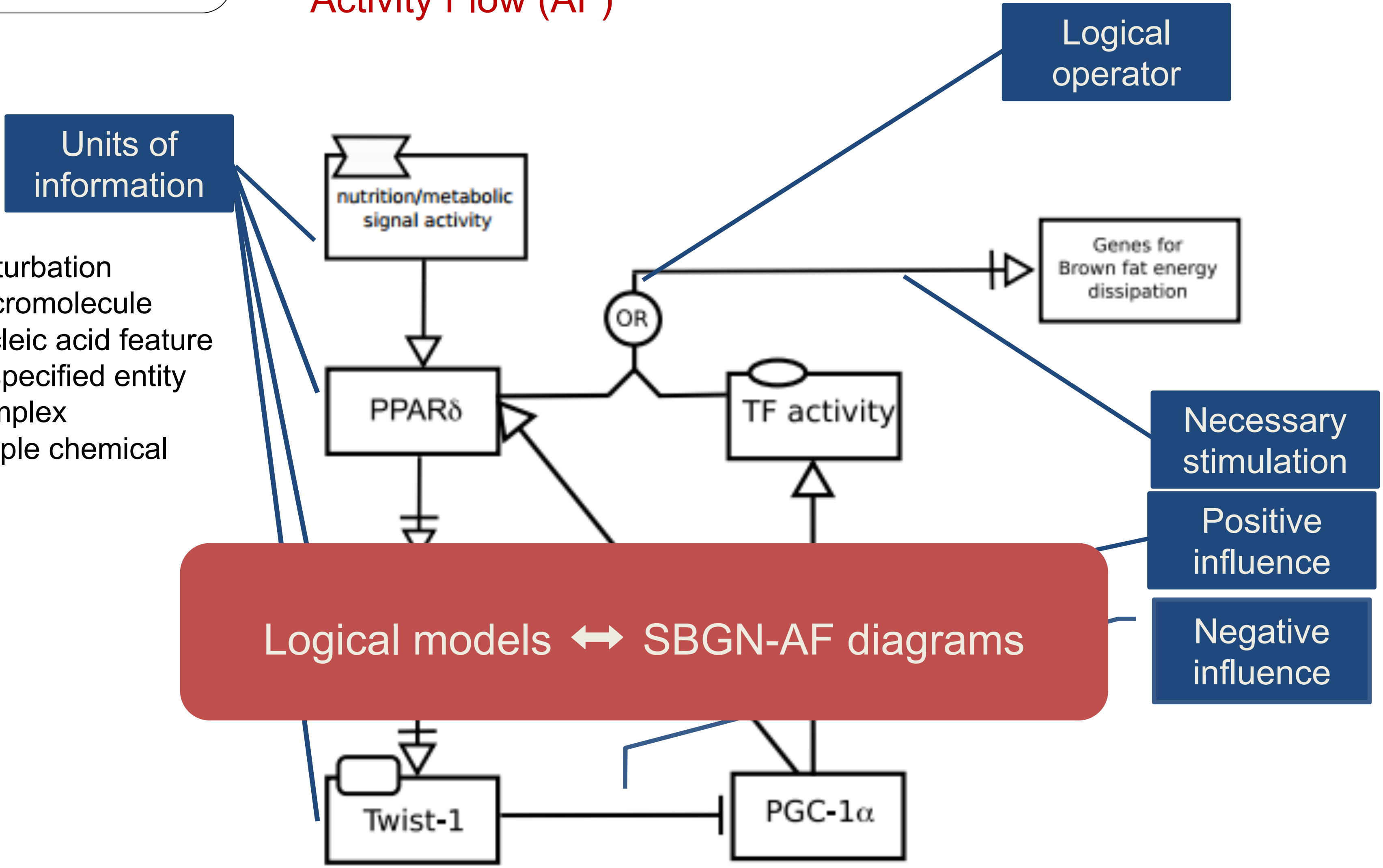
- Other types of display?
- Labels on transitions?

- At least two implementations in applications (to demonstrate interoperability)
- updated examples
- A written description of the proposal

Systems Biology Graphical Notation

SBGN

Process Description (PD),
Entity Relationship (ER),
Activity Flow (AF)



Logical operator

Units of information

Perturbation
Macromolecule
Nucleic acid feature
Unspecified entity
Complex
Simple chemical

Necessary stimulation

Positive influence

Negative influence

Logical models ↔ SBGN-AF diagrams

COMBINE archive format

A *COMBINE archive* is a single file containing the various documents (and in the future, references to documents), necessary for the description of a model and all associated data and procedure, e.g.

- simulation experiment descriptions
- all models needed to run the simulations
- associated data files

The archive is encoded using the Open Modeling EXchange format (OMEX).

Discussion

- Extended scope of logical modelling (e.g. model families, fuzzy logic, etc.)
- Are timing constraints (delays, rates, probabilities, priorities, etc.) part of a model?
- Are specifications of input behaviours part of a model?
- What types of model perturbations may be considered?

Standardisation is a collective effort!

http://co.mbine.org/events/COMBINE_2017

COMBINE 2017

Dates: ***9-13 October 2017***
Location: ***Milan, ITALY***

The COMBINE 2017 Meeting will take place in Milan, Italy, from October 9th to October 13th at the Università degli Studi di Milano Bicocca.

Stay tuned for more information coming soon.

The "Computational Modeling in Biology" Network (COMBINE) is an initiative to coordinate the development of the various community standards and formats in systems biology and related fields. COMBINE 2017 will be a workshop-style event with oral presentations, posters, and breakout sessions. The five meeting days will include talks about the COMBINE standards and associated or related standardization efforts, as well as presentations of tools using these standards. Oral presentations will be selected from the submitted abstracts. In addition, poster sessions will allow people to inform each other about their software and other projects in a setting that fosters interaction and in-depth discussion.

If you have any questions, please contact <marco.antoniotti [.at.] unimib.it>

Deadline for abstracts August 01

Acknowledgements

The CoLoMoTo members!

D Bérenguier, **SM Keating**, **A Naldi**, **MP van Iersel**, N Rodriguez, A Dräger, F Büchel, T Cokelaer, B Kowal, B Wicks, E Gonçalves, J Dorier, M Page, PT Monteiro, A von Kamp, I Xenarios, H de Jong, M Hucka, S Klamt, **D Thieffry**, **N Le Novère**, J Saez-Rodriguez, **T Helikar**

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