

SBML in 2016

Sarah Keating
... on behalf of many



SBML

1. Why ?

Brief introduction to SBML

2. Development of SBML

Level 1 -> Level 2 -> Level 3

3. SBML Level 3 and L3 packages

Current status

4. SBML Process

Organisation – Editors - Team

5. Supporting SBML

Software infrastructure available

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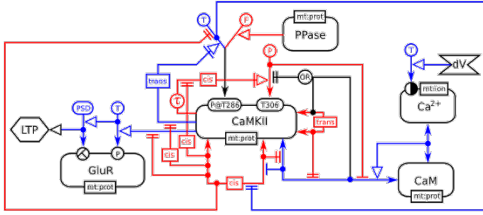
Organisation – Editors - Team

5. Supporting SBML

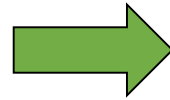
Software infrastructure available

Why standards ?

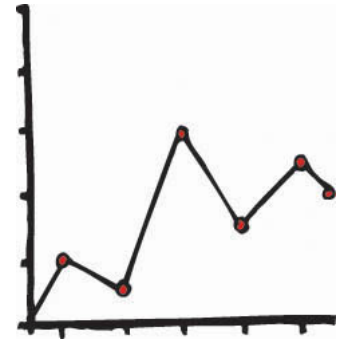
In the beginning ...



My model



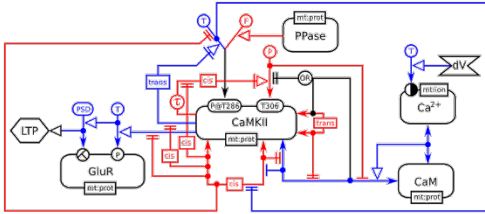
My software



My results

Why standards ?

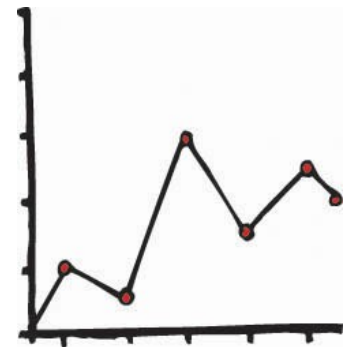
Ideally ...



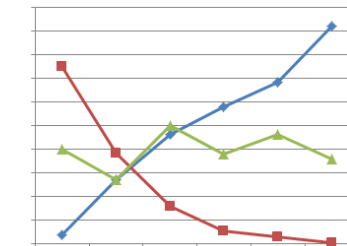
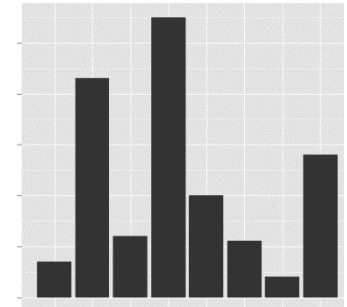
My model



Many tools



My results



Additional results



Many users



Why standards ?

Goal: reproducible and reusable models and simulations

- Need to capture both
 - **Mathematical** content
 - **Semantic** content
- Need a **software-independent** format
 - Different packages have different strengths
 - Strengths are often complementary

Overview of SBML

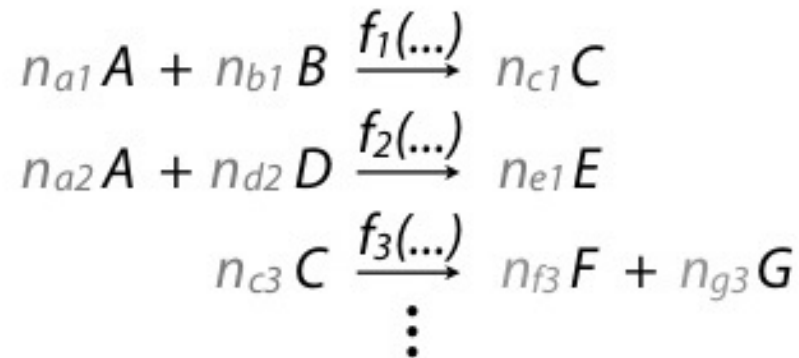
- A machine-readable format
- Tool-neutral exchange language
- Independent of modelling formalism
- Declares model not procedure
- Expressed in XML

Overview of SBML

Participants: 'species' – pools of entities of the same kind

Location: 'compartment' – container of well stirred mix

Process: 'reaction' – not necessarily biochemical



Overview of SBML

- Explicit math
- Explicit units
- Annotation on every element

X Does not store
simulation description

X Does not store
experimental data

Overview of SBML

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- Explicit units
- Annotation on every element

X Does not store
simulation description

X Does not store
experimental data



Other
standards
do

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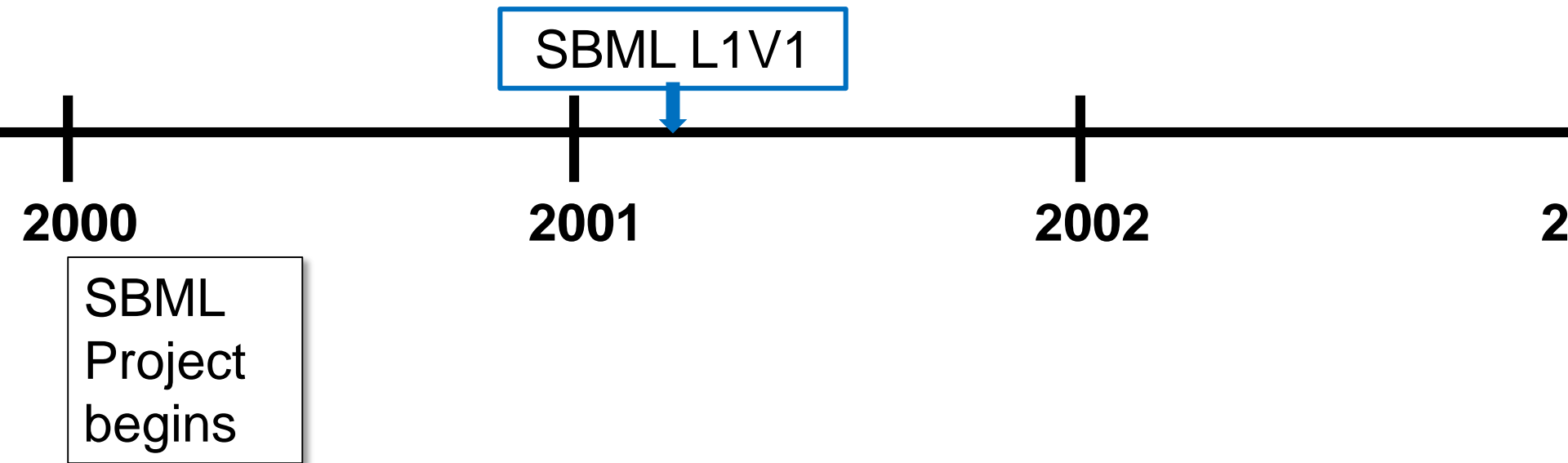
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Organisation – Editors - Team

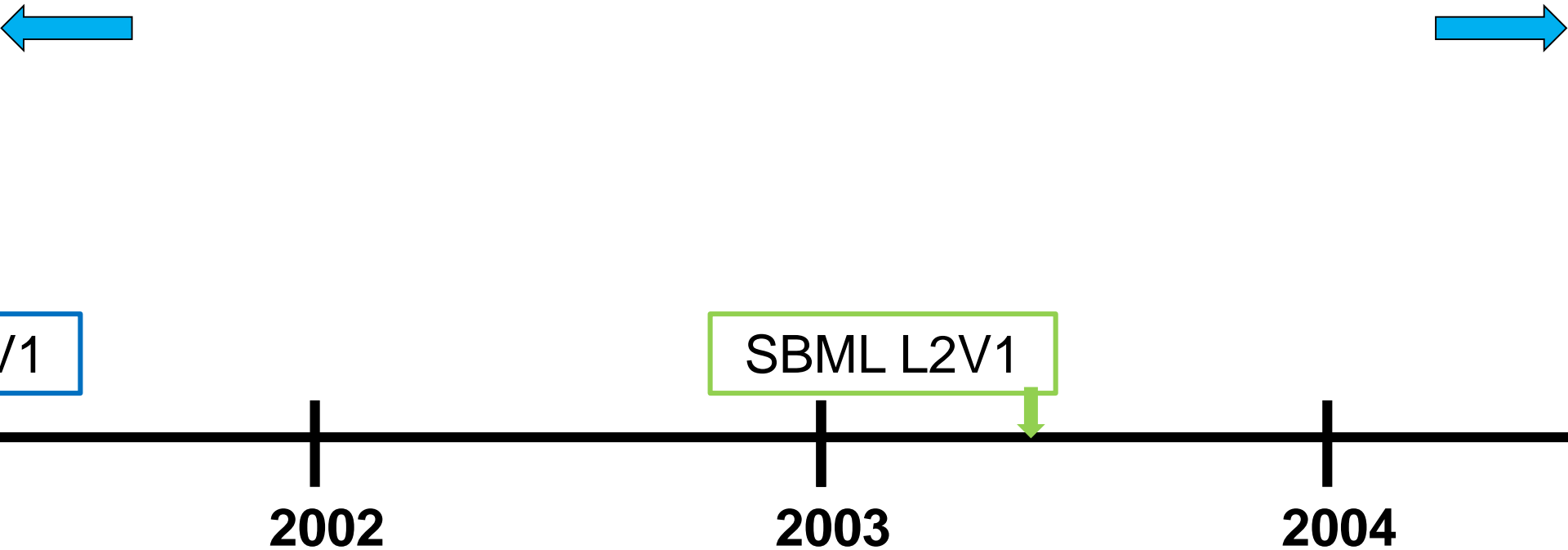
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Software infrastructure available

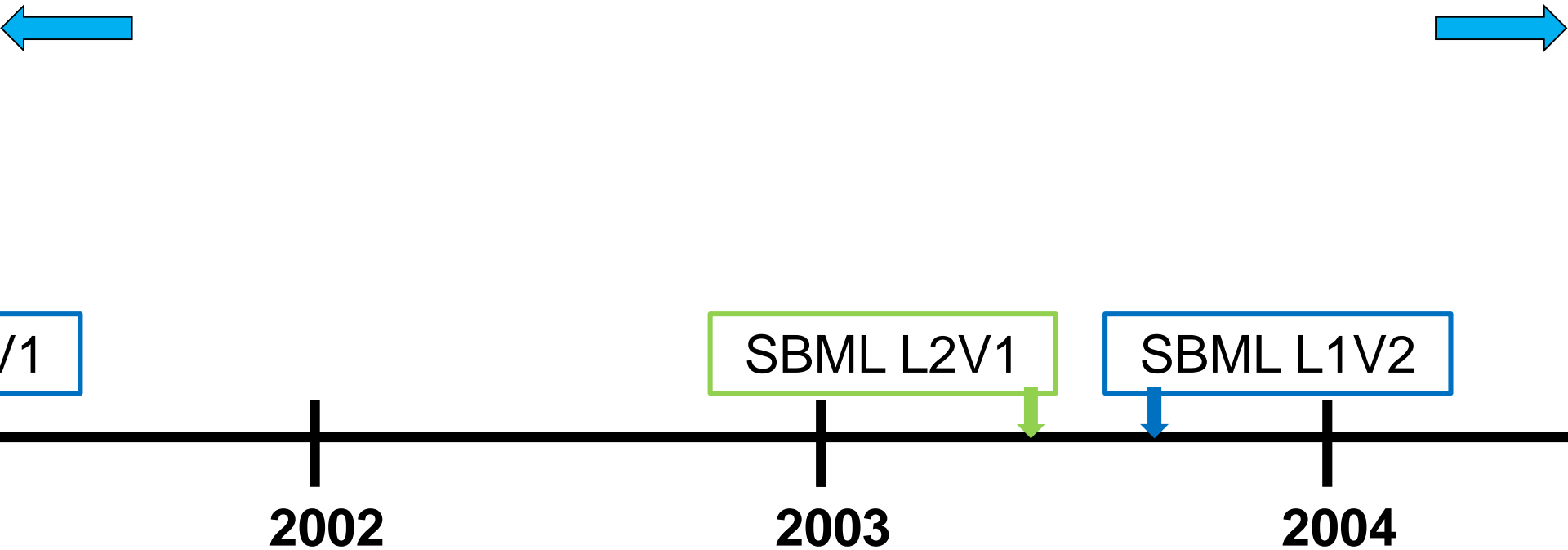
Evolution of SBML



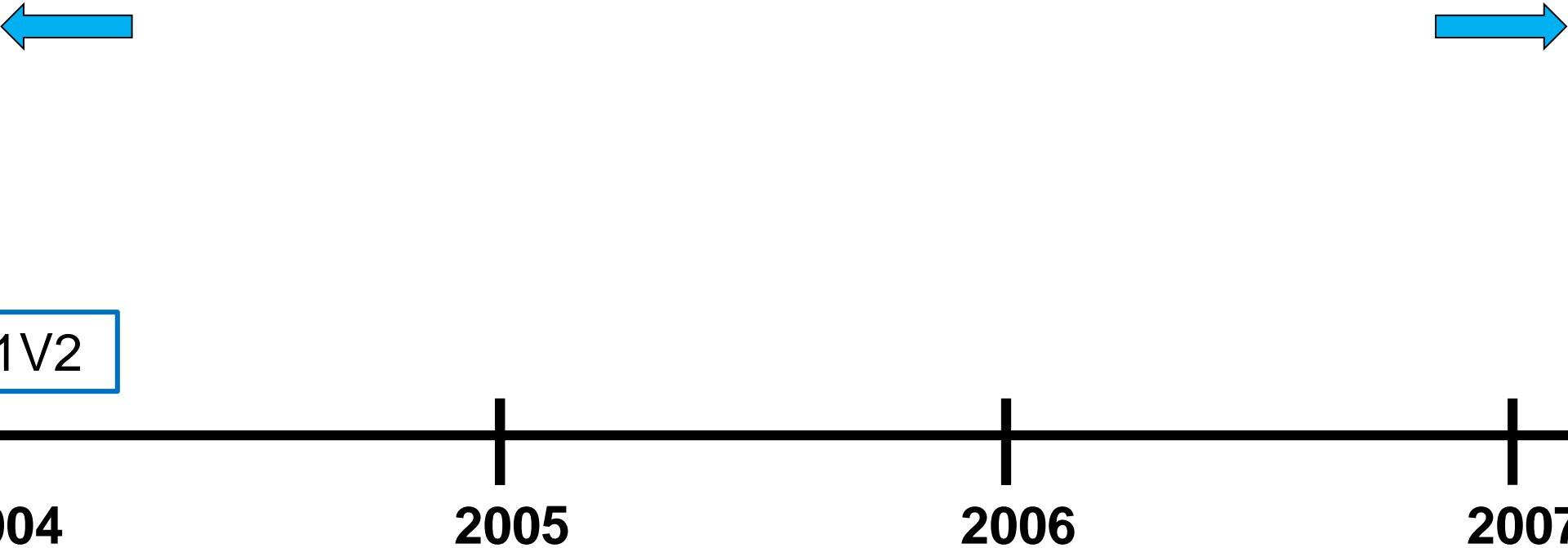
Evolution of SBML



Evolution of SBML



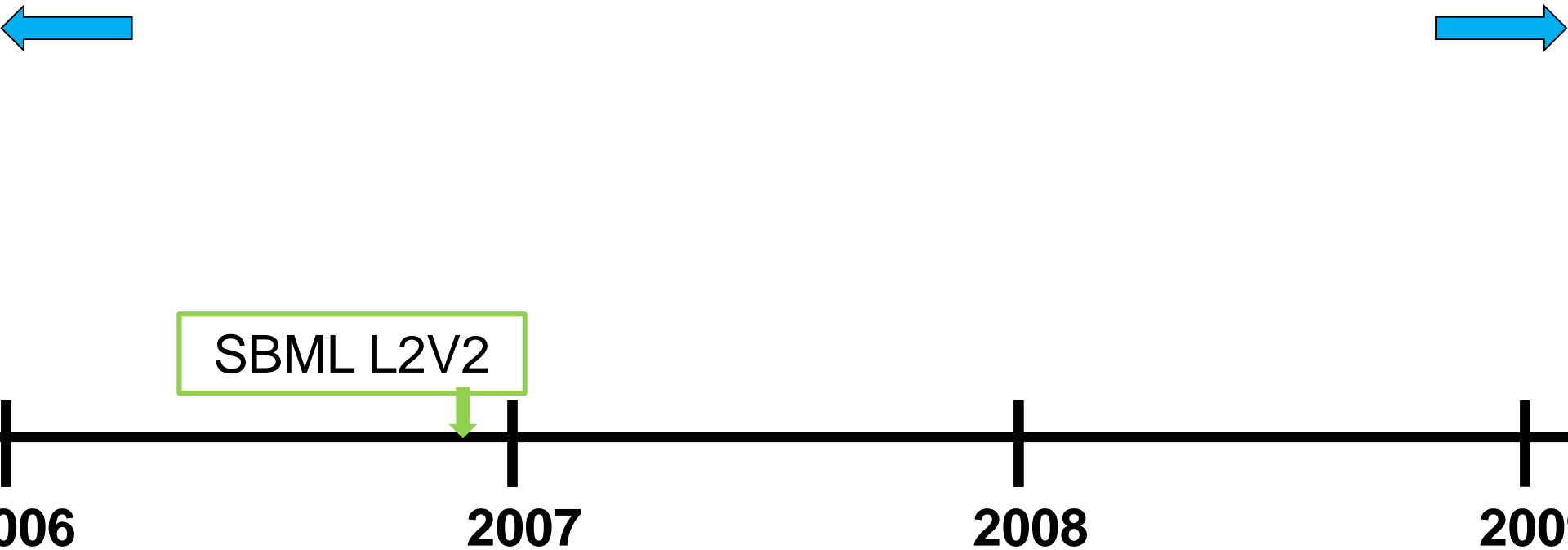
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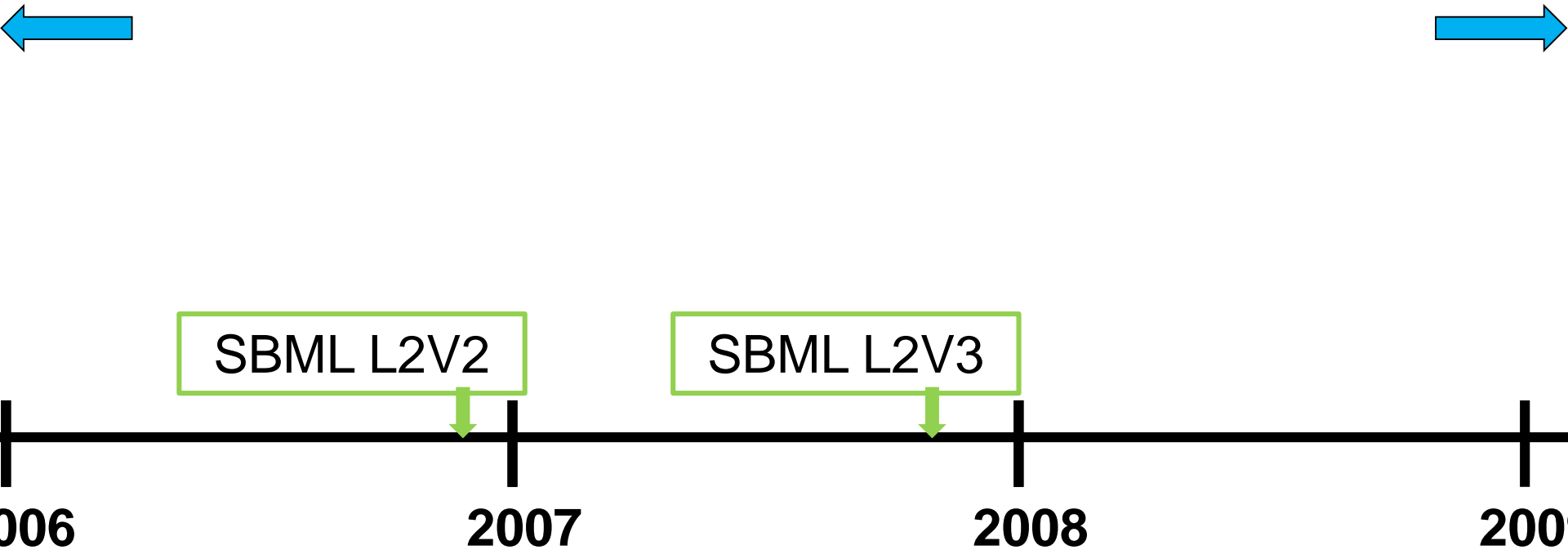
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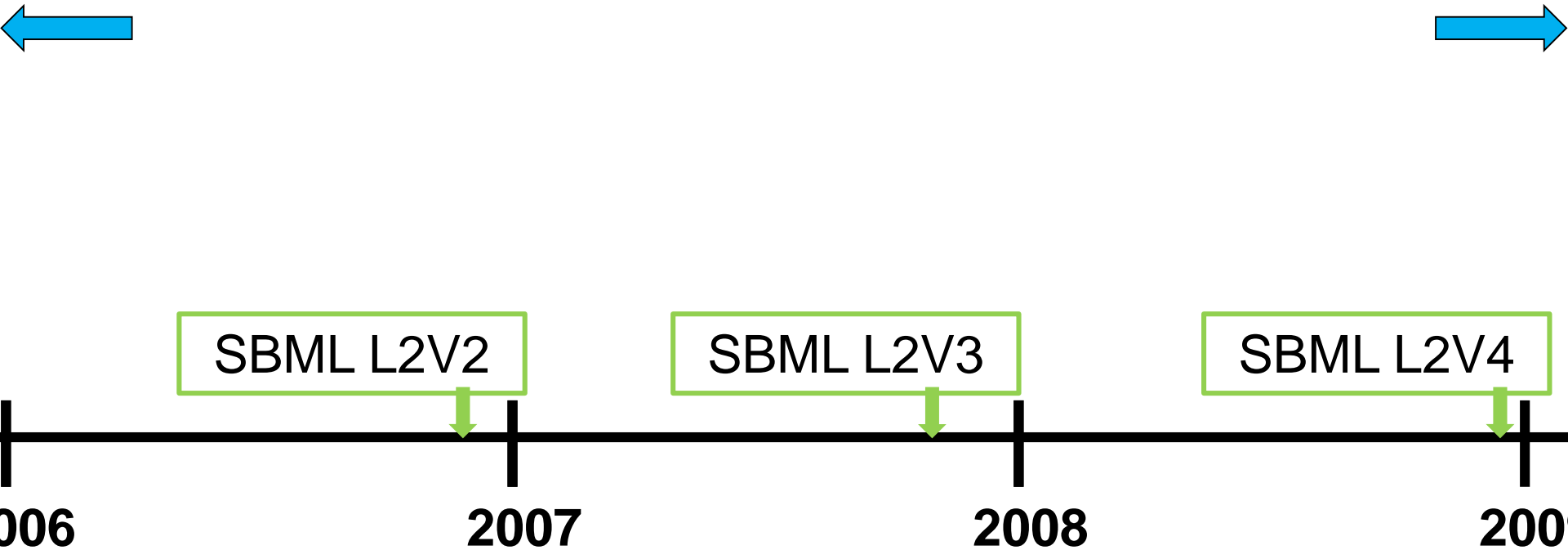
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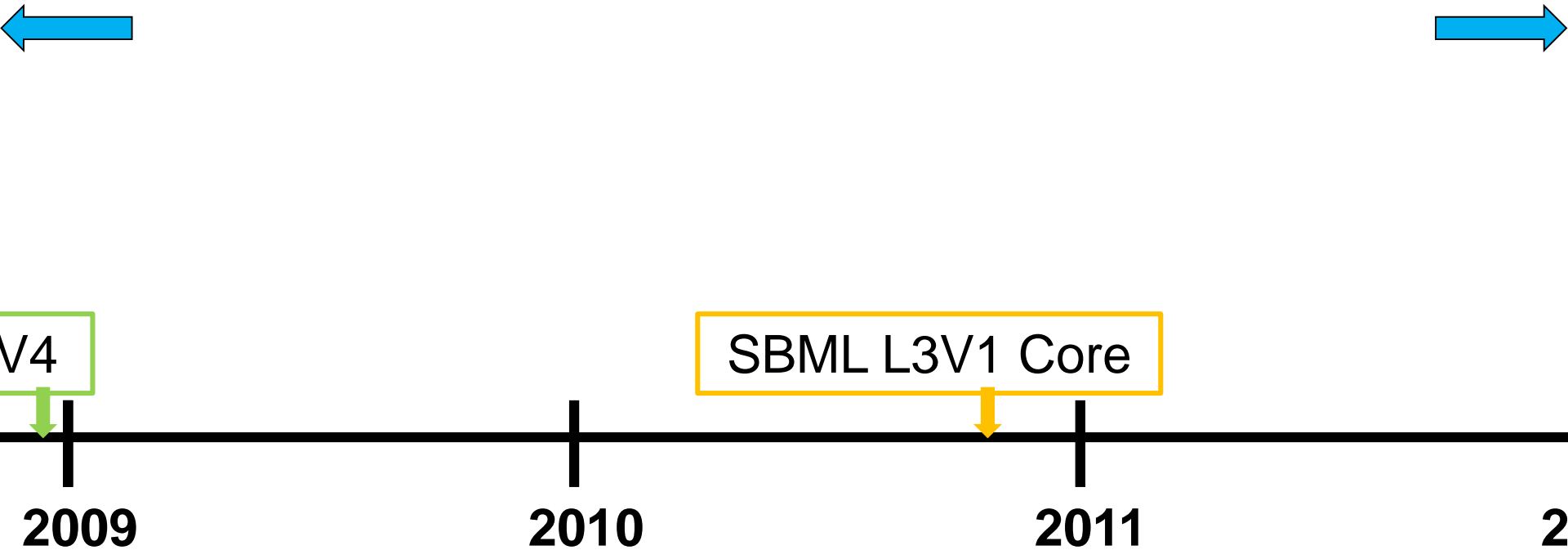
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Evolution of SBML



Evolution of SBML



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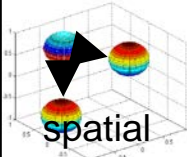
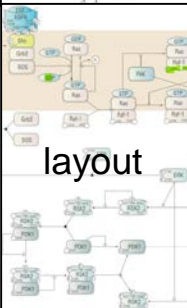

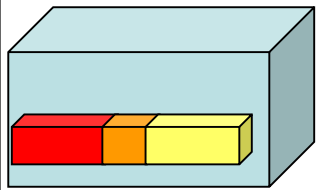
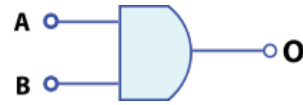
Organisation – Editors - Team

5. Supporting SBML

Software infrastructure available

SBML Level 3 Packages



 <p>spatial</p>  <p>layout</p>	<p>The Systems Biology Markup Language (SBML): Language Specification for Level 3 Version 1 Core</p> <p>Michael Hucka (Chair) California Institute of Technology, US Frank Bergmann University of Washington, US Stefan Hoops Virginia Bioinformatics Institute, US Sarah M. Harding California Institute of Technology, US Sven Sahle University of Heidelberg, DE Darren J. Wilkinson Newcastle University, GB</p> <p>sbml-editors@sbml.org</p> <p>core SBML Level 3 Version 1 Core Release 1 (Candidate) 31 December 2009</p> <p>Please report errors, ambiguities, and other issues in this document using the form at http://sbml.org/specifications/sbml-level-3/version-1/core/issue-report-form</p> <p>Corrections and other changes to this SBML language specification may appear over time. Notifications of new releases are broadcast on the mailing list sbml-dev@lists.sourceforge.net</p> <p>The latest release of the SBML Level 3 Version 1 Core specification is available at http://sbml.org/specifications/sbml-level-3/version-1/core</p> <p>This release of the specification is available at http://sbml.org/specifications/sbml-level-3/version-1/core/release-1/</p> <p>The list of known issues in all releases of SBML Level 3 Version 1 Core is available at http://sbml.org/specifications/sbml-level-3/version-1/core/known-issues/</p> <p>Formal schemas for use with XML are available at http://sbml.org/specifications/sbml-level-3/version-1/schemas/</p> <p> Systems Biology Markup Language</p>	 <p>comp</p>  <p>qual</p>
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SBML Level 3 Packages

Package name & link to info page	Label	Description	Status
Annotations	annot	Support for richer annotation syntax than the regular annotations in SBML Level 3 Core	Stalled
Arrays	arrays	Support for expressing arrays of things	Draft available
Hierarchical Model Composition	comp	A means for defining how a model is composed from other models	Released
Distributions	distrib	Support for encoding models that sample values from statistical distributions	Draft available
Dynamic Processes	dyn	Support for creating and destroying entities during a simulation	Draft available
Extended Math	math	A suite of packages that collectively allow MathML beyond the subset allowed in SBML core.	Not started
Flux Balance Constraints	fbc	Support for constraint-based (a.k.a. steady-state) models	Released
Groups	groups	A means for grouping elements	Released
Layout	layout	Support for storing the spatial topology of a network diagram; adjunct to the render package	Released
Multistate and Multicomponent Species	multi	Object structures for representing entity pools with multiple states and composed of multiple components, and reaction rules involving them	Draft available
Qualitative Models	qual	Support for models wherein species do not represent quantity of matter & processes are not reactions per se	Released
Rendering	render	Support for defining the graphical symbols and glyphs used in a diagram of the model; adjunct to the layout package	Draft available
Required Elements	req	Support for fine-grained indication of SBML elements that have been changed by the presence of another package	Draft available
Spatial Processes	spatial	Support for describing processes that involve a spatial component, and describing the geometries involved	Draft available

http://sbml.org/Documents/Specifications#SBML_Level_3_Packages

Status

Released

- Specification document complete
- Specification document approved
- Two implementations

Status

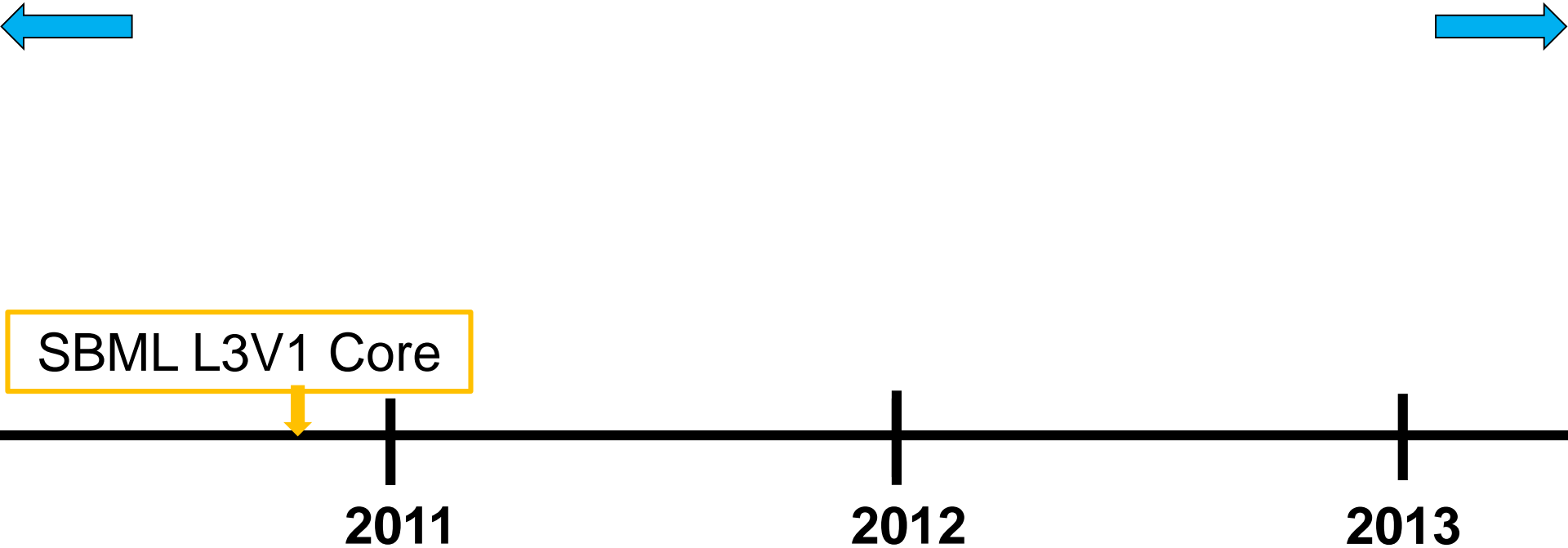
Draft available

- Specification document being worked on
- Implementations being worked on

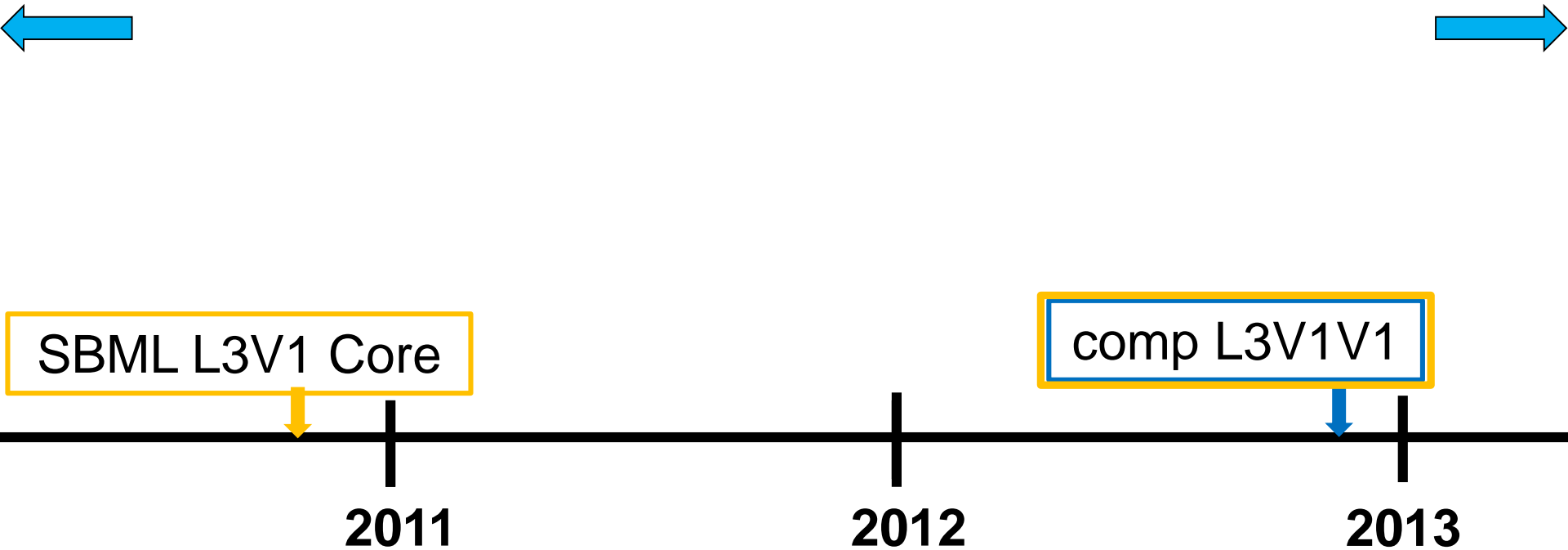


SUBJECT TO CHANGE

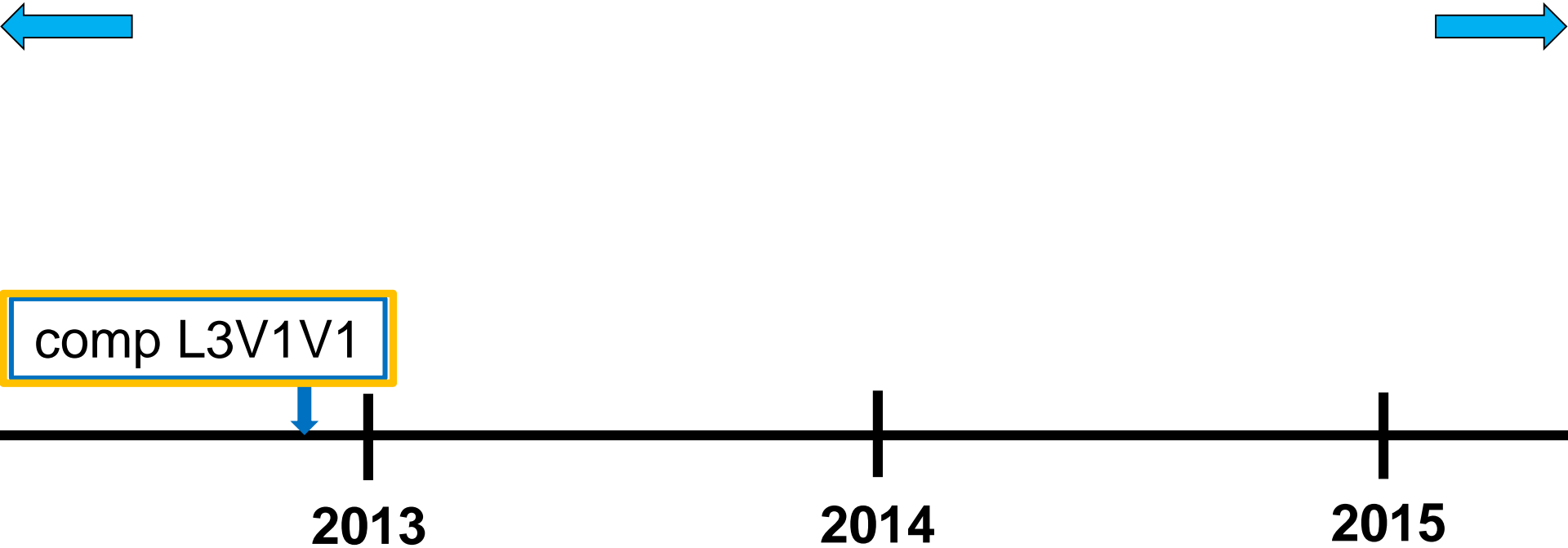
Evolution of SBML



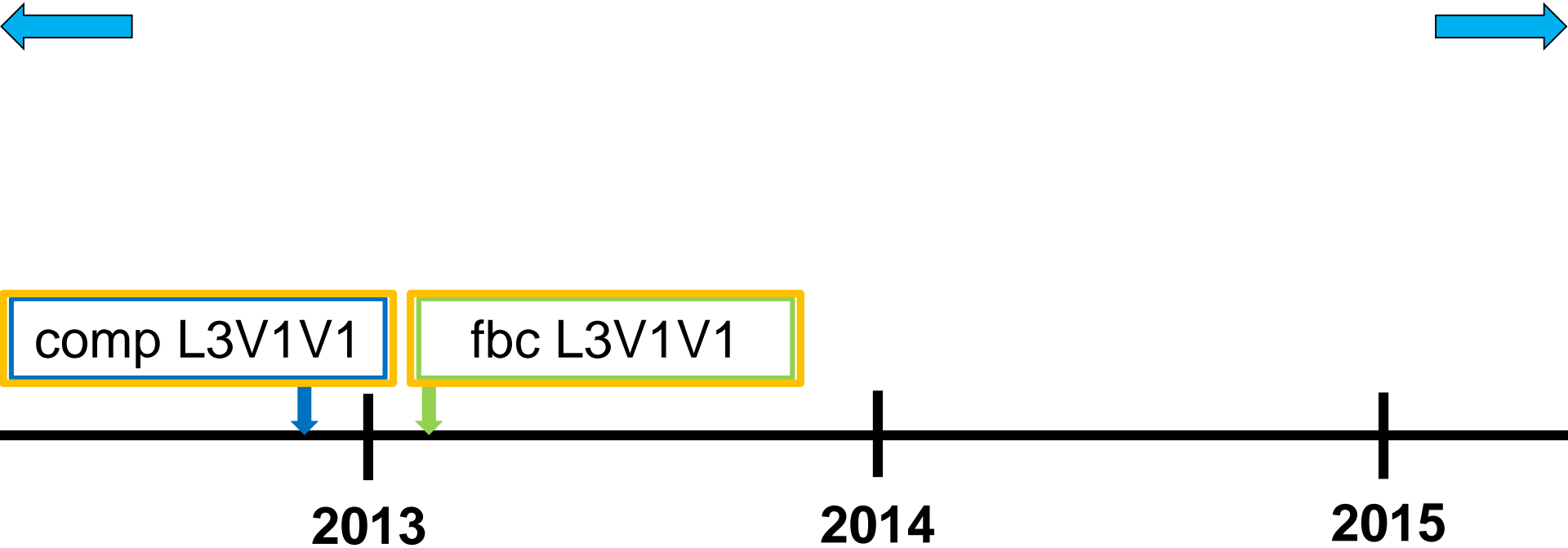
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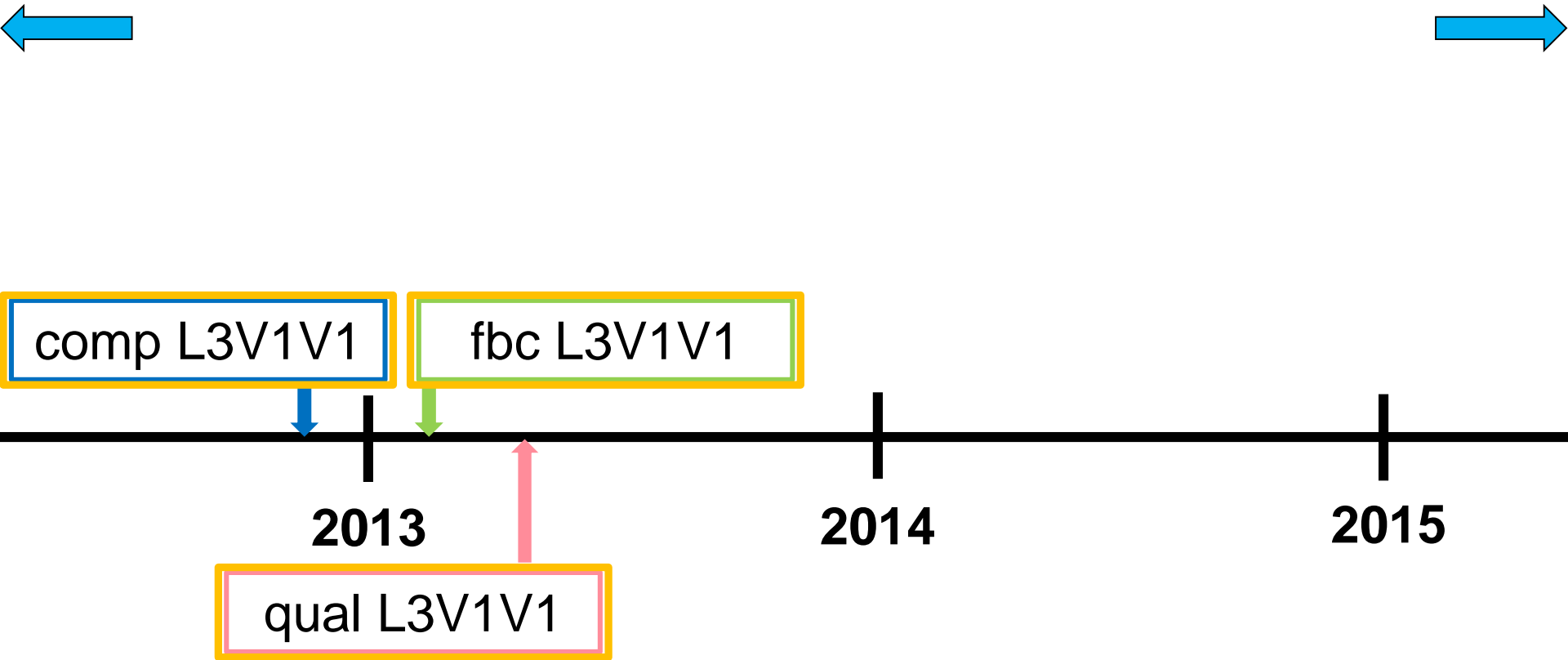
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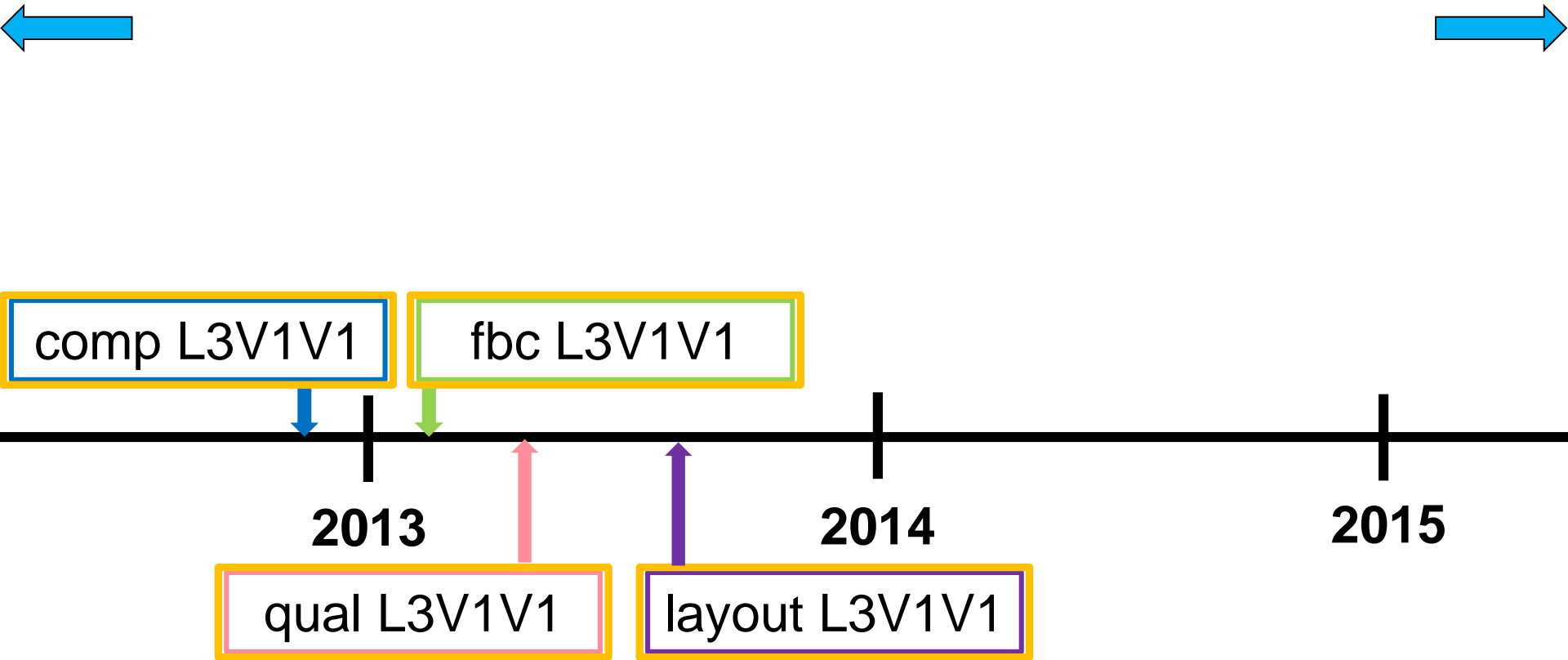
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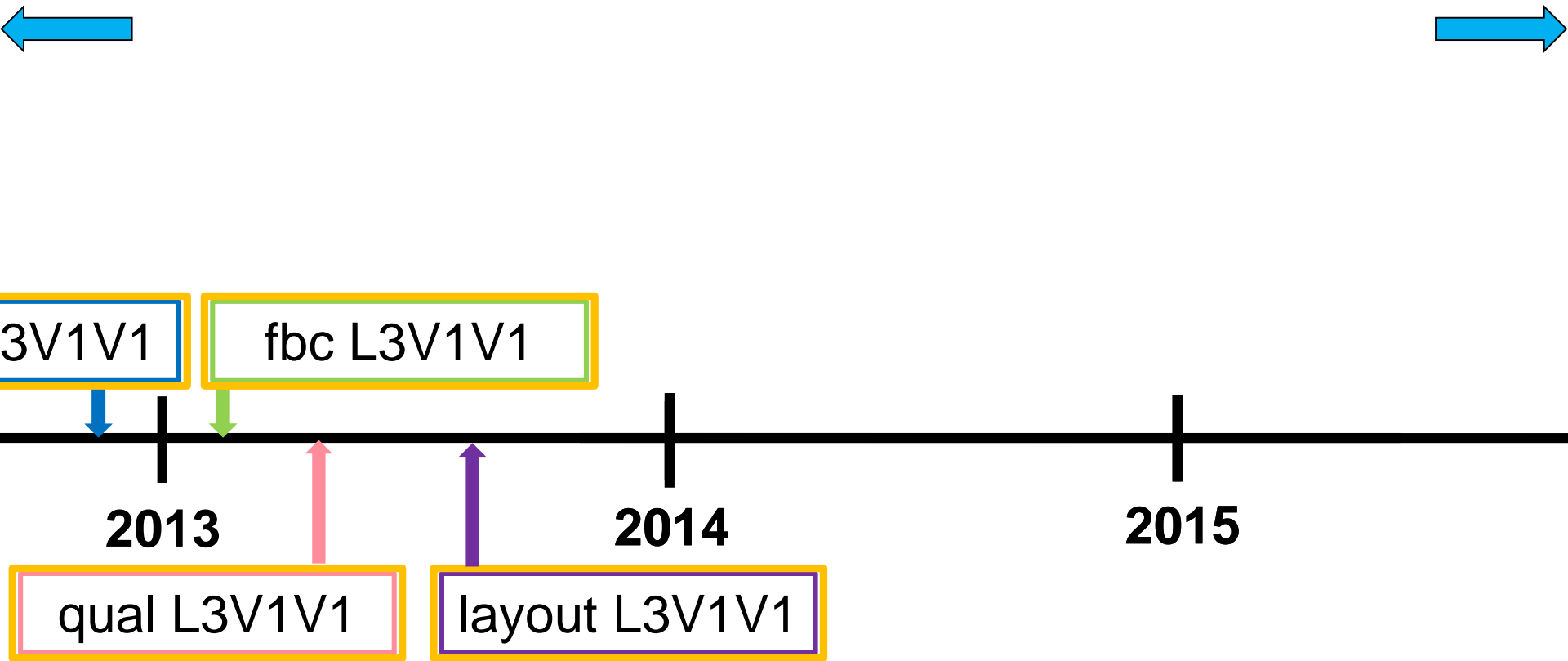
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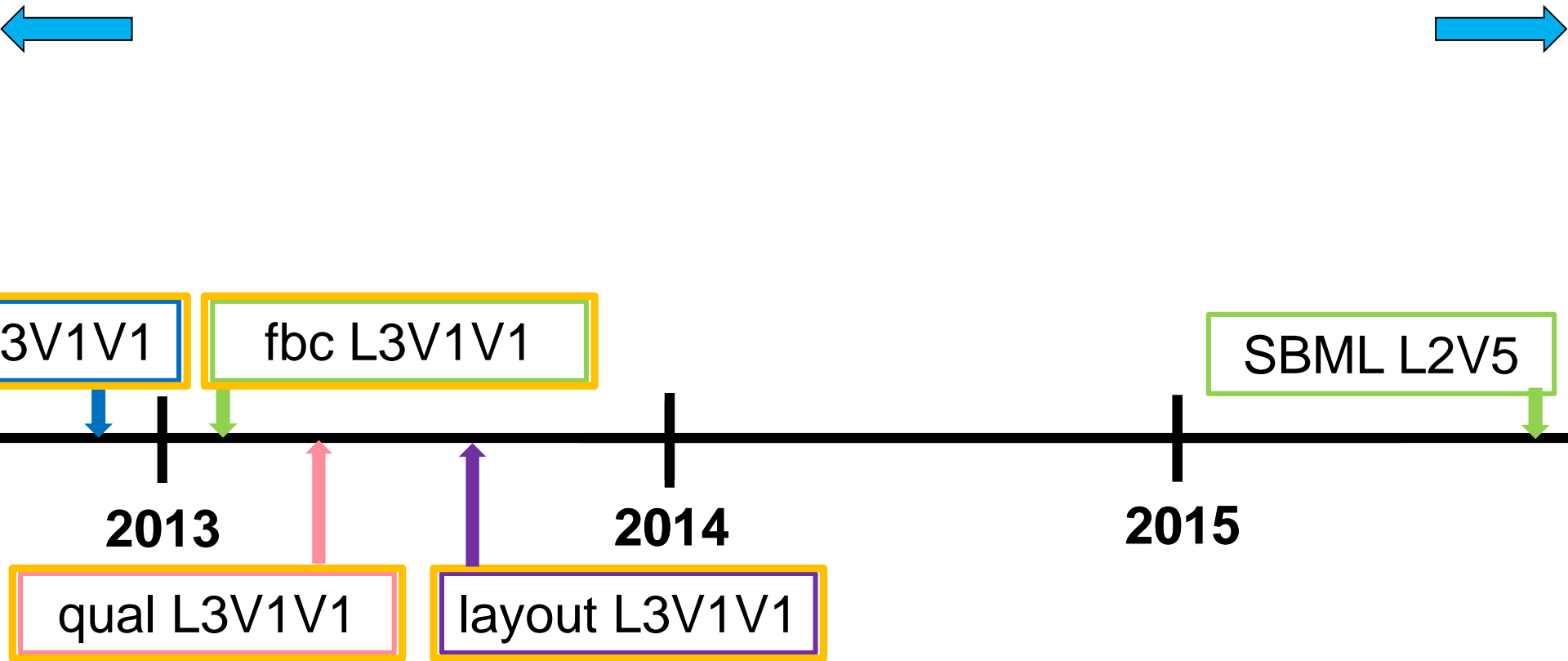
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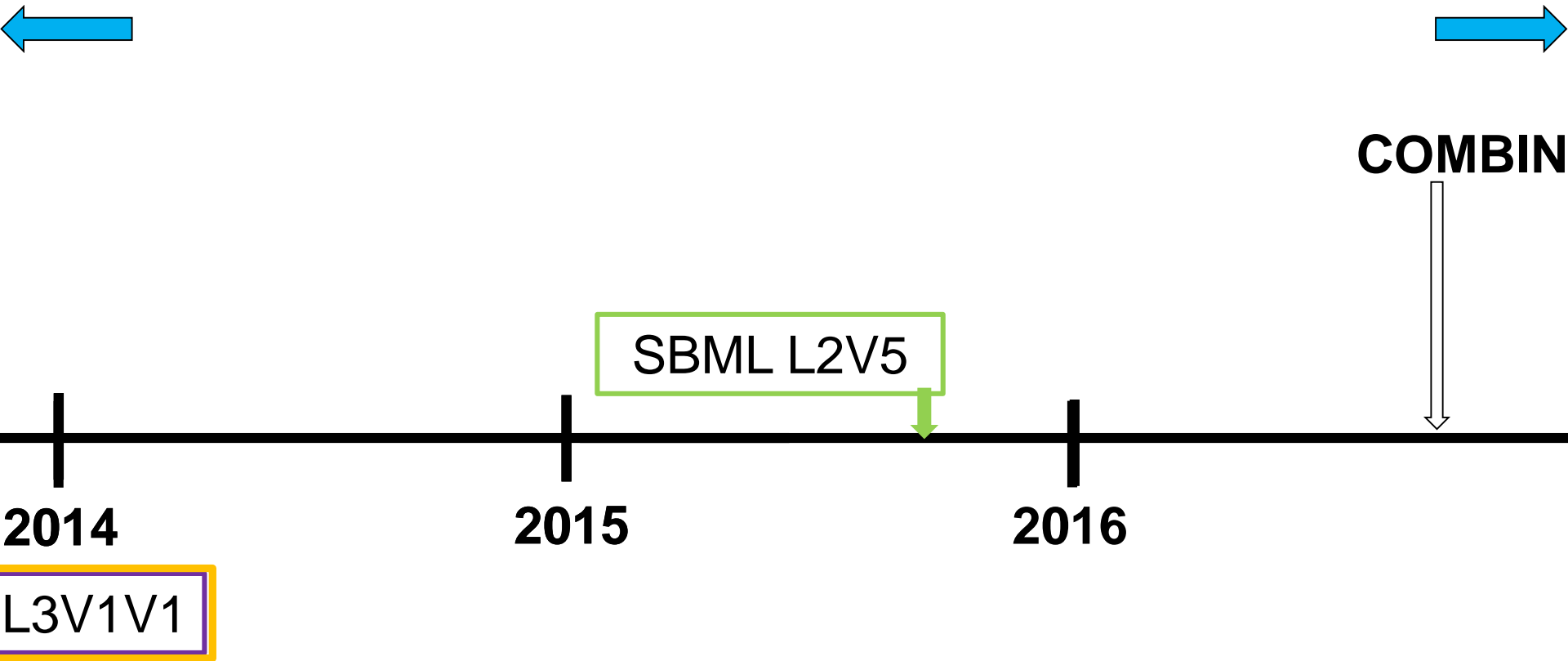
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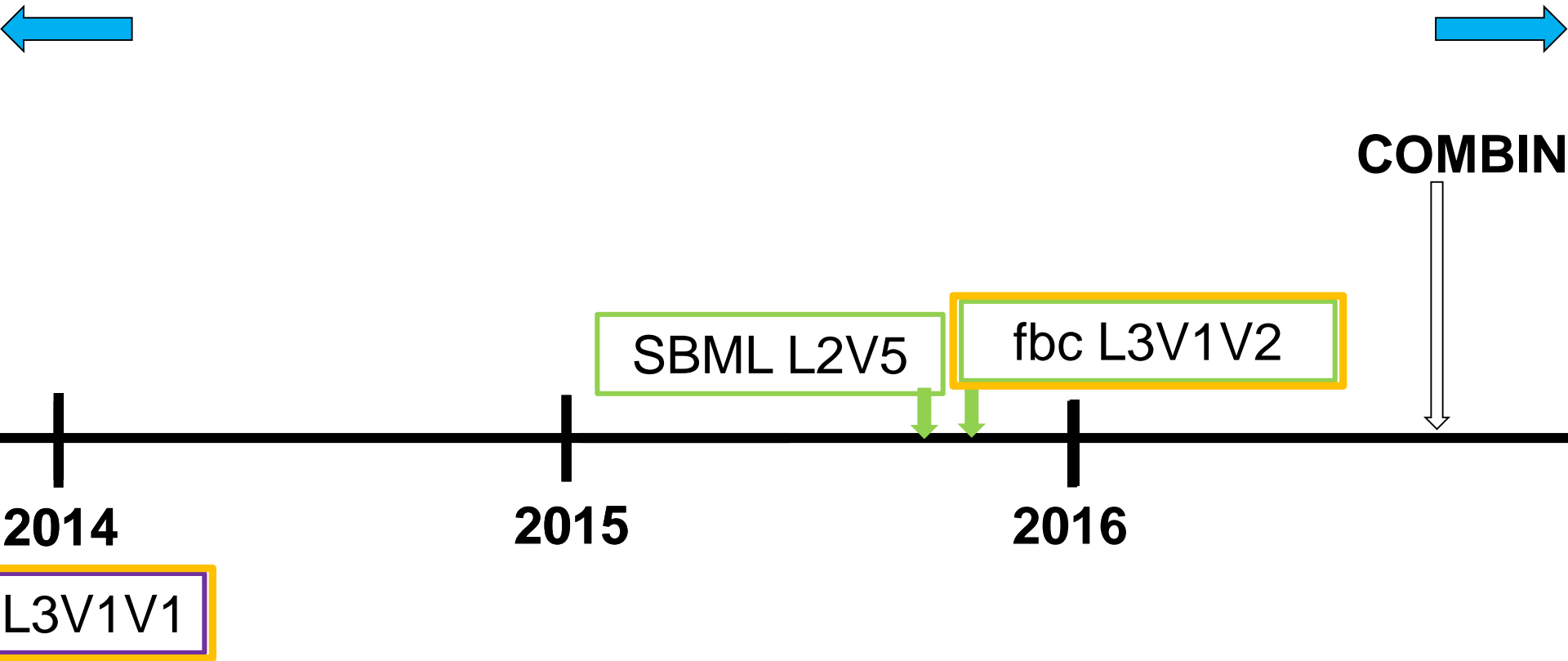
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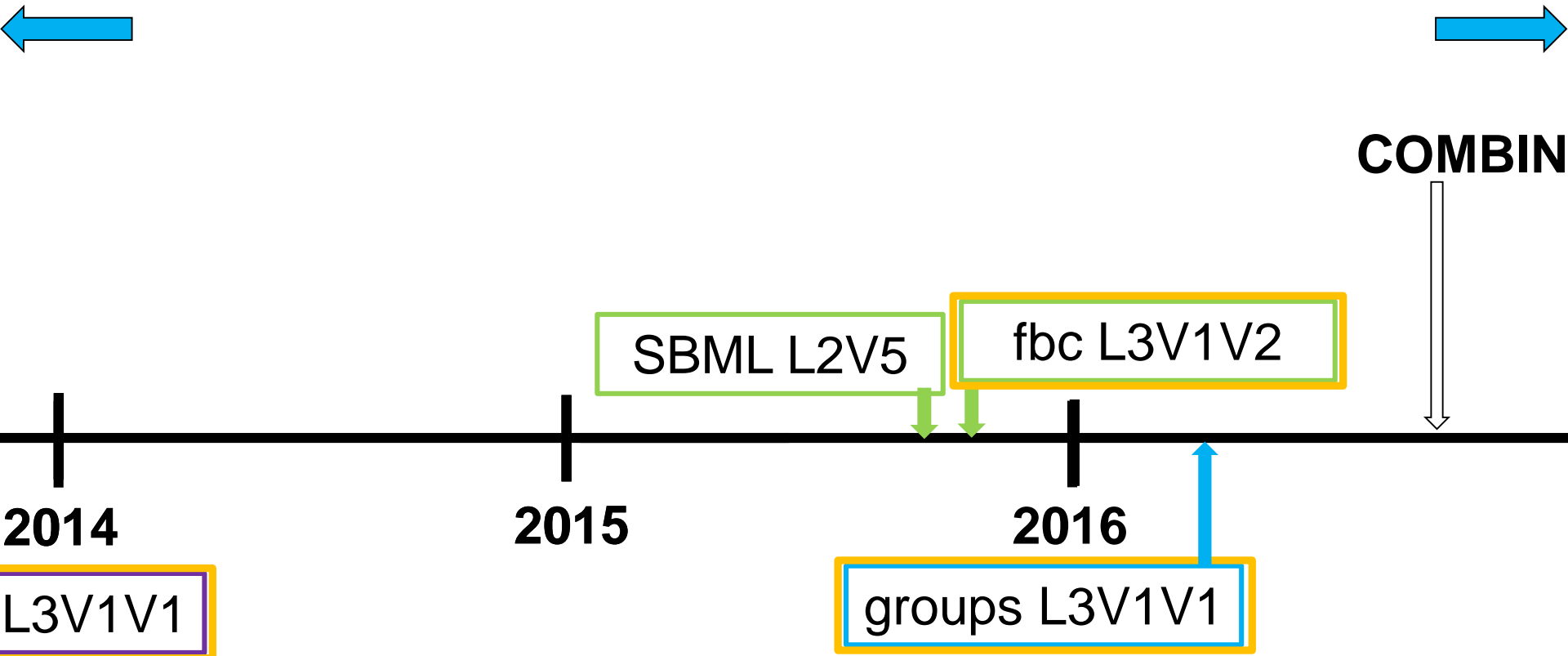
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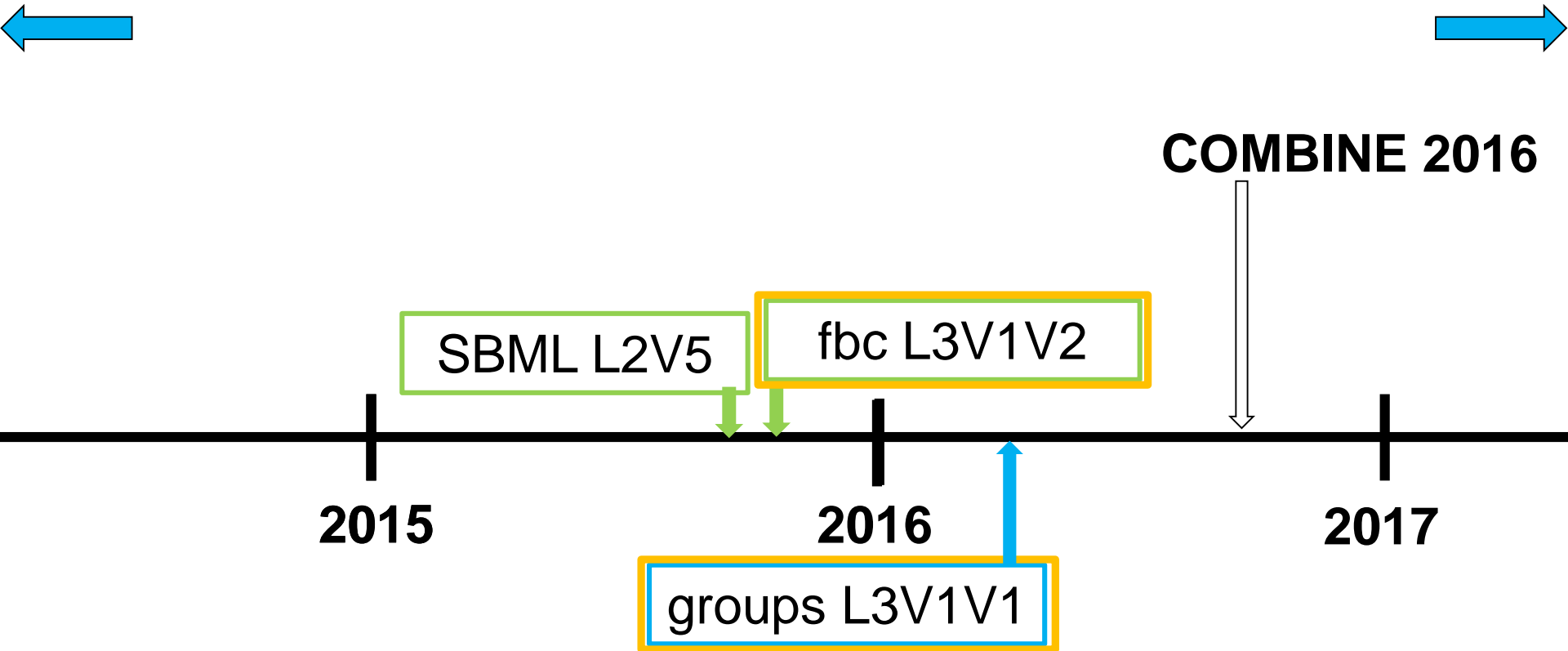
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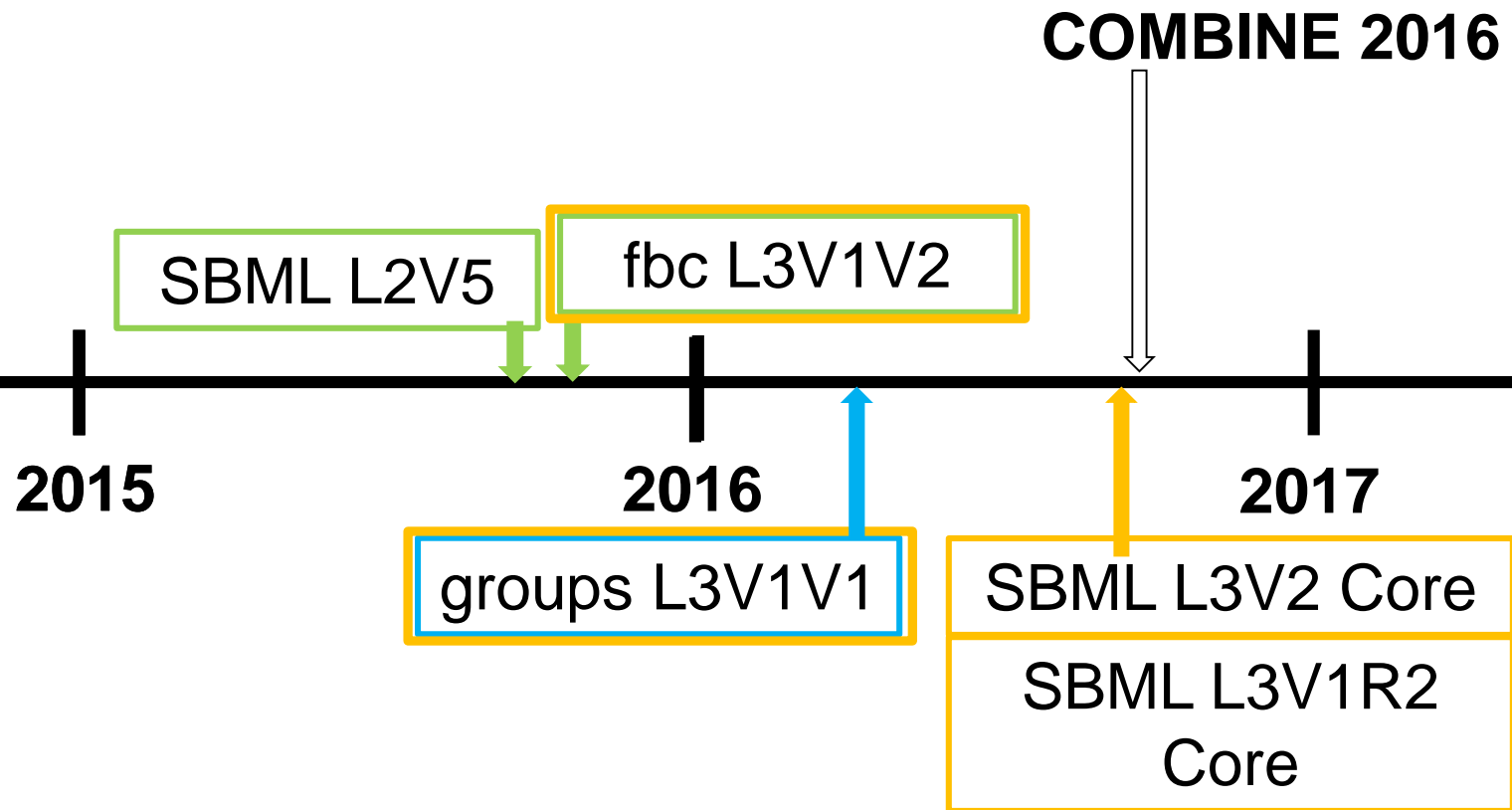
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SBML Process

- Formal process with written guidelines for
 - Development procedures
 - Achieving community consensus

http://sbml.org/Documents/SBML_Development_Process

SBML Process

- Organization
 - Elected Editors
 - Invited Scientific Advisory Board
 - Funded Team

<http://sbml.org/Documents/About>

SBML Editors



Andreas Dräger



Sarah Keating

Coordinator



Nicolas Le Novère



Brett Olivier



Dagmar Waltemath



Lucian Smith

Secretary

Current

Past

Frank Bergmann

Hamid Bolouri

Andrew Finney

Stefan Hoops

Michael Hucka

Chris Myers

Sven Sahle

Herbert Sauro

James Schaff

Darren Wilkinson

SBML Editors

- Responsibilities
 - Evaluate/act on proposals/requests/reports
- Coordinator
 - Chairs activities of the editors
- Secretary
 - Not elected; member of the funded team
 - Time to do: specifications/documentation

SBML Team

Michael Hucka (Team leader)

Frank Bergmann

Andreas Dräger

Sarah Keating

Lucian Smith

Nicolas Rodriguez

Harold Gómez

Linda Taddeo

SBML Team

- Responsibilities

- Maintain resources for supporting SBML infrastructure
 - Website
 - Forums/mailing lists
 - Participate in Events – COMBINE/HARMONY
 - Software

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Tools supporting SBML

The Systems Biology Markup Language

News Documents Downloads Forums Facilities Community Events About   


Parent pages: [SBML.org](#)

SBML Software Guide


The following pages describe SBML-compatible software packages known to us. We offer different ways of viewing the information, all drawn from the same underlying data collected from the systems' developers via our [software survey](#). The *Matrix* provides a table listing all known software and a variety of their features; the *Summary* provides general descriptions of most of the software; and the *Showcase* provides a sequential slideshow of a subset of the software.

Number of software packages listed in the matrix today: **283**.

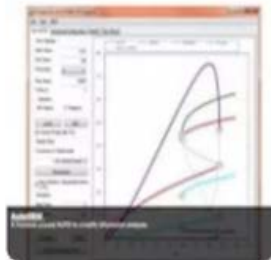
Go to the SBML Software Matrix



Go to the SBML Software Summary



Go to the SBML Software Showcase



Please [tell us about additions and updates](#).


http://sbml.org/SBML_Software_Guide

Tools supporting SBML

- Maintain a list of software supporting SBML
- Outline the facilities/level of support
- Relies on developers to keep us up to date ☺

http://sbml.org/SBML_Software_Guide

Online validator



The Systems Biology Markup Language

News Documents Downloads Forums Facilities Community Events About

Google Site Search.

Parent pages: [SBML.org](#) / [Facilities](#) / [Online SBML Validator](#)

This tests the syntax and internal consistency of an SBML file. Passing this validator does not *guarantee* correctness, but it's the best automated assessment available.

Use the form below to upload your SBML content. You can also access this service via a **network API**. By using any part of this service, you agree to the terms of the [privacy notice](#).

[Sign in](#) or [Register](#) with this service.

You can retrieve the result of a previously-scheduled validation run by entering its key here:

(E.g., 7bf66904-7d67-49bb-9127-bee77a8f96ba)

Upload File

Submit URL

Paste SBML

Upload

Drag & Drop Files

Validate now

Schedule for Validation

Select an SBML file located on your computer. The file can be uncompressed, or compressed using **zip**, **gzip** or **bzip2**.

<http://sbml.org/Facilities/Validator/>

Online validator

- Checks that an SBML file conforms to SBML specifications
- Customise checks made and the output presented
- Browser based OR RESTful network API
- Schedule long running validations

<http://sbml.org/Facilities/Validator/>

Online validator

Recent improvements

- Support for draft SBML Level 3 packages
 - Uses RelaxNG schemas to provide syntactic validation
- Links to other services for additional analysis
- Faster hardware

<http://sbml.org/Facilities/Validator/>

SBML Test-suite

- Provides over 1000 tests for SBML
 - semantic
 - stochastic
 - syntactic
- Test runner to facilitate use
- Database of results uploaded by software developers

http://sbml.org/Software/SBML_Test_Suite

SBML Test-suite

Recent additions

- Examples of use of reaction 'id' in rules
- L3V2 versions of all (applicable) tests
- L3V2 specific tests

http://sbml.org/Software/SBML_Test_Suite

SBML Test-suite

Special thanks to the developers for testing results



COPASI

iBioSim



Systems
Biology
Simulation
Core Library

CBMPy
PySCeS Constraint Based Modelling

BioUML

The Virtual Cell

SBW
ROADRUNNER



libRoadRunner

API libraries

libSBML

- Written in portable C++
- APIs for C, C++, C#, Java, JavaScript, MATLAB, Octave, Perl, PHP, Python, R, Ruby
- Other features: unit checking, converters

<http://sbml.org/Software/libSBML>

JSBML

- Pure Java
- API similar to libSBML but more Java-ish
- Additional Java features such as listeners

<http://sbml.org/Software/JSBML>

API libraries

libSBML

JSBML

- Read/write/manipulate SBML
- Validate SBML (JSBML thanks Google Summer of Code)
- Work seamlessly with all Levels and Versions of SBML
- Supports all L3 Packages (Released and drafts)
- Free, open source, LGPL

<http://sbml.org/Software/libSBML>

<http://sbml.org/Software/JSBML>



MOCCASIN

- Converts basic forms of MATLAB ODE models into SBML
- Written in Python – does NOT need MATLAB
 - parses MATLAB into AST
 - resolves ambiguous constructs
 - infers reactions using algorithm
 - Fages F., Gay S., Soliman S. “Inferring reaction systems from ordinary differential equations”, Theoretical Computer Science, 599:64-78, 2015
- uses BIOCHAM webservice

<http://sbml.org/Software/MOCCASIN>

MOCCASIN

Planned improvements

- Provide way for users to identify 'SBML' constructs
 - compartments/units
- Support more MATLAB constructs
 - if – else; switch
- Support models across multiple files
- Implement Fages et al. algorithm to use offline

<http://sbml.org/Software/MOCCASIN>

Deviser

- Facilitates design of SBML packages
- GUI form based interface can be used to generate
 - Full libSBML code for package
 - JSBML code (Deviser thanks Google Summer of Code)
 - UML diagrams
 - RNG schemas
 - Basic LaTeX docs

<https://github.com/sbmlteam/deviser>

Deviser

Planned improvements

- Release 1.0
- Generate non-SBML libraries for other XML based representations
 - SED-ML
 - UncertML
 - Combine Archive
 - ...

<https://github.com/sbmlteam/deviser>

Just released

libCombine

- Library to read/write/create CombineArchive
- Uses zipper library; depends on libSBML/has similar API
- Interrogate manifest/look at individual files/work with metadata
- Language bindings for .NET/Java/Python

<https://github.com/sbmlteam/libCombine>

Converters

- Extend converters available
- Improve/update existing converters
 - BioPax \leftrightarrow SBML (again, thanks Google Summer of Code)

http://sbfc.sourceforge.net/mediawiki/index.php?title=Main_Page

GSoC 2016

Hovakim Grabski	Russian-Armenian University, Armenia	Java support for Deviser, a code generation system for SBML libraries
Kaito Li	Funahashi Lab, Keio University, Japan	Interconvertible Layout program for CellDesigner
Devesh Khandelwal	Cluster Innovation Centre, University of Delhi, India	SBGN-ML and SBML to Escher Converter
Tramy Nguyen	Myers Research Group, University of Utah, USA	Interconversion between the systems biology modeling formats SBML and BioPAX
Roman Schulte	University of Tübingen, Germany	JSBML Validation System



Funding

Current funding:

NIH (NIGMS) R1 GM070923

MOCCASIN – Initial funding : Modeling Immunity for Biodefense
contract HHSN2662005000021C (PI: Stuart Sealton)

Institutes:

California Institute of Technology (USA)

Babraham Institute (UK)

EMBL-EBI (UK)

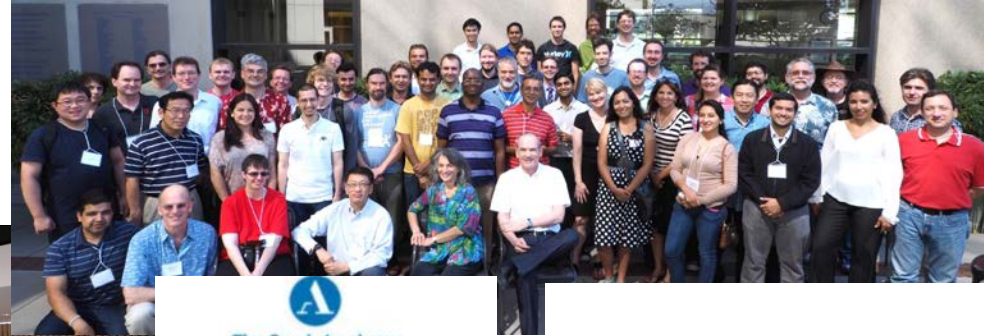
University of Heidelberg (Germany)

University of Tübingen (Germany)

Funding through the years

NIH/NIGMS (USA)	Ministry of Agriculture (Japan)
BBSRC (UK)	Ministry of Education, Culture, Sports, Science and Technology (Japan)
Google Summer of Code (USA)	DARPA IPTO Bio-Computation Program (USA)
Virtual Liver Network (BMBF, Germany)	Air Force Office of Scientific Research (USA)
MedSys project Spher4Sys (BMBF, Germany)	STRI, University of Hertfordshire (UK)
ELIXIR (EU)	Molecular Sciences Institute (USA)
Keio University (Japan)	JST ERATO Kitano Symbiotic Systems Project (Japan)
Drug Disease Model Resources (EU-EFPIA)	JST ERATO-SORST Program (Japan)
National Science Foundation (USA)	International Joint Research Program of NEDO (Japan)

Acknowledgments



Memorial Sloan Kettering
Cancer Center.



The Systems
Biology
Institute



Stanford University

Universität
Rostock

