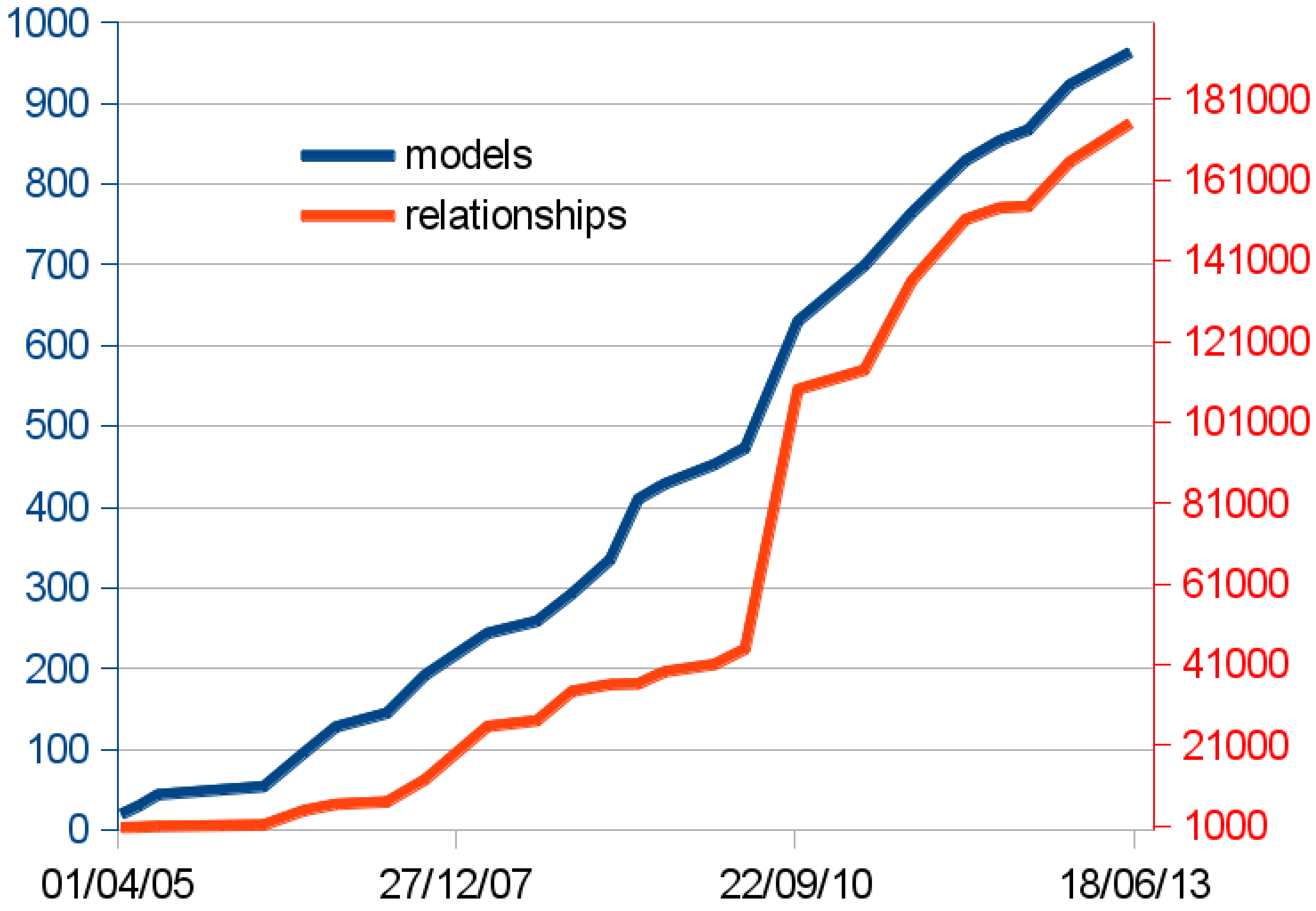
the combine
computational modeling in biology network

Interoperable Standards For modelling in biology

Rising interest in models from new stakeholders

- “Biologists”: computational models look “useful”, “serious”
- Publishers: computational articles are respectable,
  can be published in high profile journals
- Funding agencies: Models could help with the major challenges
  (read “science that can be sold to citizen/electors”):
  Health, Food, Energy...
- Industries: Models could help with the major challenges
  (read “new opportunities to make money”):
  Pharmas, crops, biofuels ...

Computational models on the rise



BioModels Database (published models branch) growth since its creation

http://www.ebi.ac.uk/biomodels/

We need to share:

Model descriptions

Simulation descriptions

Parametrisations

In order to:

Verify

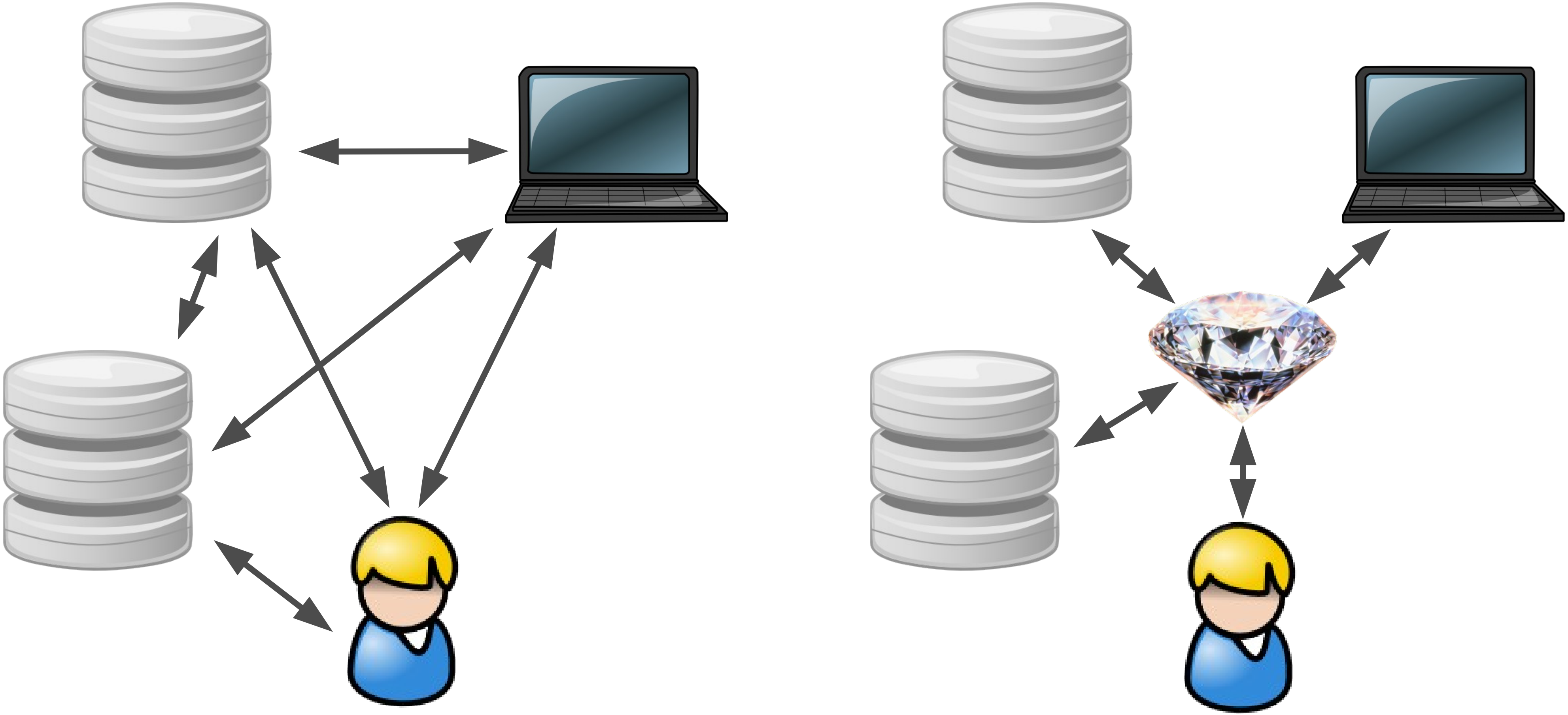
Re-use

Modify

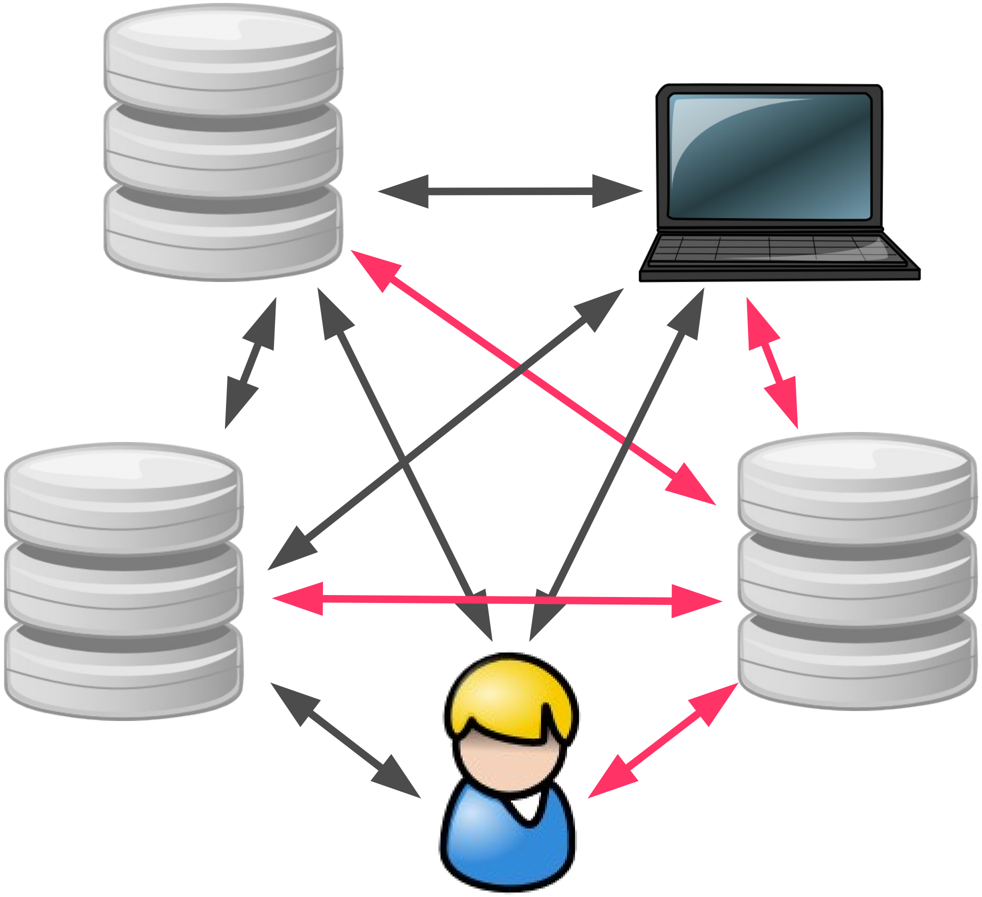
Build upon

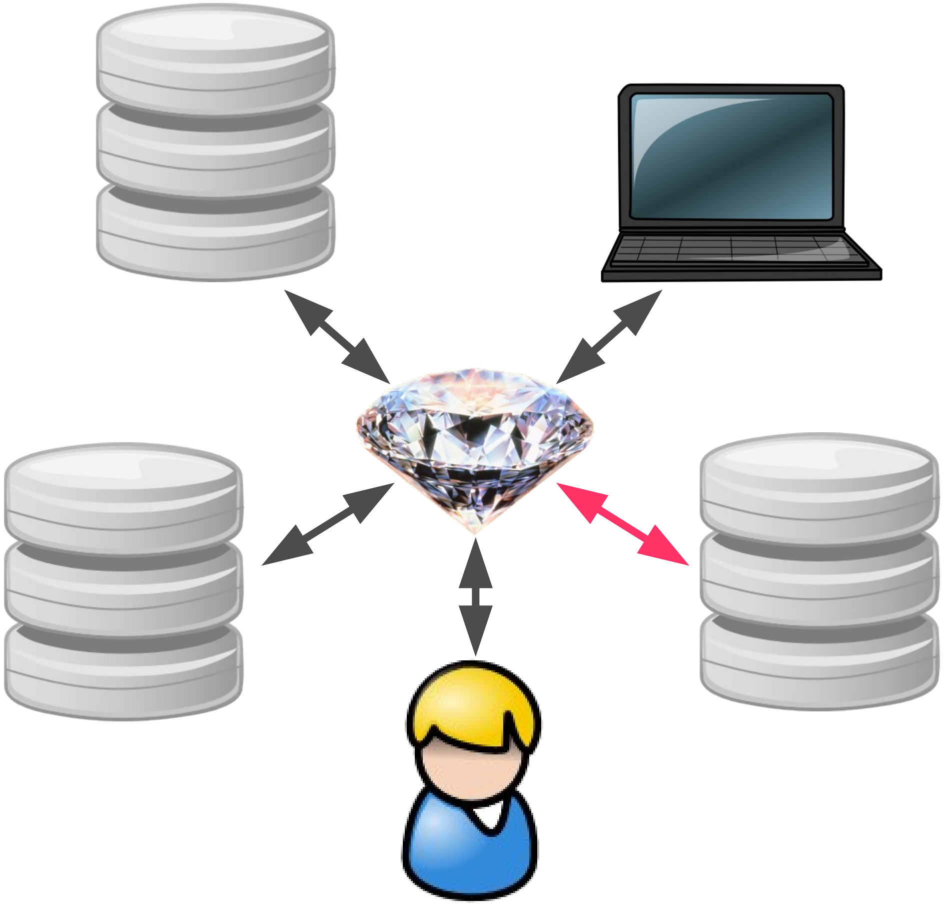
Integrate with

What are standards good for (1)?



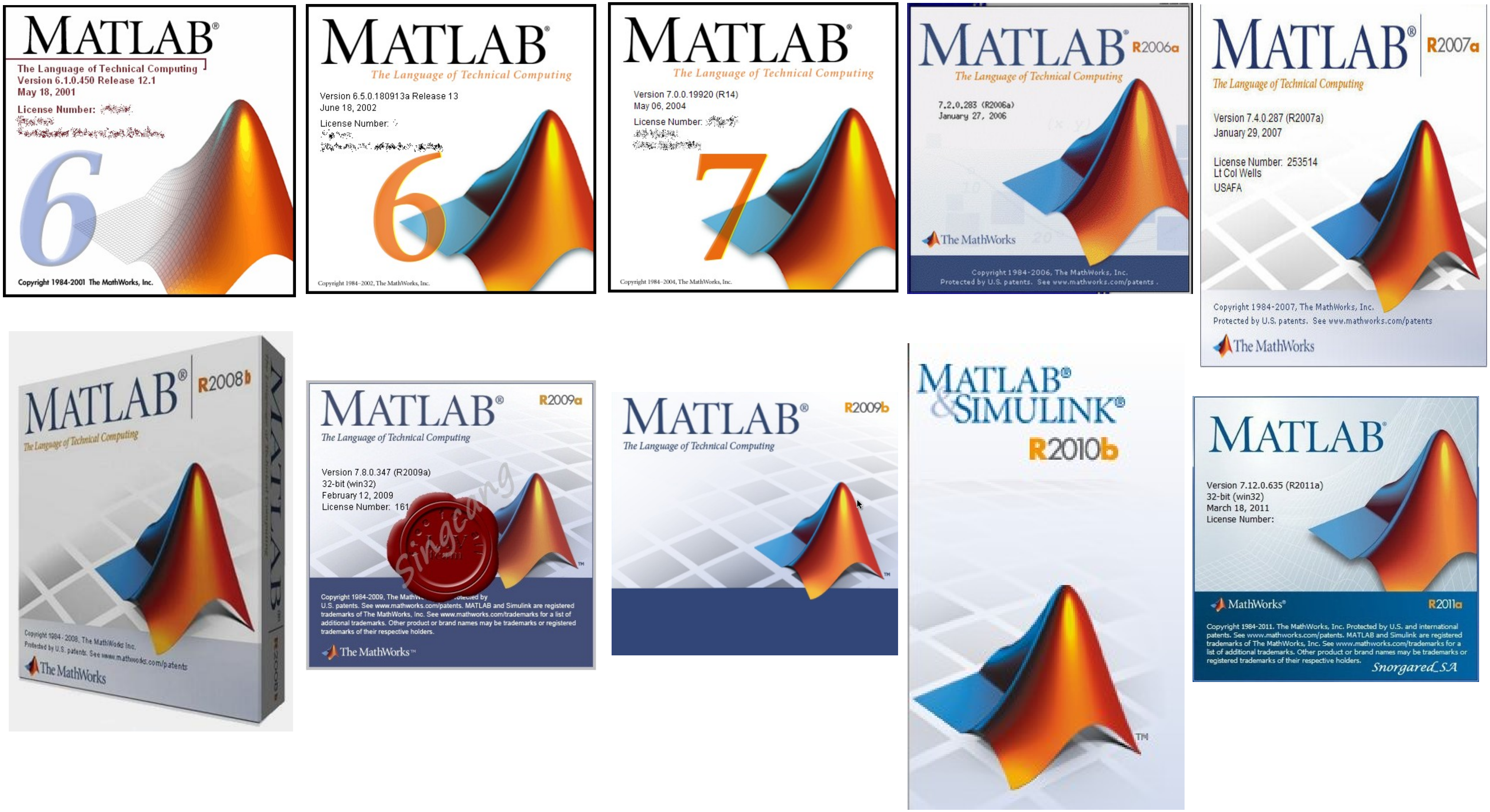
What are standards good for (1)?





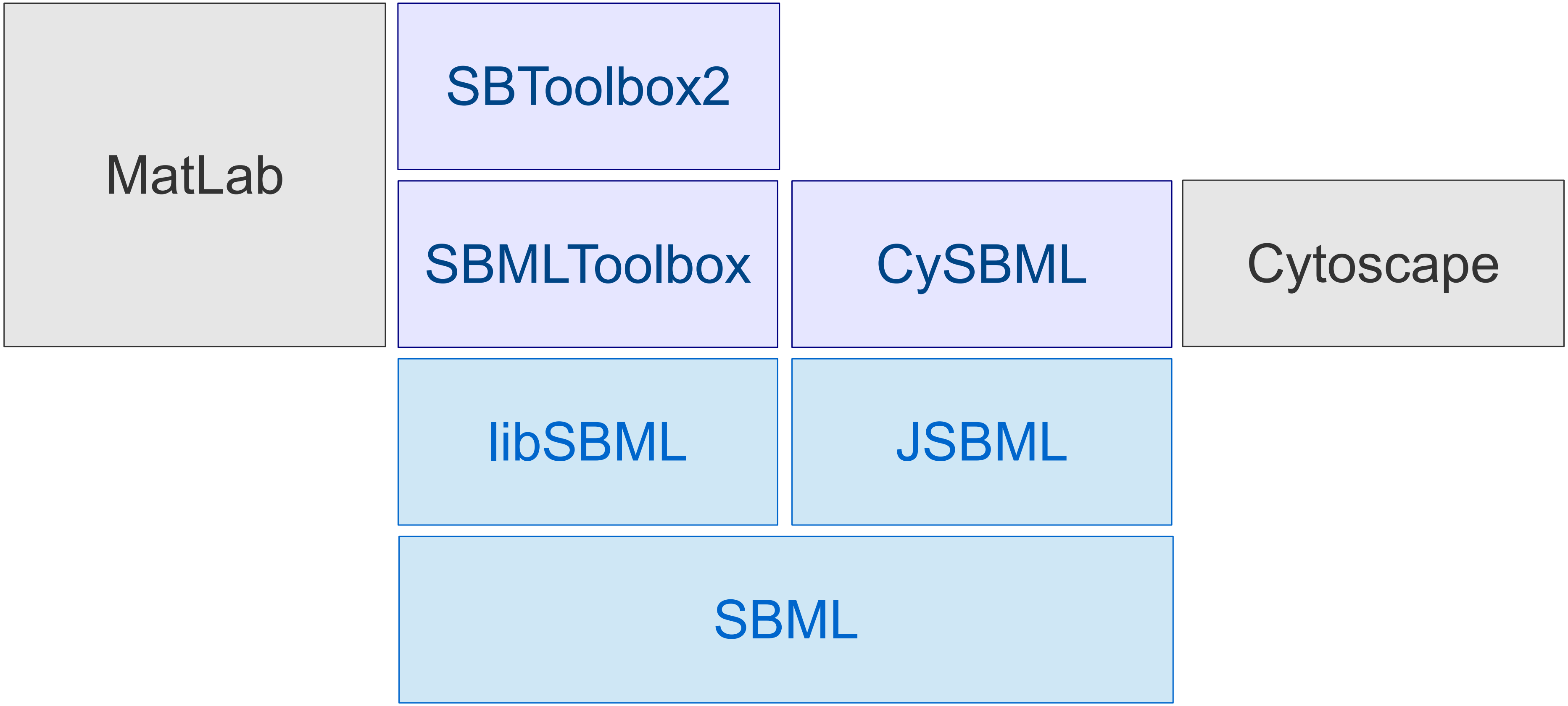
N tools require N conversions for exchange and not N(N-1)/2

What are standards good for (2)?



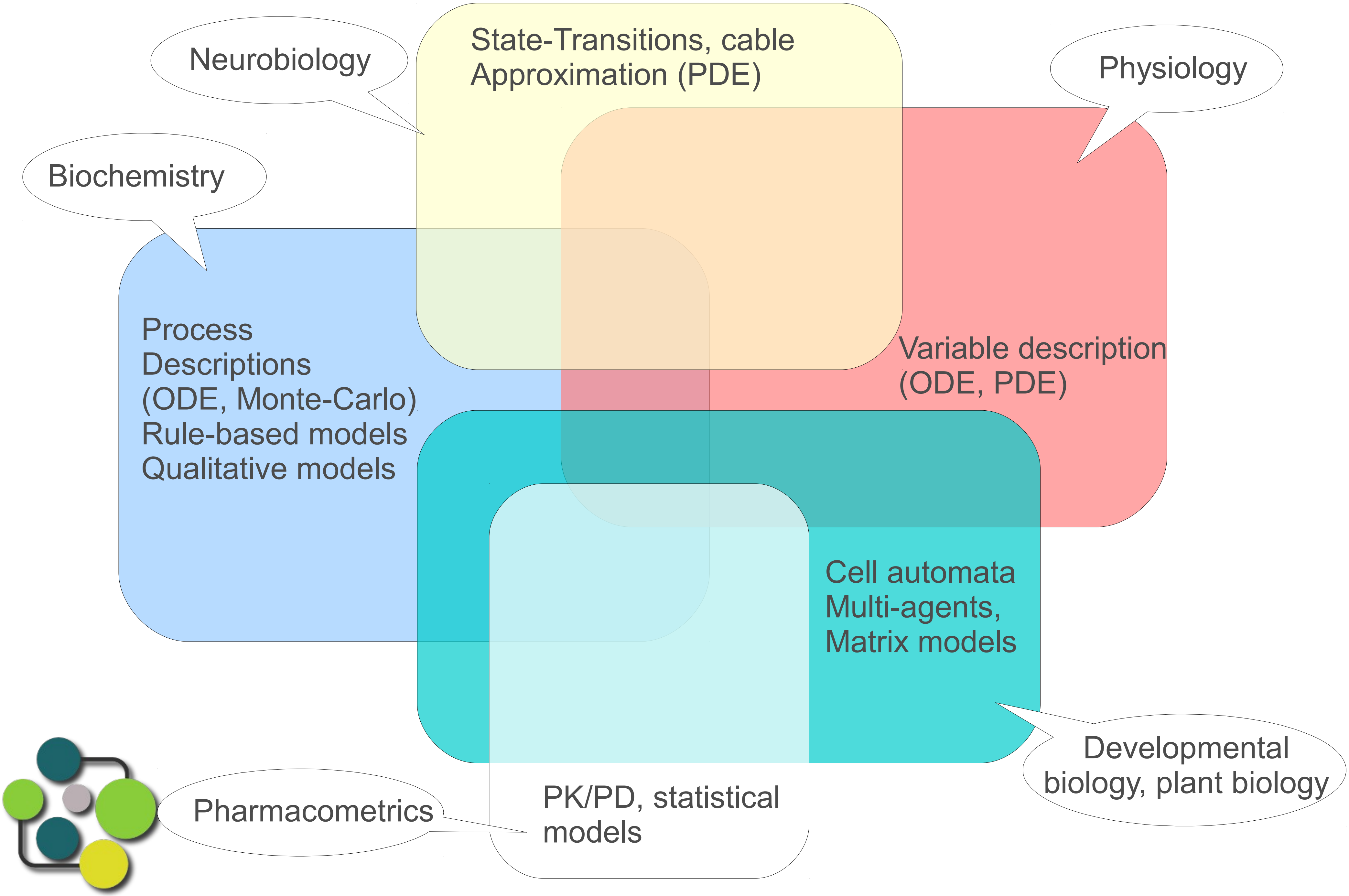
Open standards are more stable than proprietary formats

What are standards good for (3)?



Open standards can be built on. They generate new science

Many alternative modelling approaches



Neurobiology

State-Transitions, cable
Approximation (PDE)

Physiology

Biochemistry

Process
Descriptions
(ODE, Monte-Carlo)
Rule-based models
Qualitative models

Variable description
(ODE, PDE)

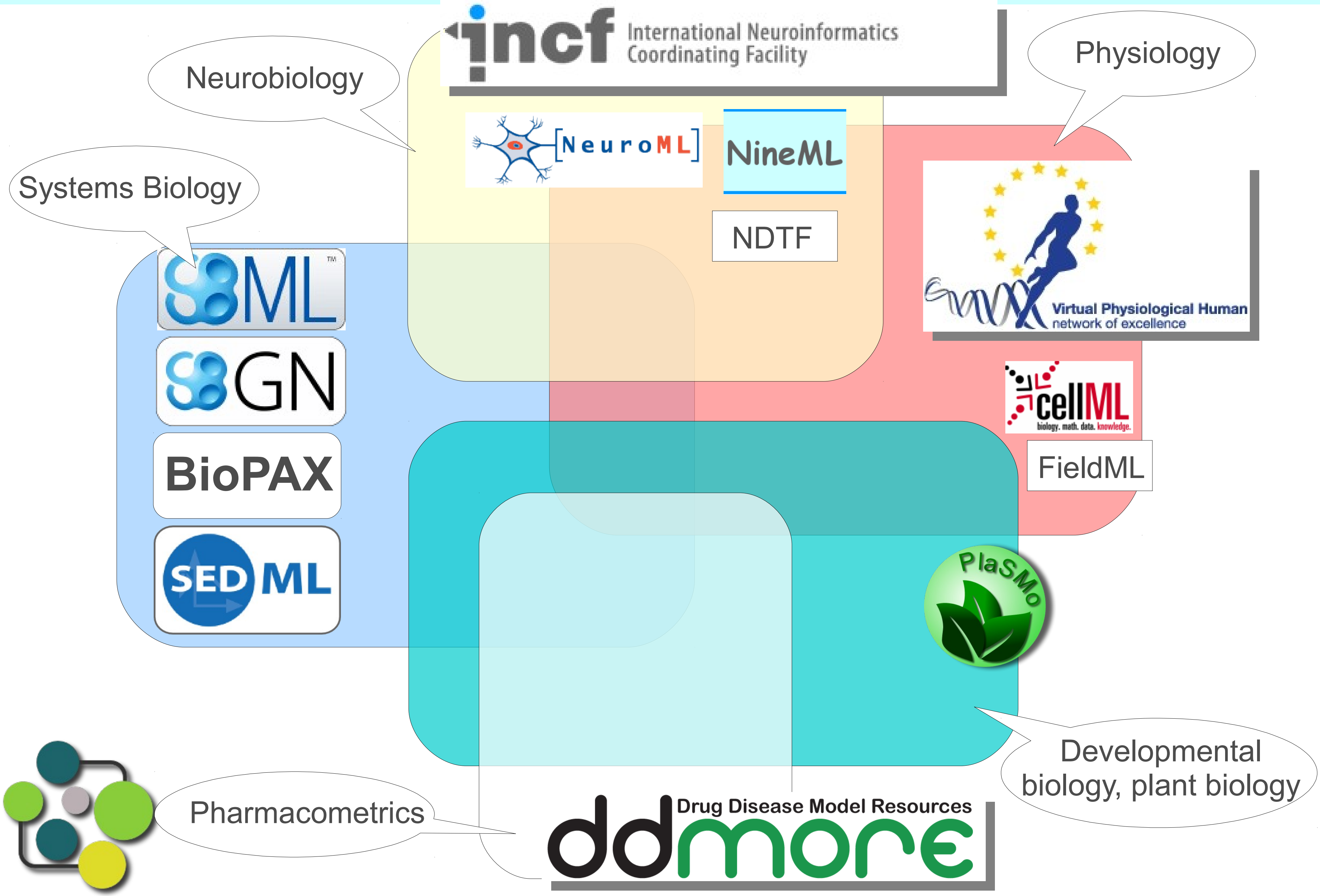
Cell automata
Multi-agents,
Matrix models

Developmental
biology, plant biology

Pharmacometrics

PK/PD, statistical
models

Parallel and redundant efforts



Neurobiology

incf International Neuroinformatics Coordinating Facility

NeuroML

NineML

NDTF

Physiology

Virtual Physiological Human network of excellence

cellML biology. math. data. knowledge.

FieldML

Systems Biology

SBML™

SBGN

BioPAX

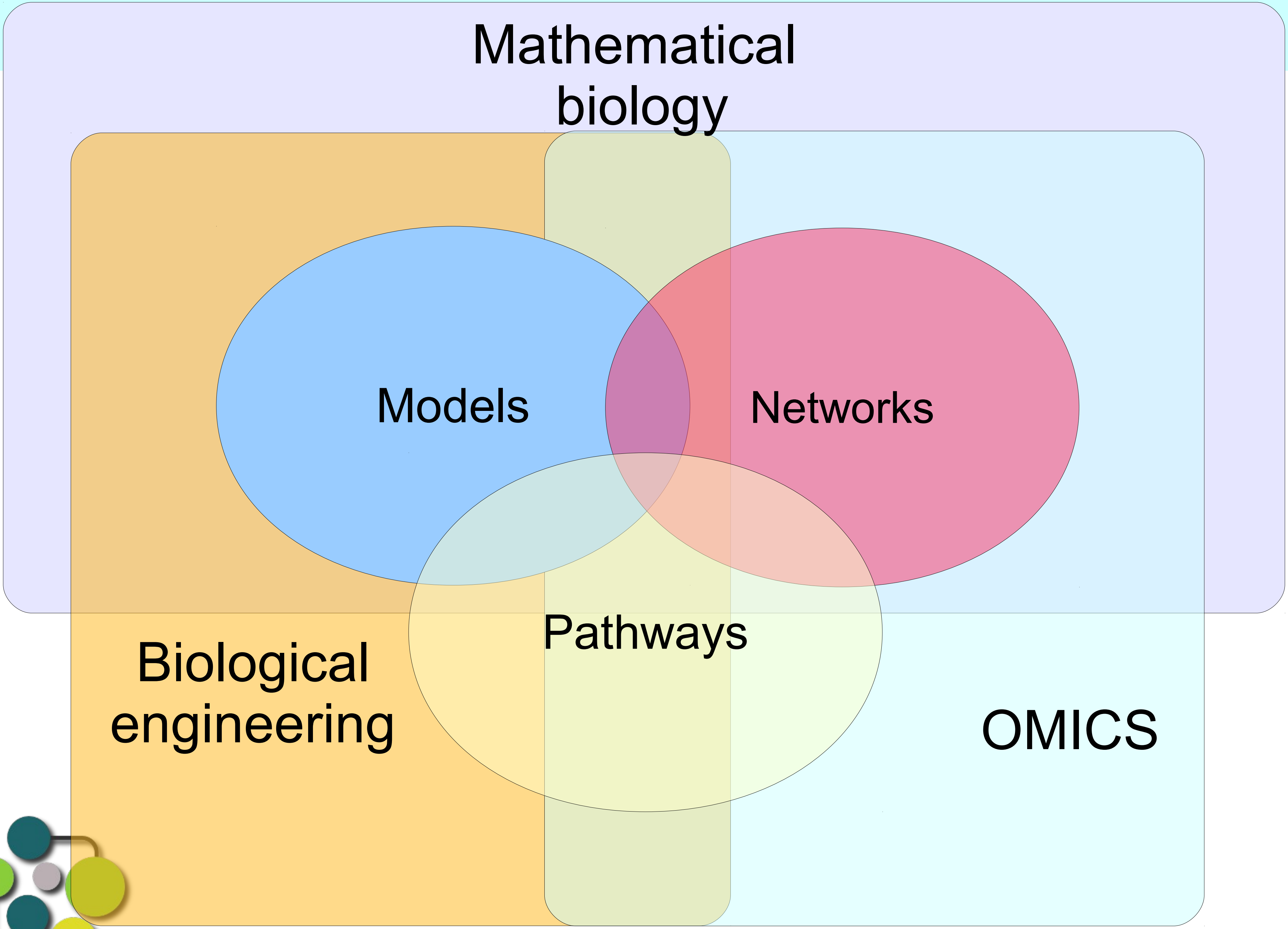
SED ML

PlaSMo

Developmental biology, plant biology

Pharmacometrics

ddmore Drug Disease Model Resources



Mathematical biology

Models

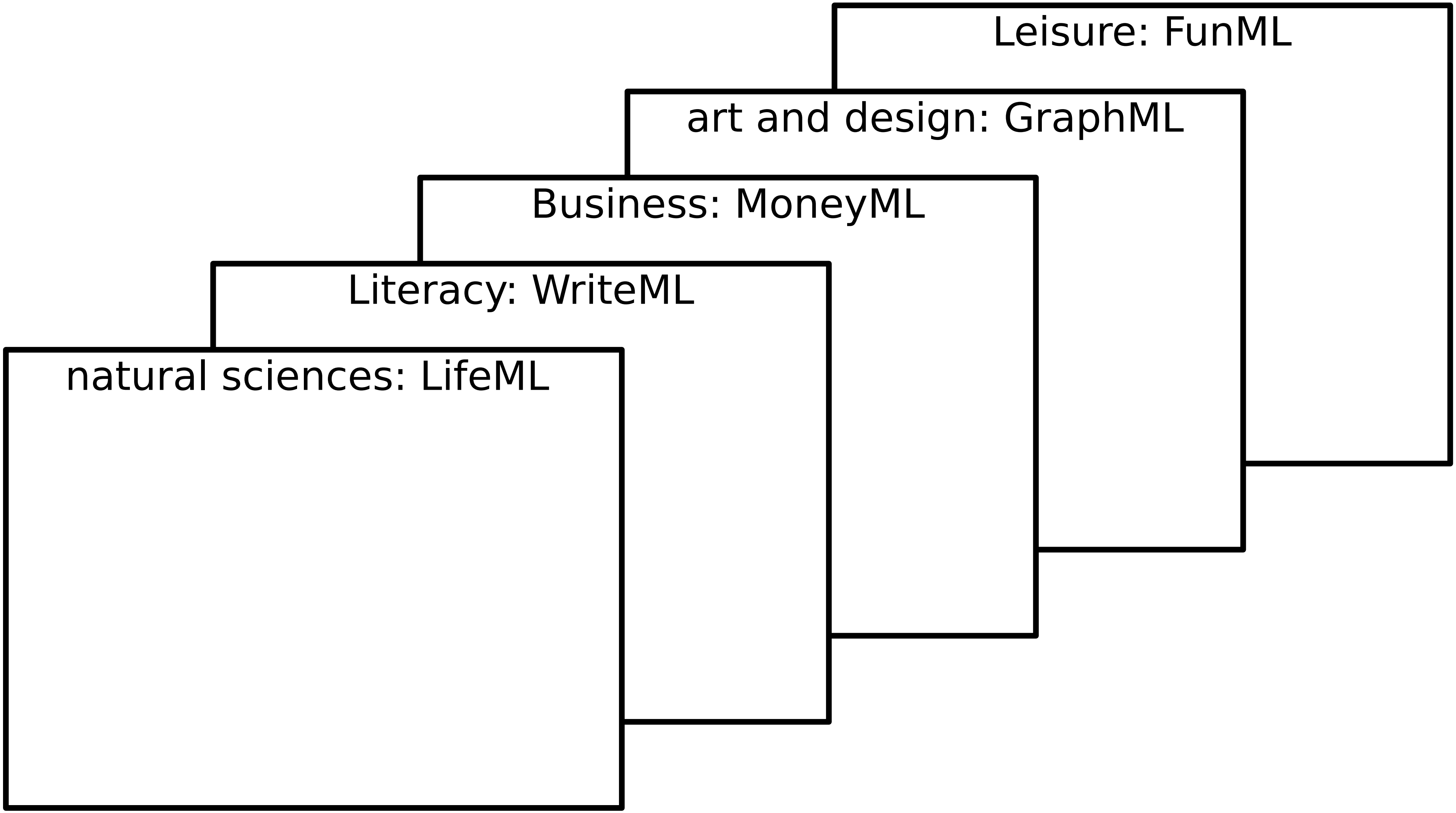
Networks

Pathways

Biological engineering

OMICS

What if the world-wide web was built like this?



Leisure: FunML

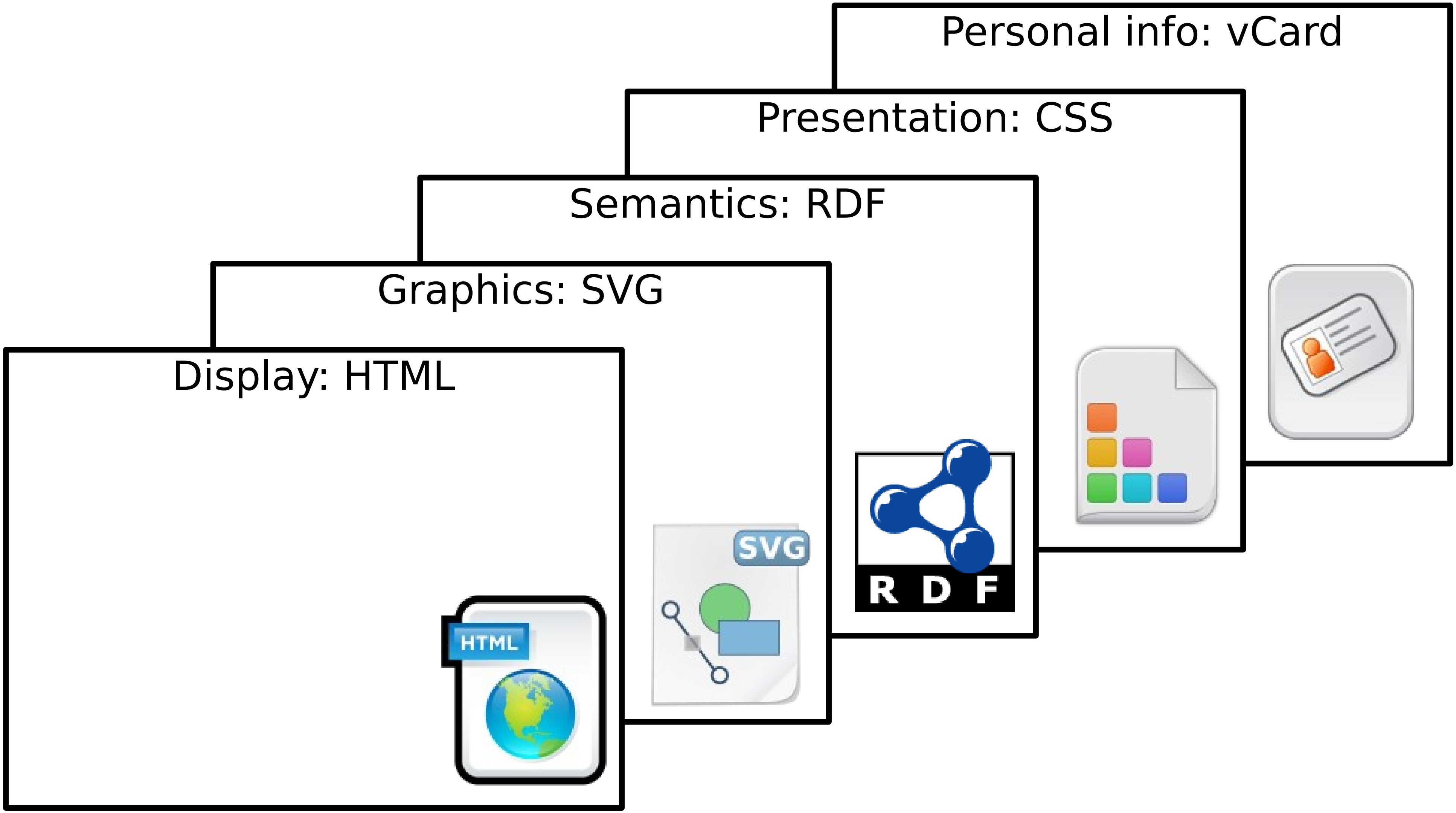
art and design: GraphML

Business: MoneyML

Literacy: WriteML

natural sciences: LifeML

The correct way to do it



Personal info: vCard

Presentation: CSS

Semantics: RDF

Graphics: SVG

Display: HTML

Overarching standardisation structure

the combine

computational modeling in biology network

The “WorldWide Web consortium” of modelling in biology

http://co.mbine.org/

Mission 1: Coordinating development of standards

	Model descriptions	Simulations and analysis	results
Minimal requirements	MIRIAM	MIASE	
Data-models	SBML™ SBGN cellML biology. math. data. knowledge.	SED ML	NuML
Terminologies	SBO	KISAO	TEDDY

Three types of COMBINE standards

- **CORE STANDARDS:** Efforts fulfilling COMBINE criteria and aiming at following COMBINE rules and interoperate with other COMBINE standards

SBML™ SED ML BioPAX SBGN cellML
biology. math. data. knowledge.

- **ASSOCIATED EFFORTS:** Standards that are not representation formats, but aiming at enrich or bridge the core standards

MIRIAM identifiers.org SBO KISAO

- **RELATED EFFORTS:** Formats developed by other communities, that complement or interoperate with COMBINE formats, and that we would like to see joining COMBINE or collaborating closely to COMBINE

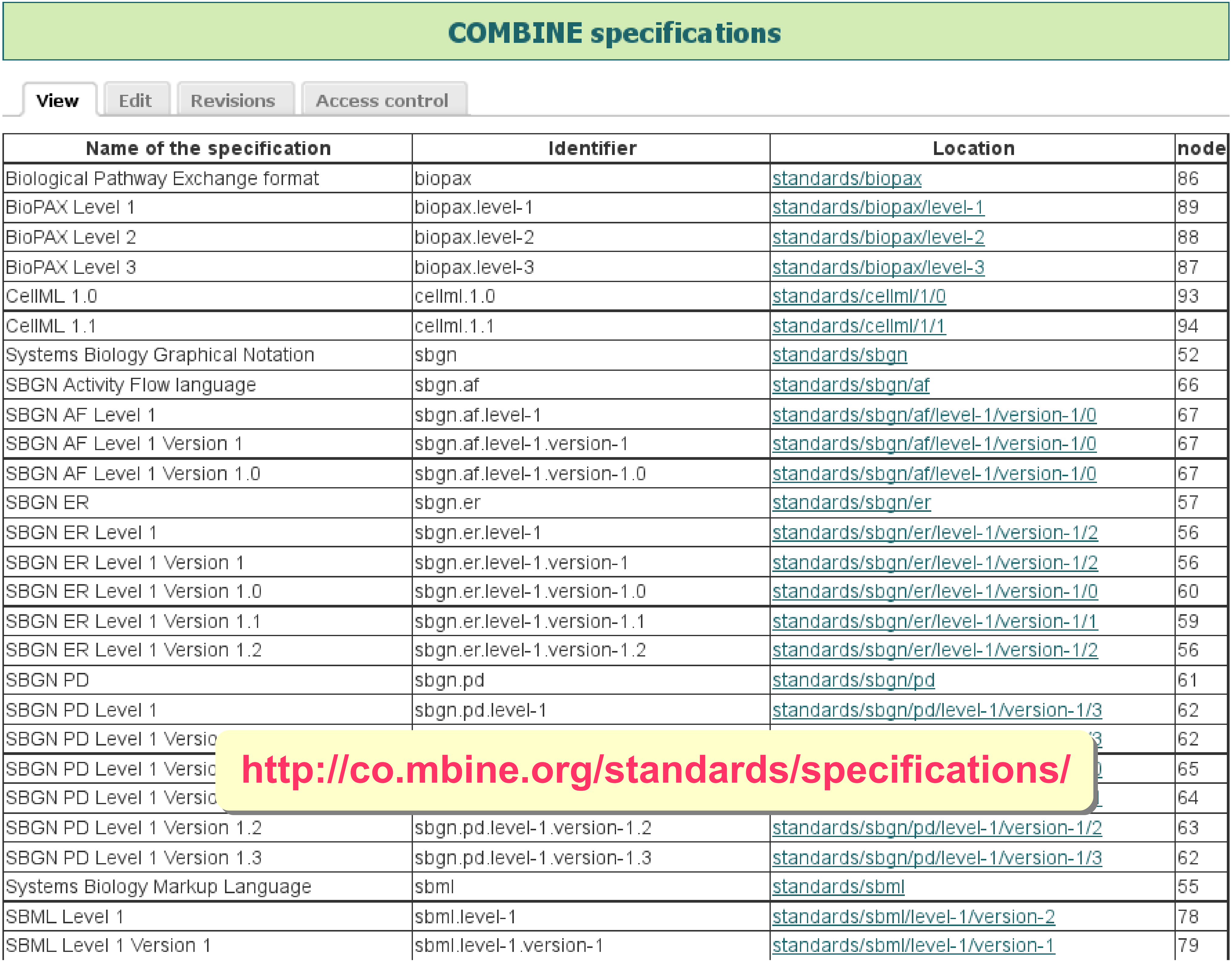
[NeuroML] **NuML** SBOL

NineML **FieldML** **PharmML** **PSI-MI**

COMBINE does NOT aim to take over the development of the standard formats, but to help coordinating and supporting this process

Format specification infrastructure

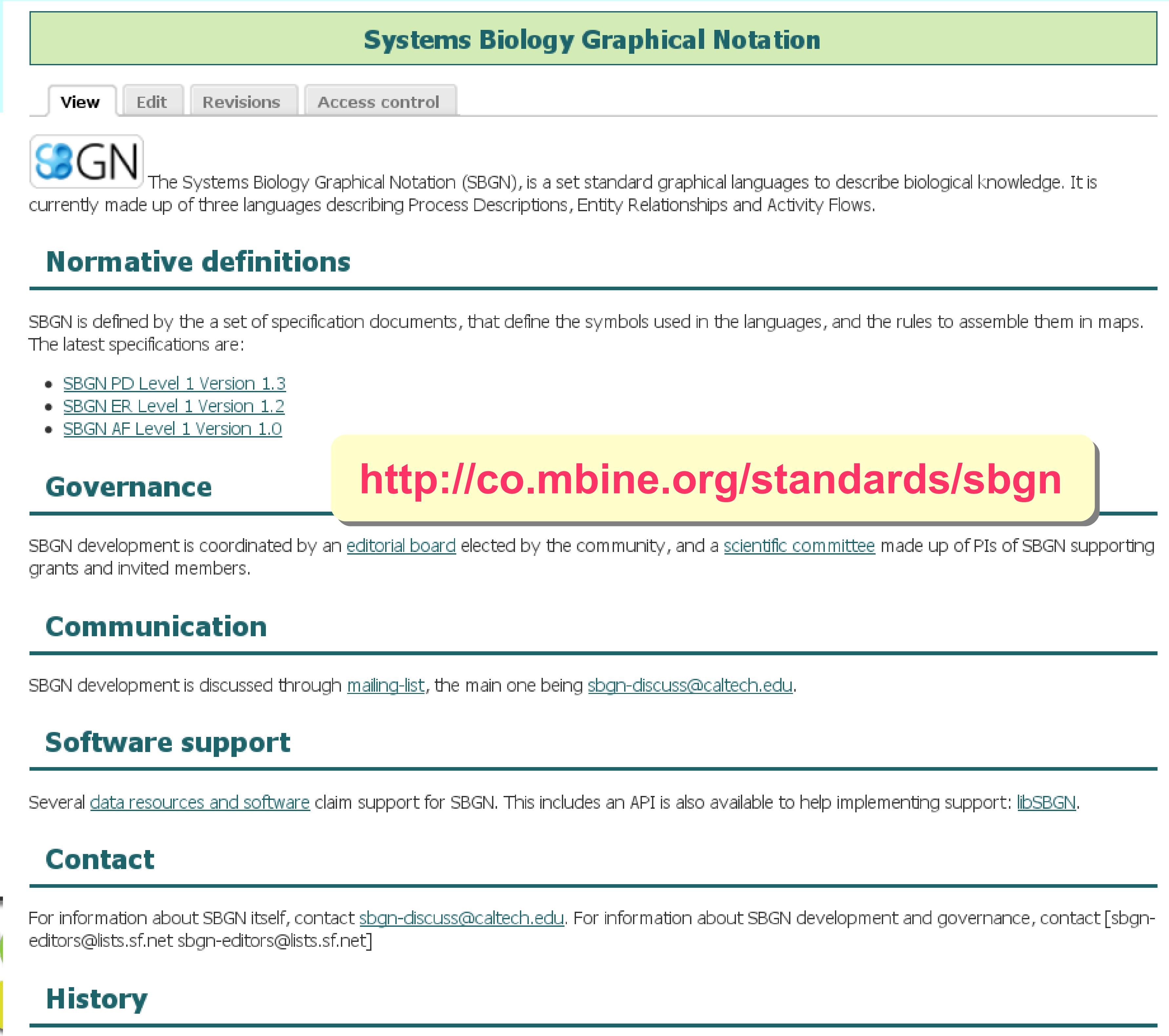
- Each format comes with many different flavors, described in many different specification documents.
- Format specifications are distributed in different ways, through different websites.
- The means of distribution for format specifications evolve over time, making hard to consistently refer to them.
- Trying to find reliable third parties proved difficult (e.g. Nature Precedings).
- We need a consistent way of naming specification documents



COMBINE specifications

Name of the specification	Identifier	Location	node
Biological Pathway Exchange format	biopax	standards/biopax	86
BioPAX Level 1	biopax.level-1	standards/biopax/level-1	89
BioPAX Level 2	biopax.level-2	standards/biopax/level-2	88
BioPAX Level 3	biopax.level-3	standards/biopax/level-3	87
CellML 1.0	cellml.1.0	standards/cellml/1/0	93
CellML 1.1	cellml.1.1	standards/cellml/1/1	94
Systems Biology Graphical Notation	sbgn	standards/sbgn	52
SBGN Activity Flow language	sbgn.af	standards/sbgn/af	66
SBGN AF Level 1	sbgn.af.level-1	standards/sbgn/af/level-1/version-1/0	67
SBGN AF Level 1 Version 1	sbgn.af.level-1.version-1	standards/sbgn/af/level-1/version-1/0	67
SBGN AF Level 1 Version 1.0	sbgn.af.level-1.version-1.0	standards/sbgn/af/level-1/version-1/0	67
SBGN ER	sbgn.er	standards/sbgn/er	57
SBGN ER Level 1	sbgn.er.level-1	standards/sbgn/er/level-1/version-1/2	56
SBGN ER Level 1 Version 1	sbgn.er.level-1.version-1	standards/sbgn/er/level-1/version-1/2	56
SBGN ER Level 1 Version 1.0	sbgn.er.level-1.version-1.0	standards/sbgn/er/level-1/version-1/0	60
SBGN ER Level 1 Version 1.1	sbgn.er.level-1.version-1.1	standards/sbgn/er/level-1/version-1/1	59
SBGN ER Level 1 Version 1.2	sbgn.er.level-1.version-1.2	standards/sbgn/er/level-1/version-1/2	56
SBGN PD	sbgn.pd	standards/sbgn/pd	61
SBGN PD Level 1	sbgn.pd.level-1	standards/sbgn/pd/level-1/version-1/3	62
SBGN PD Level 1 Versio		3	62
SBGN PD Level 1 Versio		0	65
SBGN PD Level 1 Versio		1	64
SBGN PD Level 1 Version 1.2	sbgn.pd.level-1.version-1.2	standards/sbgn/pd/level-1/version-1/2	63
SBGN PD Level 1 Version 1.3	sbgn.pd.level-1.version-1.3	standards/sbgn/pd/level-1/version-1/3	62
Systems Biology Markup Language	sbml	standards/sbml	55
SBML Level 1	sbml.level-1	standards/sbml/level-1/version-2	78
SBML Level 1 Version 1	sbml.level-1.version-1	standards/sbml/level-1/version-1	79

http://co.mbine.org/standards/specifications/



Systems Biology Graphical Notation

The Systems Biology Graphical Notation (SBGN), is a set standard graphical languages to describe biological knowledge. It is currently made up of three languages describing Process Descriptions, Entity Relationships and Activity Flows.

Normative definitions

SBGN is defined by the a set of specification documents, that define the symbols used in the languages, and the rules to assemble them in maps. The latest specifications are:

- SBGN PD Level 1 Version 1.3
- SBGN ER Level 1 Version 1.2
- SBGN AF Level 1 Version 1.0

http://co.mbine.org/standards/sbgn

Governance

SBGN development is coordinated by an editorial board elected by the community, and a scientific committee made up of PIs of SBGN supporting grants and invited members.

Communication

SBGN development is discussed through mailing-list, the main one being sbgn-discuss@caltech.edu.

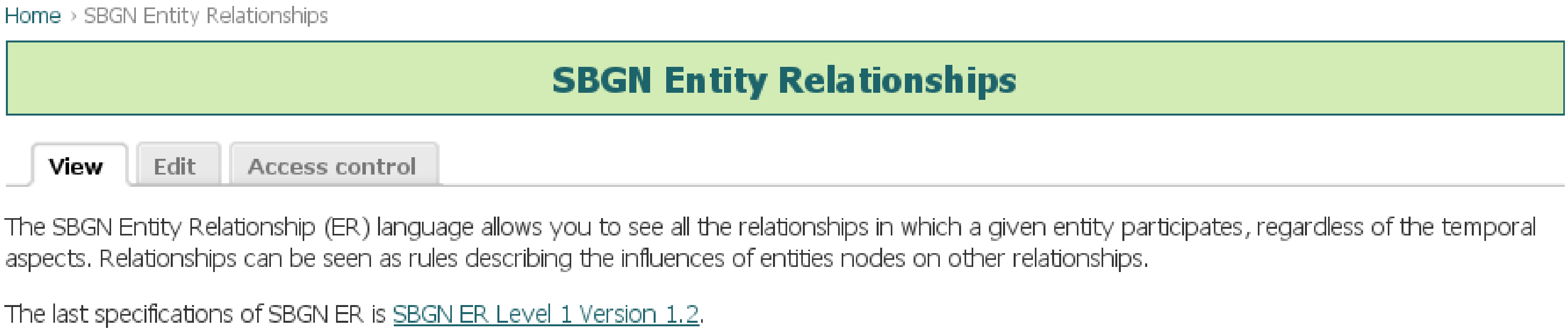
Software support

Several data resources and software claim support for SBGN. This includes an API is also available to help implementing support: libSBGN.

Contact

For information about SBGN itself, contact sbgn-discuss@caltech.edu. For information about SBGN development and governance, contact [sbgn-editors@lists.sf.net sbgn-editors@lists.sf.net]

History

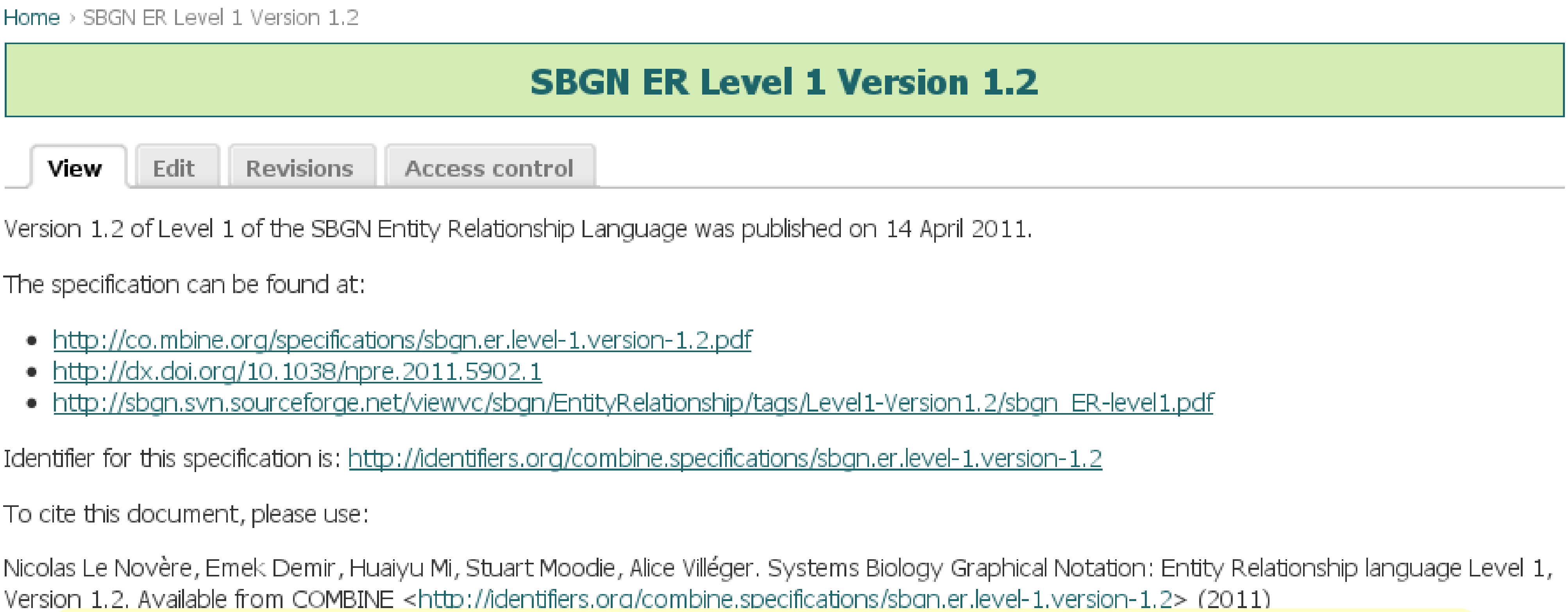


SBGN Entity Relationships

The SBGN Entity Relationship (ER) language allows you to see all the relationships in which a given entity participates, regardless of the temporal aspects. Relationships can be seen as rules describing the influences of entities nodes on other relationships.

The last specifications of SBGN ER is SBGN ER Level 1 Version 1.2.

http://co.mbine.org/standards/sbgn/er



SBGN ER Level 1 Version 1.2

Version 1.2 of Level 1 of the SBGN Entity Relationship Language was published on 14 April 2011.

The specification can be found at:

- http://co.mbine.org/specifications/sbgn.er.level-1.version-1.2.pdf
- http://dx.doi.org/10.1038/npre.2011.5902.1
- http://sbgn.svn.sourceforge.net/viewvc/sbgn/EntityRelationship/tags/Level1-Version1.2/sbgn_ER-level1.pdf

Identifier for this specification is: http://identifiers.org/combine.specifications/sbgn.er.level-1.version-1.2

To cite this document, please use:

Nicolas Le Novère, Emek Demir, Huaiyu Mi, Stuart Moodie, Alice Villéger. Systems Biology Graphical Notation: Entity Relationship language Level 1, Version 1.2. Available from COMBINE <http://identifiers.org/combine.specifications/sbgn.er.level-1.version-1.2> (2011)

http://co.mbine.org/standards/sbgn/er/level-1/version-1/2

So many meetings ...

BioPAX face 2 face

SBML forum

SBGN meeting

SBML hackathon

BioModels training camp

SuperHackathon

CellML workshop

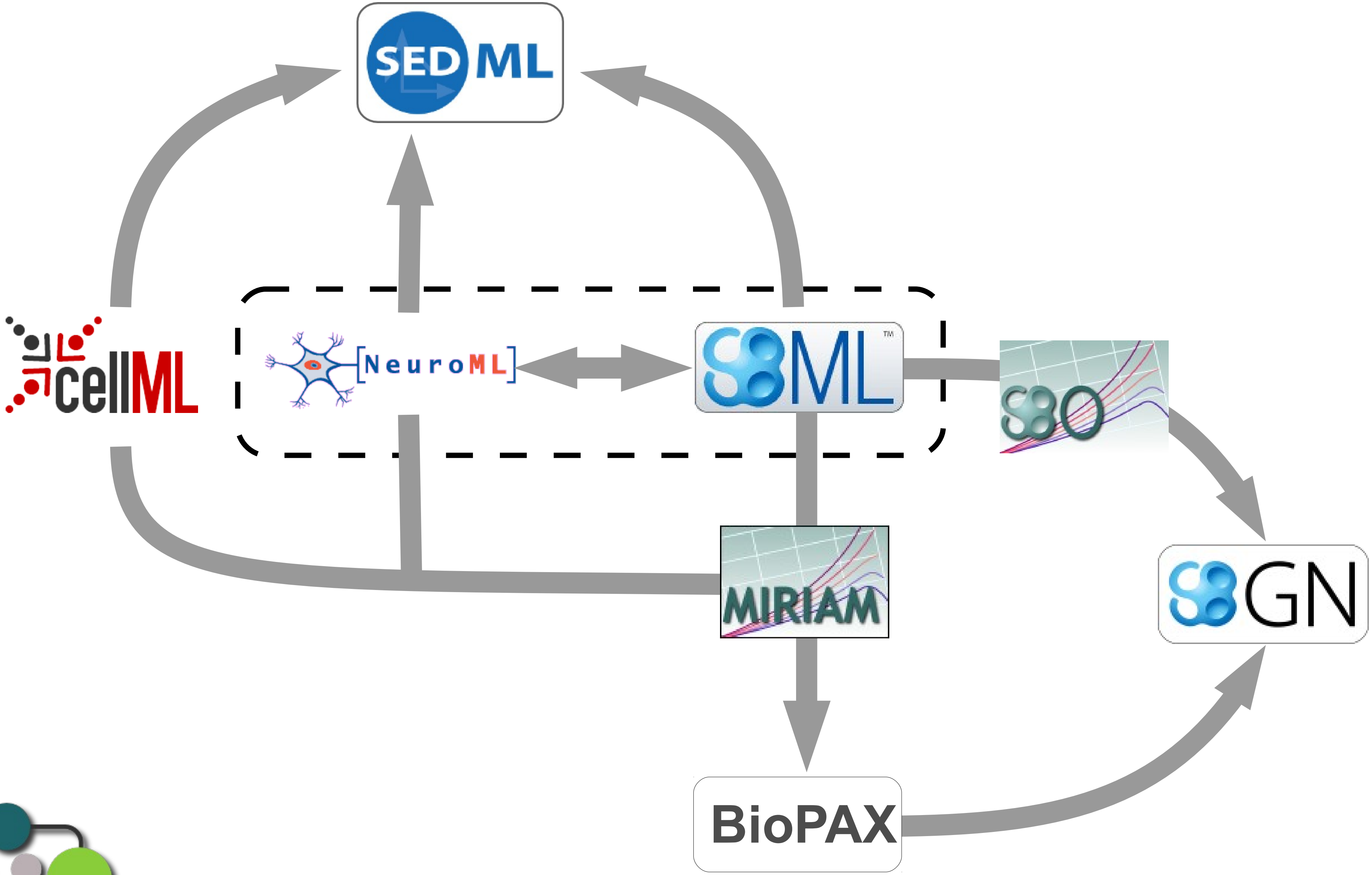
NeuroML workshop

Multiple involvements

Authors on several publications describing “our” standards:

Mirit Aladjem (BioPAX, SBGN), *Frank Bergmann* (SBGN, SED-ML), *Emek Demir* (BioPAX, SBGN), *Mélanie Courtot* (SBGN, SBO/KiSAO), *Andrew Finney* (BioPAX, SBML, SBO/KiSAO), *Igor Goryanin* (SBGN, SBML), *Stefan Hoops* (SBO/KiSAO, SED-ML), *Michael Hucka* (BioPAX, SBGN, SBML, SBO/KiSAO, SED-ML), *Peter Hunter* (CellML, SBML), *Nick Juty* (SBML, SBO/KiSAO), *Douglas Kell* (SBGN, SBO/KiSAO), *Hiroaki Kitano* (SBML, SBGN), *Fedor Kolpakov* (SBGN, SED-ML), *Nicolas Le Novère* (BioPAX, SBGN, SBML, SBO/KiSAO, SED-ML), *Pedro Mendes* (SBML, SBO/KiSAO), Huaiyu Mi (BioPAX, SBGN), *David Nickerson* (CellML, SED-ML), *Poul Nielsen* (CellML, SBML), *Sven Sahle* (SBGN, SED-ML), *Herbert Sauro* (SBGN, SBML), *Jacky Snoep* (SBGN, SBO/KiSAO), *Alice Villéger* (SBGN, SBO/KiSAO), *Dagmar Waltemath* (SBO/KiSAO), *Sarala Wimalaratne* (BioPAX, SBGN, SBO/KiSAO) ....

Interoperable standards = coupled development



Mission 2: Coordinating meetings

COMBINE coordinate the organisation of common meetings, where developers of all standards and related tools can gather together:

- Efficient collaboration and synergy
- Money saving
- Time saving

http://co.mbine.org/events

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

COMBINE Annual forum

Workshop-style event with oral presentations plus discussion, poster and breakout sessions. It is aimed at further developing the standards. The meetings cover the COMBINE standards and associated or related standardization efforts. The participants are everyone wishing to participate to the development of the standards.

- COMBINE 2010: October 6–9, Edinburgh, UK
- COMBINE 2011: September 3-7, Heidelberg, DE
- COMBINE 2012: August 15-19, Toronto, CA
- COMBINE 2013: September 16-20, Paris, FR
- COMBINE 2014: Los Angeles, USA

HARMONY hackathons

Hackathon-type meetings, with a focus on development of the support for standards, their interoperability and software infrastructure. Focus is not on general discussions or oral presentations but hands-on hacking and interaction between people focused on practical development of standards and supporting software. The participants are generally developers.

- HARMONY 2011: April 18-22, New-York City, USA
- HARMONY 2012; May 21-25, Maastricht, NL
- HARMONY 2013: May 20-23, Farmington, USA
- HARMONY 2014: April 20-15, Manchester, UK
- HARMONY 2015: Wittenberg, DE

End-user meetings

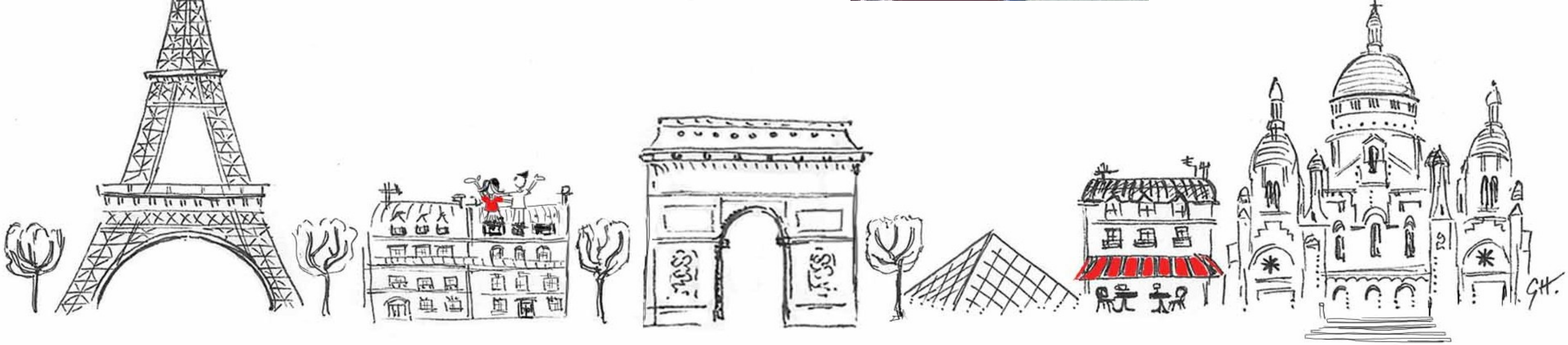
Attached to major scientific events such as the ICSB, COMBINE meetings are organised to communicate with scientists who benefit from our standards, primarily through their software tools. Those meetings are made up of tutorials, demo and non-technical presentations.

- Satellite of ICSB 2013: Copenhagen = You!
- Satellite of ICSB 2014: Melbourne

COMBINE forum 2013

institutCurie

- September 16 to 20
- Institut Curie, Paris
- Registration deadline: <u>September 9th</u>
- http://co.mbine.org/events/COMBINE_2013
- Local organiser: Eric Bonnet



Thank-you

BioPAX, CellML, SBML, SED-ML editors

Developers of related ontologies and software

Organisers of meetings and efforts to support our standards

The community of Computational Systems Biology

NIGMS

EMBL

BBSRC
bioscience for the future

NEDO

elixir

cnrs

MEMORIAL SLOAN-KETTERING CANCER CENTER
ESTABLISHED 1884

ENFIN
Enabling Systems Biology

CAM

UCONN HEALTH CENTER

Netherlands Consortium for
Systems Biology

nbic
netherlands
bioinformatics
centre

Universiteitsfonds Limburg
| SWOL |

OntarioGenomicsInstitute

OICR
Ontario Institute
for Cancer Research

UM
Maastricht
University

National
Human Genome
Research Institute

INSTITUT DES
SYSTEMES
COMPLEXES
ISC
PARIS ÎLE DE FRANCE

HITS

virtual liver
network

DFG

FONDATION
PIERRE-GILLES
DE GENNES
POUR LA RECHERCHE