



Heidelberg Institute for
Theoretical Studies



The NormSys Registry For Modeling Standards in Systems and Synthetic Biology

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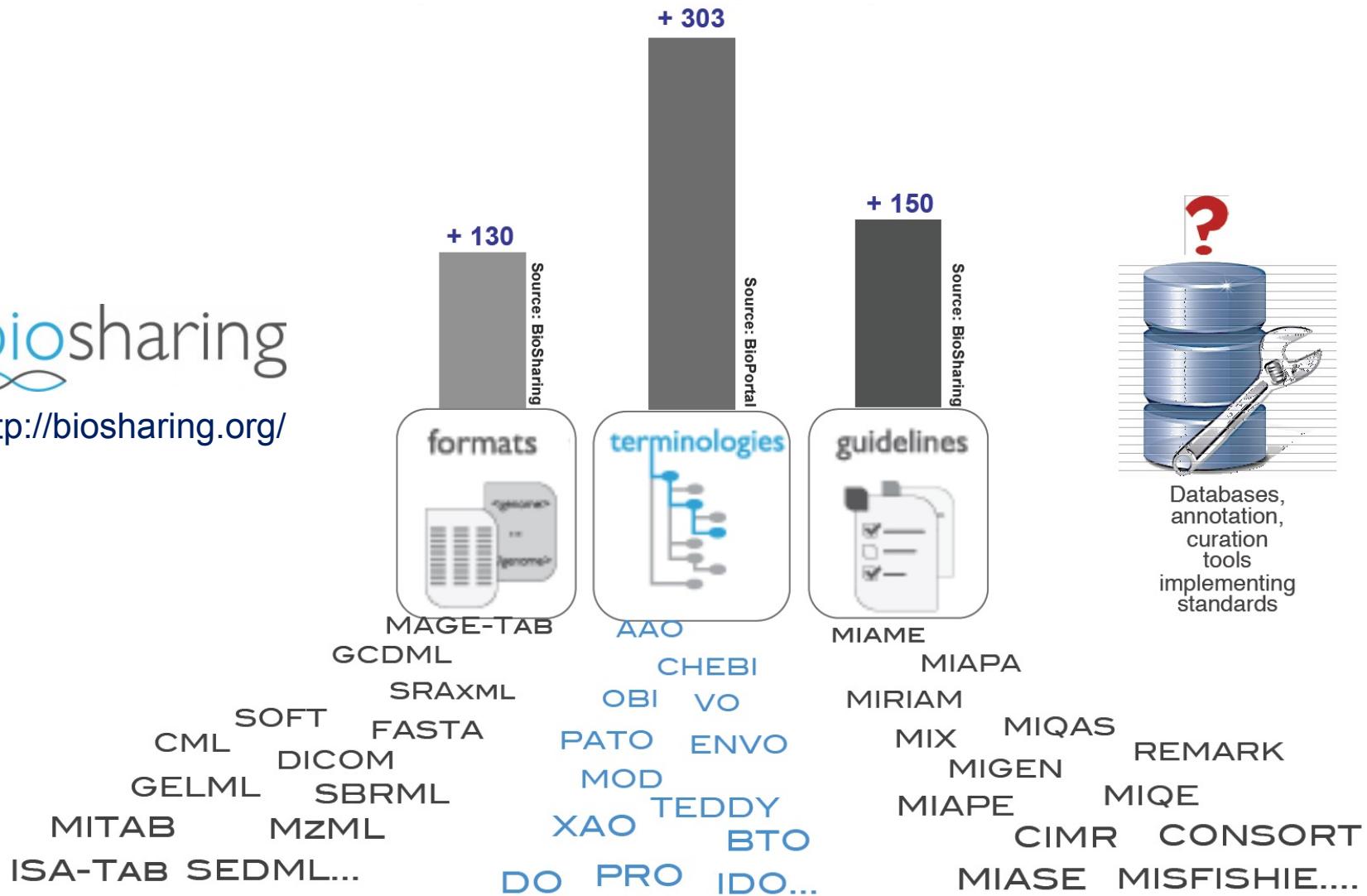
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De-facto Standards in Biology & Biotechnology



<http://biosharing.org/>



Supported by:

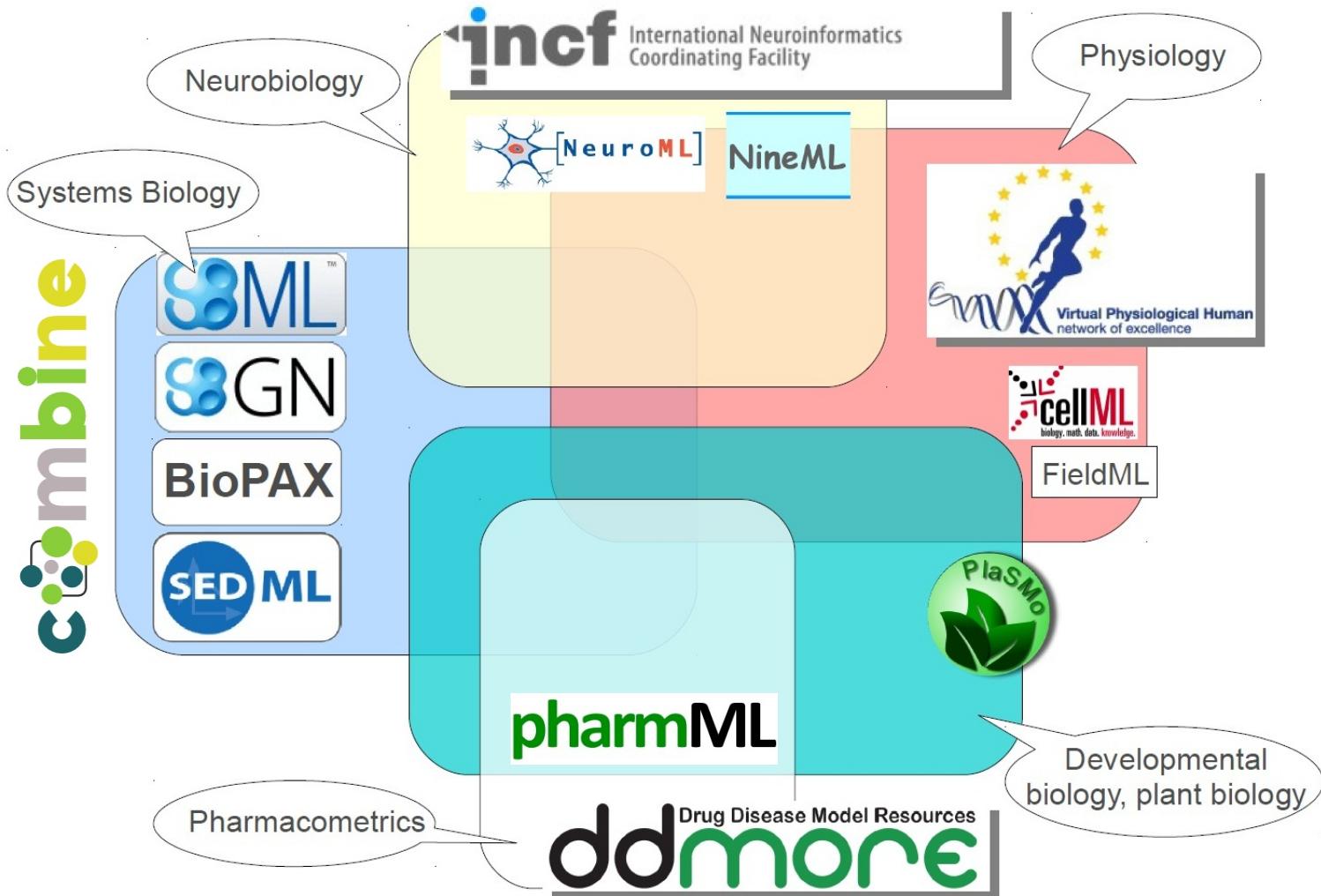


Source: Susanna-Assunta Sansone (University of Oxford, UK)



NORMSYS

Community Modelling Standards in Different Fields



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Source: Nicolas Le Novère (Babraham Institute, Cambridge, UK)



So many standards...

HOW STANDARDS PROLIFERATE:

(SEE: A/C CHARGERS, CHARACTER ENCODINGS, INSTANT MESSAGING, ETC)

SITUATION:
THERE ARE
14 COMPETING
STANDARDS.

14?! RIDICULOUS!
WE NEED TO DEVELOP
ONE UNIVERSAL STANDARD
THAT COVERS EVERYONE'S
USE CASES.

YEAH!



SOON:

SITUATION:
THERE ARE
15 COMPETING
STANDARDS.

NormSys – Project Aims and Challenges

- Identification and **classification** of modelling standards
- Transfer from **grassroots** to **approved standards**
- Bring together all stakeholders
 - Standard developers providing the standards → **YOU**
 - Research initiatives and **industries** using and applying the standards
 - Publishers and **Journals** distributing (standardized) data and models
 - Funders having interest in sustainability and reuse of scientific results
 - Standardization bodies providing support for the standardization process
- How to **publish** and **distribute** the standards?
- How to **convince** the communities to apply standards?
- How to **certify** implementation of standards?



<http://www.normsys.org>

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NormSys Registry for Modelling Standards

- **Information** resource for community standards
- **Comparison** of their main characteristics and features
- **Classification** by fields of application (with examples)
- **Transformation** options between the standards
- **Bundled links** to corresponding web resources: specifications, websites, publications, repositories, APIs...
- Direct links to **validation** tools for models
- **Faceted browsing** and search by different criteria
- Initial focus on commonly used community standards: COMBINE standards and related efforts

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The NormSys Registry for Modeling Standards

This registry aims at surveying standard formats for computational modeling in biology. It not only lists the standards, but also compares their major features, their possible fields of biological application and use cases (including model examples), as well as their relationships, commonalities and differences. This registry provides a common entry point for modelers and software developers who plan to apply the standards for their respective case of application, and serves them with detailed information and links to the standards, their specifications and APIs.

The information provided in this system does not claim to be complete or all-encompassing, nor can we guarantee any absence of defectiveness. However, we collect and assemble the information to the best of our knowledge and belief to assist in selecting the appropriate standard format for your specific requirements. Please note that the system is work in progress and is constantly revised and extended. Any feedback and suggestions for corrections or improvements, as well as for new fields of applications to be included (with example models) are highly welcome.

<http://normsys.h-its.org/>

Format Classes

Systems Biology Markup Language (SBML)

[Formats](#)[Details](#)

CellML

[Formats](#)[Details](#)

Systems Biology Graphical Notation (SBGN)

[Formats](#)[Details](#)

Simulation Experiment Description Markup Language (SED-ML)

[Formats](#)[Details](#)

Pharmacometrics Markup Language (pharmML)

[Formats](#)[Details](#)

NeuroML

[Formats](#)[Details](#)

FieldML

[Formats](#)[Details](#)

Synthetic Biology Open Language (SBOL)

[Formats](#)[Details](#)

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Show results for:

Select

Format

or filter by

Format class

✓ CellML

FieldML

NeuroML

Pharmacometrics Markup Language (pharmML)

Simulation Experiment Description Markup Language (SED-ML)

Synthetic Biology Open Language (SBOL)

Systems Biology Graphical Notation (SBGN)

Systems Biology Markup Language (SBML)

Software

Api language

Supported biological scale

molecular

cellular

tissue

Standard Formats

Displaying: 1 Found: 1 Total: 16

CellML 1.1

CellML 1.1

Synopsis

describes models as a network of components, representing abstract concepts, that are connected through well-defined Interfaces.

CellML-based exchange format developed by the University of Auckland in collaboration with Physiome Sciences, Inc. CellML 1.1 has a modular architecture allowing a modeller to build complex systems of models that expand and reuse previously published models. CellML is a standard XML-based format for encoding contextual information for a model. CellML 1.1 can be used in conjunction with CellML Metadata to provide a complete description of the structure and underlying mathematics of biological models. A repository of over 200 electrophysiological, mechanical, signal processing and metabolic pathway models is available at www.cellml.org.*

*(Autumn A. Cuellar et al. SIMULATION December 2003 79: 740-747, doi:10.1177/0037549703040939)

	Biological Applications	Class	Details	License	Links	Transformations	APIs	Validator						
Format	Multi-organism Process	Cell Cycle	Signaling	Pharmacokinetic	Pharmacodynamics	Metabolic Process	Immune Response	Circadian Rhythm	Regulation of Gene Expression	Electrophysiology	Neuronal Network	Multicellular Organismal Process	Regulation of Growth	Predatory Behavior
CellML 1.1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

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Show results for:

Select

Format

or filter by

Format class

 Systems Biology Markup Language (S*

Biological application

Modeling formalism

Software

Api language

Supported biological scale

- molecular
- cellular
- tissue
- organ
- organism
- ecosystem

Spatial representation

- Compartment
- Dimensions

Standard Formats

Displaying: 1 Found: 1 Total: 16

SBML L3V1 Core

Systems Biology Markup Language Level 3 Version 1 Core

Synopsis

Representation of biological processes as a set of processes, that are converting pools of entities into other pools entities.

Description

Systems Biology Markup Language (SBML), a free, open, XML-based format for representing biochemical reaction networks. SBML is a software-independent language for describing models common to research in many areas of computational biology, including cell signaling pathways, metabolic pathways, gene regulation, and others.*

*(M. Hucka et al. Bioinformatics (2003) 19 (4): 524-531)

[Biological Applications](#) [Class](#) [Details](#) [License](#) [Links](#) [Transformations](#) [APIs](#) [Validator](#)

Publication Date

© 10/2010

Authors

 Hucka, Michael
 Sahle, Sven

 Bergmann, Frank
 Schaff, James

 Hoops, Stefan
 Smith, Lucian

 Keating, Sarah
 Wilkinson, Darren

Organizations

- combine

Biological Scales

Scale	molecular	cellular	tissue	organ	organism	ecosystem
Support	intrinsic	potential	potential	unknown	unknown	potential



Spatial representation

- Compartment
- Dimensions
- Gradients
- SpatialStructures

Support for Units

Filter

Support

intrinsic

potential

potential

unknown

unknown

potential

Spatial Representation

Spatial Representation Level	Compartment	Dimensions	Gradients	SpatialStructures
Support	intrinsic	intrinsic	unknown	unknown

[Modeling Formalisms](#) for this format

[Software support](#) for this format

[Examples](#) for this format

Advantage

- Multiscale Models 

Modularity:

no

Components Relation
Flat Network:

no

Supported Math

MathML Support:

yes

Full MathML Support:

no

Unit Support

Unit Required:

no

Support:

intrinsic

Description

units are more like a form of annotation; every transformation of values implied by units must be encoded explicitly

Annotation Support

Miriram Support:

yes

identifiers.org Support:

yes



Spatial representation

- Compartment
- Dimensions
- Gradients
- SpatialStructures

Support for Units

Filter

Support	Intrinsic	potential	potential	unknown	unknown	potential
---------	-----------	-----------	-----------	---------	---------	-----------

Spatial Representation

Spatial Representation Level	Compartment	Dimensions	Gradients	SpatialStructures
Support	Intrinsic	Intrinsic	unknown	unknown

Multiscale Models

Models that are capable to integrate multiple biological scales at once.

antage

Multiscale Models 

Modularity:

no

Components Relation

Flat Network:

no

Supported Math

MathML Support:

yes

Full MathML Support:

no

Unit Support

Unit Required:

no

Support:

intrinsic

Description

units are more like a form of annotation; every transformation of values implied by units must be encoded explicitly

Annotation Support

Miriram Support:

yes

identifiers.org Support:

yes



Show results for:

Select

Format

or filter by

Format class

Systems Biology Markup Language (f)

Biological application

Modeling formalism

Software

Api language

Supported biological scale

molecular

Standard Formats

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Biological Applications	Class	Details	License	Links	Transformations	APIs	Validator
Webpage	Specification			Publication			
	<ul style="list-style-type: none">SBML			<ul style="list-style-type: none">The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models.			
Model repository	Software Repository			<ul style="list-style-type: none">SBML Software Guide			



Show results for:

Select

Format

Standard Formats

Displaying: 1 Found: 1 Total: 16

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Biological Applications	Class	Details	License	Links	Transformations	APIs	Validator
SBML L3V1 Core	—	libAntimony CellDesigner Arcadia	—	—	SBML2SBGNML	—	—
CellML 1.1	libAntimony	—	—	—	—	—	—
SBGN PD L1 V1.3	—	—	—	—	—	—	—
NeuroML 2 beta 3	jNeuroML	—	—	—	—	—	—
SBOL v2.0	iBioSim	—	—	—	—	—	—
SBGN-ML 0.2	—	—	—	—	—	—	—

Software

Api language

Supported biological scale

- molecular
- cellular
- tissue
- organ
- organism
- ecosystem

Spatial representation

- Compartment

NORMSYS

Show results for:

Select

Software

libAntimony

or

Search by name

filter by

Formats

Biophysics v1.8.1
CellML 1.1
ChannelML v1.8.1
FieldML v0.5

(hold ctrl for multiple selection or to deselect)

Software

Displaying: 1 Found: 1 Total: 13

libAntimony

Formats

- [Systems Biology Markup Language Level 3 Version 1 Core](#)
- [CellML 1.1](#)

Links

Software

- [libAntimony](#)

Contact

Copyright

Imprint

About

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Output

Input

SBML L3V1 Core

CellML 1.1

SBGN PD L1 V1.3

NeuroML 2 beta 3

SBOL v2.0

SBGN-ML 0.2

SBML L3V1 Core

—

libAntimony

CellDesigner
Arcadia

jNeuroML

—
SBML2SBGNML

CellML 1.1

libAntimony

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SBGN PD L1 V1.3

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NeuroML 2 beta 3

jNeuroML

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SBOL v2.0

iBioSim

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SBGN-ML 0.2

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Biological Applications

Format Transformation



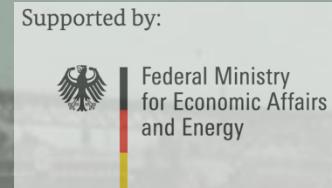
Biological Application	Format												Biological Applications		Format Transformation	
	SBML L3V1 Core	CellML 1.1	SBGN ER L1 V1.2	SBGN PD L1 V1.3	SBGN AF L1 V1.0	MorphML v1.8.1	NeuroML 2 beta 3	PharmML v0.6	SBOL v2.0	SBOL Visual v1.0.0	ChannelML v1.8.1	Biophysics v1.8.1	NetworkML v1.8.1			
Multi-organism Process	✓	✓	—	—	—	—	—	—	—	—	—	—	—	—	—	
Cell Cycle	✓	✓	✓	—	—	—	—	—	—	—	—	—	—	—	—	
Signaling	✓	✓	✓	✓	✓	—	—	—	—	—	—	—	—	—	—	
Single Cell Morphology	—	—	—	—	—	✓	✓	—	—	—	—	—	—	—	—	
Pharmacokinetic	✓	✓	—	—	—	—	—	✓	—	—	—	—	—	—	—	
Pharmacodynamics	✓	✓	—	—	—	—	—	✓	—	—	—	—	—	—	—	
Izhikevich-based Neuron Models	✓	—	—	—	—	—	✓	—	—	—	—	—	—	—	—	
Synthetic Gene Regulatory Network	✓	—	✓	✓	✓	—	—	—	✓	✓	—	—	—	—	—	
Metabolic Process	✓	✓	—	✓	—	—	—	✓	—	—	—	—	—	—	—	
Immune Response	✓	✓	—	—	✓	—	—	—	—	—	—	—	—	—	—	
Circadian Rhythm	✓	✓	✓	—	—	—	✓	—	—	—	—	—	—	—	—	
Regulation of Gene Expression	✓	✓	✓	✓	✓	—	—	—	✓	✓	—	—	—	—	—	
Electrophysiology	✓	✓	—	—	—	—	✓	—	—	✓	✓	✓	✓	—	—	

NormSys – Project Aims and Challenges

- Identification and **classification** of modelling standards
- Transfer from **grassroots** to **approved standards**
- Bring together all stakeholders
 - Standard developers providing the standards → **YOU**
 - Research initiatives and **industries** using and applying the standards
 - Publishers and **Journals** distributing (standardized) data and models
 - Funders having interest in sustainability and reuse of scientific results
 - Standardization bodies providing support for the standardization process
- How to **publish** and **distribute** the standards?
- How to **convince** the communities to apply standards?
- How to **certify** implementation of standards?



<http://www.normsys.org>



Research Communities

Develop and apply *de facto* community standards in grass-roots initiatives



Industries
Need certified
standards



Standardisation Bodies



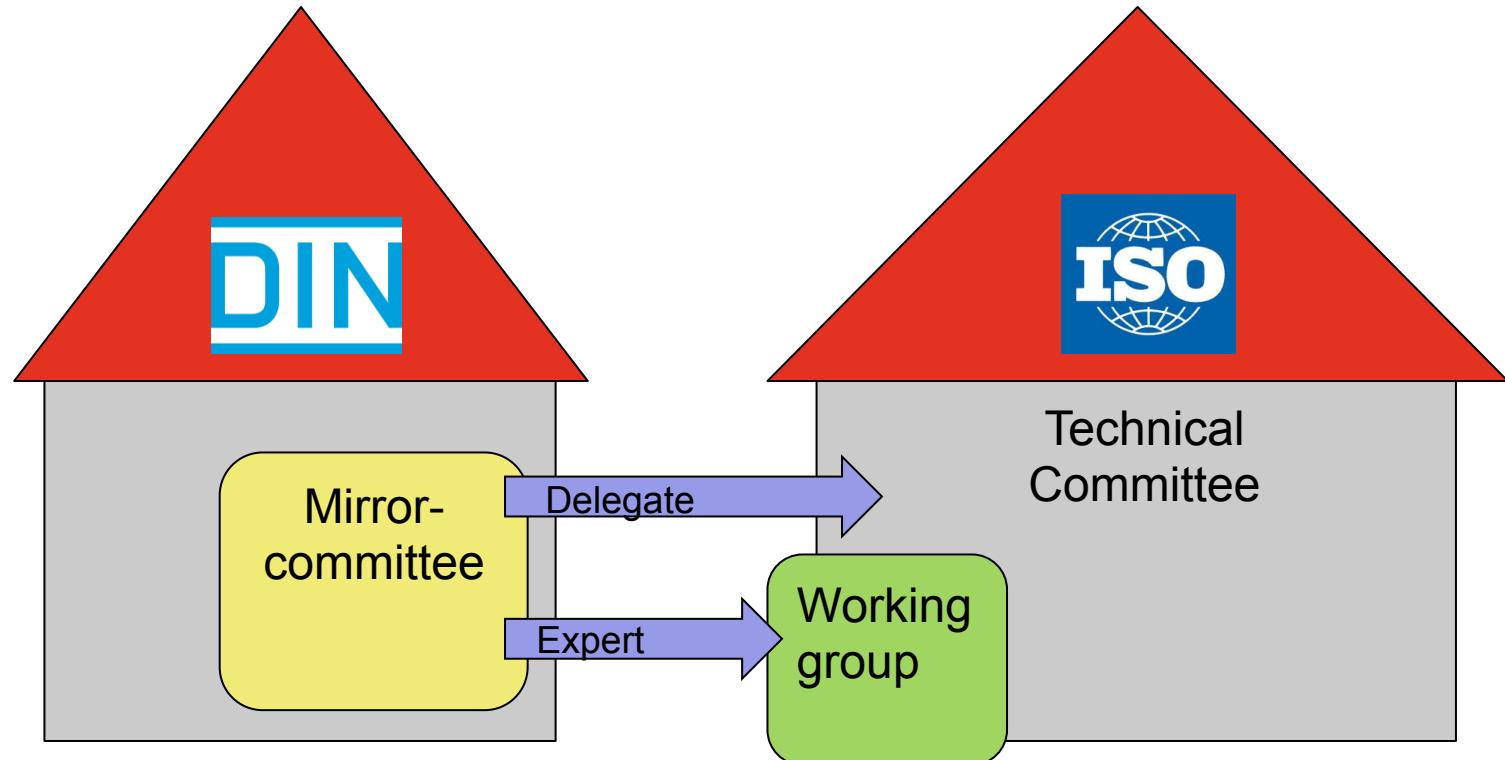
Help to distribute and promote standards



Standardisation Organizations



Standardisation Organisations: How do they work?



National

International

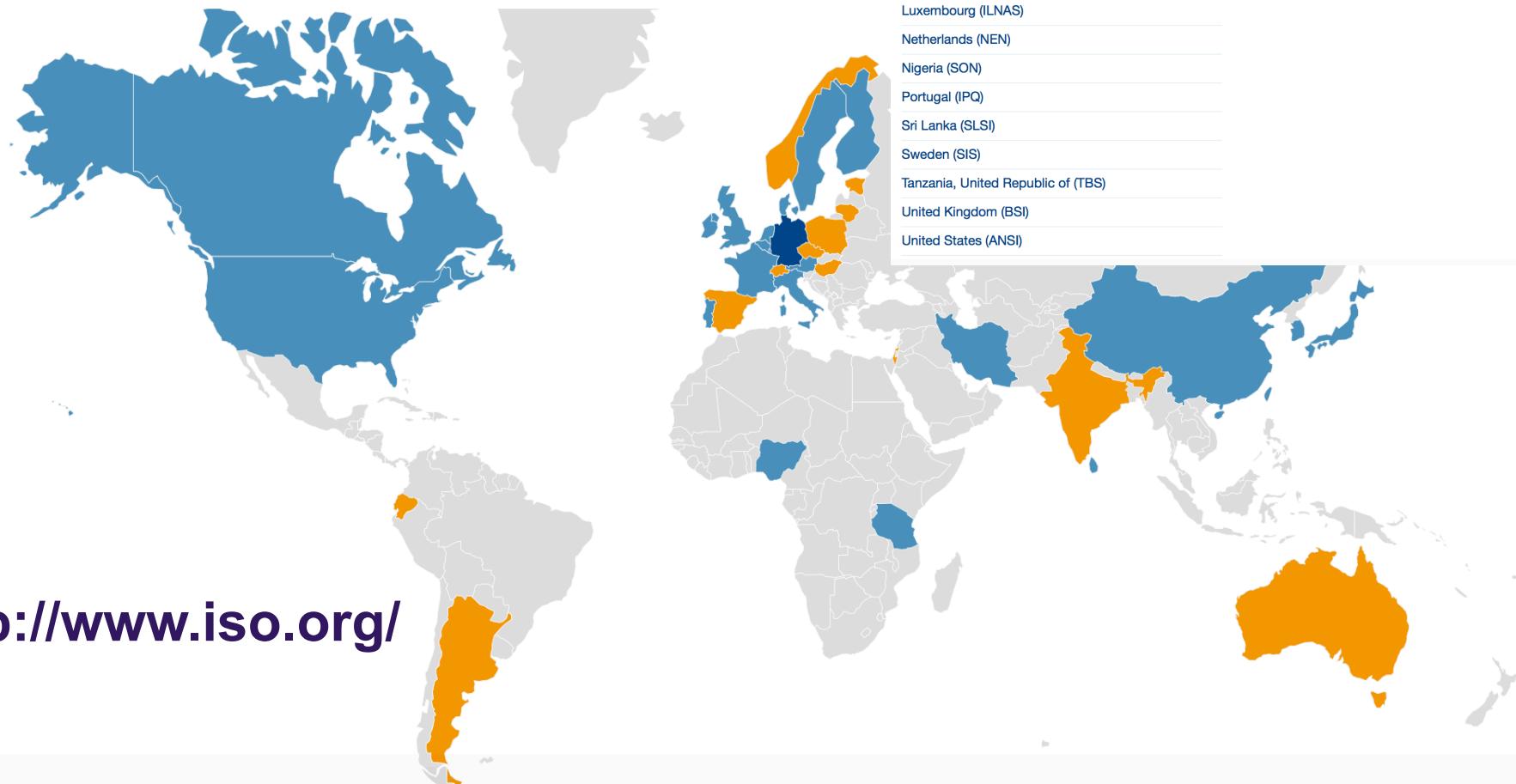
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Source: DIN – German Institute for Standardisation



ISO/TC 276 - Biotechnology



<http://www.iso.org/>

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ISO/TC 276 Biotechnology

[About](#)[Contact details](#)[Structure](#)[Liaisons](#)[Meetings](#)[Tools](#)

Subcommittees/Working Groups:

Subcommittee/Working Group	Title
ISO/TC 276/WG 1	Terminology Convenor: Pablo Serrano , BPI e.V. (Germany) <i>The convener can be reached through the secretariat</i>
ISO/TC 276/WG 2	Biobanks and bioresources Convenor: Georges Dagher , INSERM (France) <i>The convener can be reached through the secretariat</i>
ISO/TC 276/WG 3	Analytical methods Convenor: Sheng Lin-Gibson , NIST (USA) <i>The convener can be reached through the secretariat</i>
ISO/TC 276/WG 4	Bioprocessing Convenor: Tatsuo Heki , FUJIFILM (Japan) <i>The convener can be reached through the secretariat</i>
ISO/TC 276/WG 5	Data processing and integration Convenor: Martin Golebiewski , HITS (Germany) <i>The convener can be reached through the secretariat</i>

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HITS

Developing an ISO standard for applying and connecting community modelling standards

ISO/TC 276 Biotechnology WG 5 (Data Processing and Integration) has started to work on a draft for a new ISO standard in the life sciences:

„Minimal requirements for downstream data processing and integration workflows for interfacing and linking heterogeneous data, models and corresponding metadata“

Framework („hub“) standard making references to existing community standards:

- References to formats for processed life science data and computer models
- References to minimal reporting guidelines for data, models and metadata
- Definition of interfacing between data sets, models and metadata
- Standards for describing workflow elements and their interplay in modelling biological systems

Need for a meta-standard for standards

Example: Great Baltimore fire of 1904



Individual fire hydrants depending on region
with 600 variations of hose couplings
→ Need for a standard for general interfaces

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HITS



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Theoretical Studies



<http://normsys.h-its.org/>

Concept & project lead: Martin Golebiewski

Design: Jill Zander

Implementation: Nils Wötzel

Content: Martin Golebiewski, Alexander Nikolaew

Collaboration partners:

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Babette Regierer (LifeGlimmer GmbH, Berlin, D)



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