Describing the whole life-cycle of modelling in neuroscience

Models at the core of integrative systems bio/physio/neurobiology

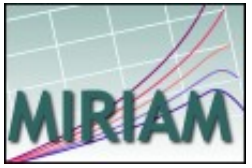
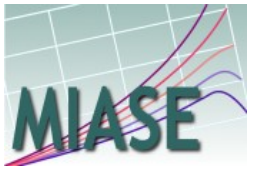
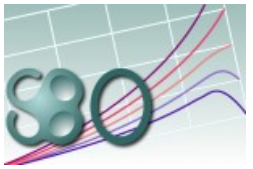
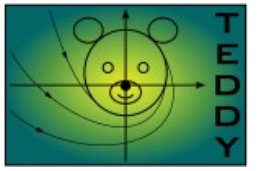
- As any kind of output from scientific research, models must be available to the scientific community: Results based on a model that is not distributed cannot be verified and falsified. This is not valid and useful science
- Computational models must be exchanged:
  computer storable and readable
- Computational models must be related to relevant experimental datasets:
  expressive relationships and robust links
- Computational models must be amenable to many different analyses:
  standard API
- Computational models must allow modification, split, merge:
  Encoded according a suitable design

Models at the core of integrative systems bio/physio/neurobiology

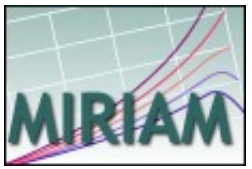
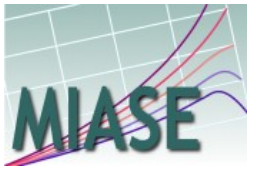
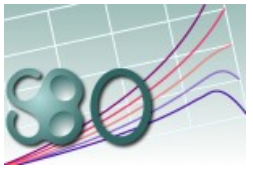
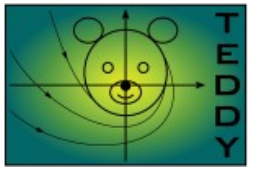
- As any kind of output from scientific research, models must be available to the scientific community: Results based on a model that is not distributed cannot be verified and falsified. This is not valid and useful science
- Computational models must be exchanged:
  computer storable and readable
- Computational models must be related to relevant experimental datasets:
  expressive relationships and robust links
- Computational models must be amenable to many different analyses:
  standard API
- Computational models must allow modification, split, merge:
  Encoded according a suitable design

➔ Standardisation is unavoidable!

A “complete” (?) mosaic of standards for Computational Systems Biology models

	Models	Simulation	Results
Minimal requirements			
Data-models			SBRML
Ontologies			

Model description

	Models	Simulation	Results
Minimal requirements			
Data-mode			SBRML
Ontologies			

Born in Tokyo

What is SBML?

The Systems Biology Markup Language is a way to **exchange and reuse** (and hopefully **interface**) descriptions of quantitative models in “Systems Biology”, in fact mostly well-stirred chemical kinetics so far.

It is not a procedural language.

It is not a programming language.

It is not a format for specific software configuration files

(only 3 of the 7 SBML founding software still in operation).

Tools are supposed to understand the whole of SBML but not obligatory make use of everything (will not be true for Level 3).

Development philosophy: Start small, get good support, extend.

SBML itself re-uses other standards: MathML, XHTML, RDF, existing ontologies.

It is supported by a community large, diverse, active and **evolving.**

Global structure of an SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="3" version="1"·
      xmlns="http://www.sbml.org/sbml/level3/version1/core">
  <model>
    <listOfFunctionDefinitions> <!-- --> </listOfFunctionDefinitions>
    <listOfUnitDefinitions> <!-- --> </listOfUnitDefinitions>
    <listOfCompartments> <!-- --> </listOfCompartments>
    <listOfSpecies> <!-- --> </listOfSpecies>
    <listOfParameters> <!-- --> </listOfParameters>
    <listOfInitialAssignments> <!-- --> </listOfInitialAssignments>
    <listOfRules> <!-- --> </listOfRules>
    <listOfConstraints> <!-- --> </listOfConstraints>
    <listOfReactions> <!-- --> </listOfReactions>
    <listOfEvents> <!-- --> </listOfEvents>
  </model>
</sbml>
```

Global structure of an SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="3" version="1"·
      xmlns="http://www.sbml.org/sbml/level3/version1/core">
  <model>
    <listOfFunctionDefinitions> <!-- --> </listOfFunctionDefinitions>
    <listOfUnitDefinitions> <!-- --> </listOfUnitDefinitions>
    <listOfCompartments> <!-- --> </listOfCompartments>
    <listOfSpecies> <!-- --> </listOfSpecies>
    <listOfParameters> <!-- --> </listOfParameters>
    <listOfInitialAssignments> <!-- --> </listOfInitialAssignments>
    <listOfRules> <!-- --> </listOfRules>
    <listOfConstraints> <!-- --> </listOfConstraints>
    <listOfReactions> <!-- --> </listOfReactions>
    <listOfEvents> <!-- --> </listOfEvents>
  </model>
</sbml>
```

variables

relationships

A very simple SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4">
  <model>
    <listOfCompartments>
      <compartment id="cell" />
    </listOfCompartments>
    <listOfSpecies>
      <species id="A" compartment="cell" initialConcentration="1"/>
      <species id="B" compartment="cell" initialConcentration="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="kon" value="1"/>
    </listOfParameters>
    <listOfReactions>
      <reaction>
        <listOfReactants>
          <speciesReference species="A" />
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="B" />
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times />
              <ci>kon</ci>
              <ci>A</ci>
              <ci>cell</ci>
            </apply>
          </math>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

Reusing existing standards

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4">
  <model>
    <listOfCompartments>
      <compartment id="cell" />
    </listOfCompartments>
    <listOfSpecies>
      <species id="A" compartment="cell" initialConcentration="1"/>
      <species id="B" compartment="cell" initialConcentration="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="kon" value="1"/>
    </listOfParameters>
    <listOfReactions>
      <reaction>
        <listOfReactants>
          <speciesReference species="A" />
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="B" />
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times />
              <ci>kon</ci>
              <ci>A</ci>
              <ci>cell</ci>
            </apply>
          </math>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

MathML

A more realistic example ...

```
<species·
    id="A"·
    name="a-tubulin"
    compartment="cell"
    initialAmount="1000"
    substanceUnits="item"
    hasOnlySubstanceUnits="true"
    boundaryCondition="true"
    constant="false"
    charge="0"
    metaid="PX"
    sboTerm="SBO:0000245" >
  <notes>
    <body xmlns="http://www.w3.org/1999/xhtml">
      <p>One of the components of a microtubule</p>
    </body>
  </notes>
  <annotation>
    <rdf:RDF·
        xmlns:bqbiol="http://biomodels.net/biology-qualifiers/"·
        xmlns:bqmodel="http://biomodels.net/model-qualifiers/"
        xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#">
      <rdf:Description rdf:about="#PX">
        <bqbiol:is>
          <rdf:Bag>
            <rdf:li rdf:resource="urn:miriam:uniprot:P68370"/>
            <rdf:li rdf:resource="urn:miriam:obo.go:GO%3A0045298"/>
          </rdf:Bag>
        </bqbiol:is>
      </rdf:Description>
    </rdf:RDF>
  </annotation>
</species>
```

Reusing existing standards again

XHTML

RDF

```
<species·
    id="A"·
    name="a-tubulin"
    compartment="cell"
    initialAmount="1000"
    substanceUnits="item"
    hasOnlySubstanceUnits="true"
    boundaryCondition="true"
    constant="false"
    charge="0"
    metaid="PX"
    sboTerm="SBO:0000245" >
  <notes>
    <body xmlns="http://www.w3.org/1999/xhtml">
      <p>One of the components of a microtubule</p>
    </body>
  </notes>
  <annotation>
    <rdf:RDF·
        xmlns:bqbiol="http://biomodels.net/biology-qualifiers/"·
        xmlns:bqmodel="http://biomodels.net/model-qualifiers/"
        xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#">
      <rdf:Description rdf:about="#PX">
        <bqbiol:is>
          <rdf:Bag>
            <rdf:li rdf:resource="urn:miriam:uniprot:P68370"/>
            <rdf:li rdf:resource="urn:miriam:obo.go:GO%3A0045298"/>
          </rdf:Bag>
        </bqbiol:is>
      </rdf:Description>
    </rdf:RDF>
  </annotation>
</species>
```

SBML is not limited to biochemistry!

Rate Rules can describe the temporal evolution of any quantitative parameter, e.g. transmembrane voltage;

Events can describe any discontinuous change, e.g. neurotransmitter release or repolarisation;

A species is an entity participating to a reaction, **not always** a **chemical** entity:

- It can be a molecule
- It can be a cell
- It can be an organ
- It can be an organism

➔ SBML is about process descriptions

BioModels Home | Browse models | Submit | Search

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

BIOMD0000000020 - Hodgkin-Huxley1952 squid-axon

SBML L2 V1 | Other formats | Actions | Submit Model Comment/Bug

Model | Overview | Math | Physical entities | Parameters

Reference Publication

Publication ID: 12991237

J Physiol 1952 Aug;117(4):500-44.
A quantitative description of membrane current and its application to conduction and excitation in nerve.
HODGKIN AL, HUXLEY AF.
[more]

Model

Original Model: *Unspecified*

Submitter: Nicolas Le Novère

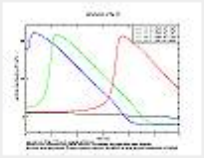
Submission Date: 2005-09-13T13:22:40+00:00

Last Modification Date: 2009-03-05T23:37:11+00:00

Creation Date: 2005-03-31T13:09:21+00:00

Creators: Maria Schilstra
Catherine Lloyd

Curation Result:

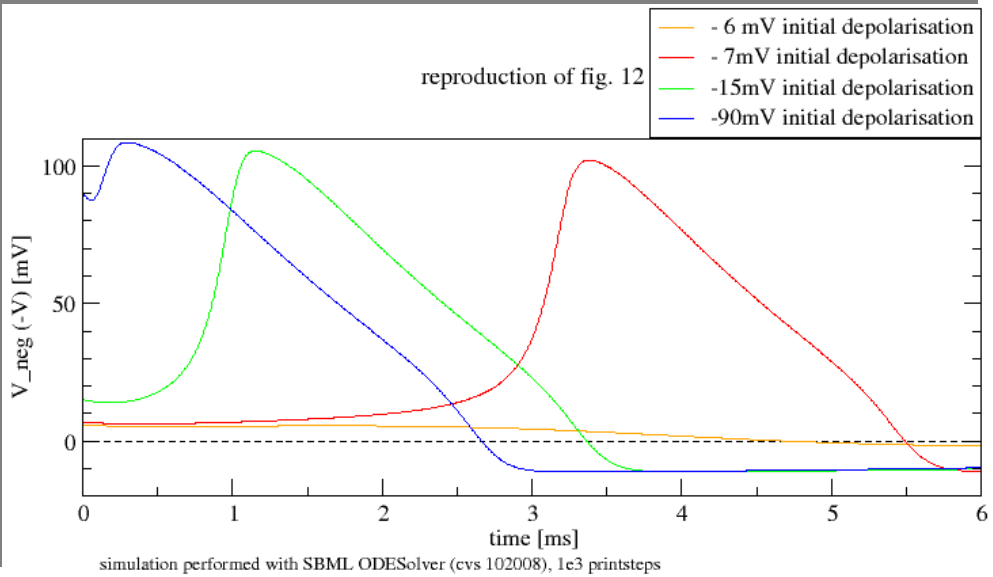


set #1	bqbiol:is	**Taxonomy** Loligo forbesi
set #2	bqbiol:isVersionOf	**Gene Ontology** voltage-gated potassium channel activity **Gene Ontology** voltage-gated sodium channel activity **Gene Ontology** action potential propagation

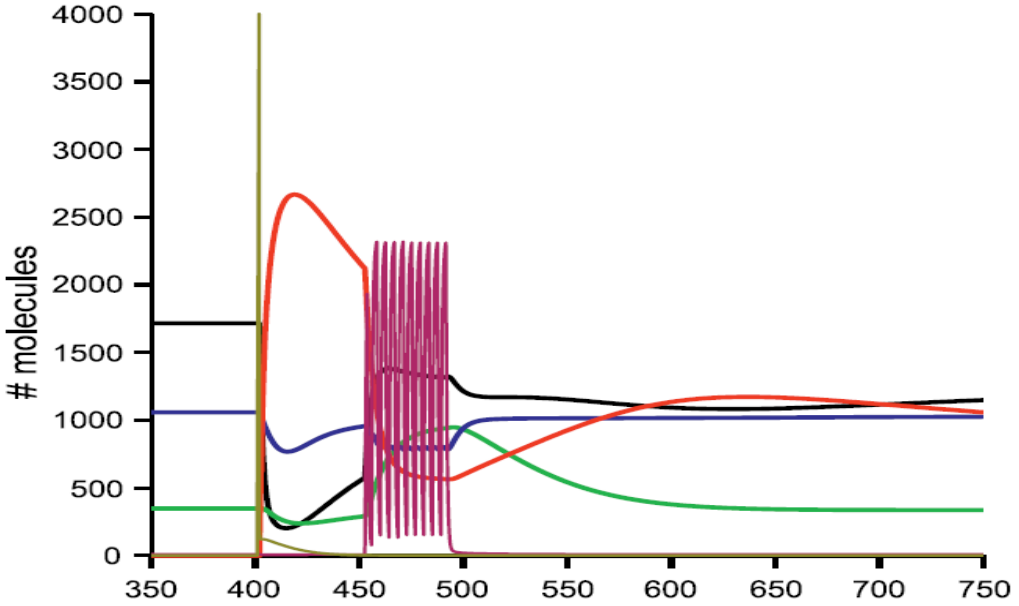
Not

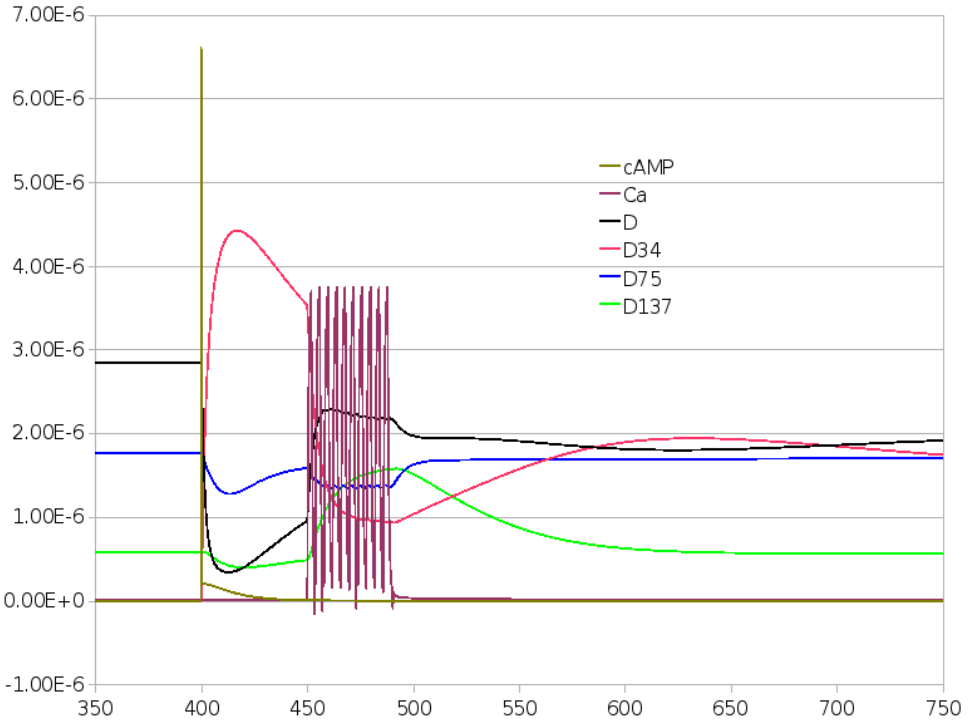
This model originates from BioModels Database: A Database of Annotated Pub
For more information see the terms of use.
To cite BioModels Database, please use Le Novère N., Bornstein B., Broicher A., C
J.L., Hucka M. (2006) BioModels Database: A Free, Centralized Database of Curated
Nucleic Acids Res., 34: D689-D691.

Developed by BioModels Team of Computational Neurobiology Group in European Bi



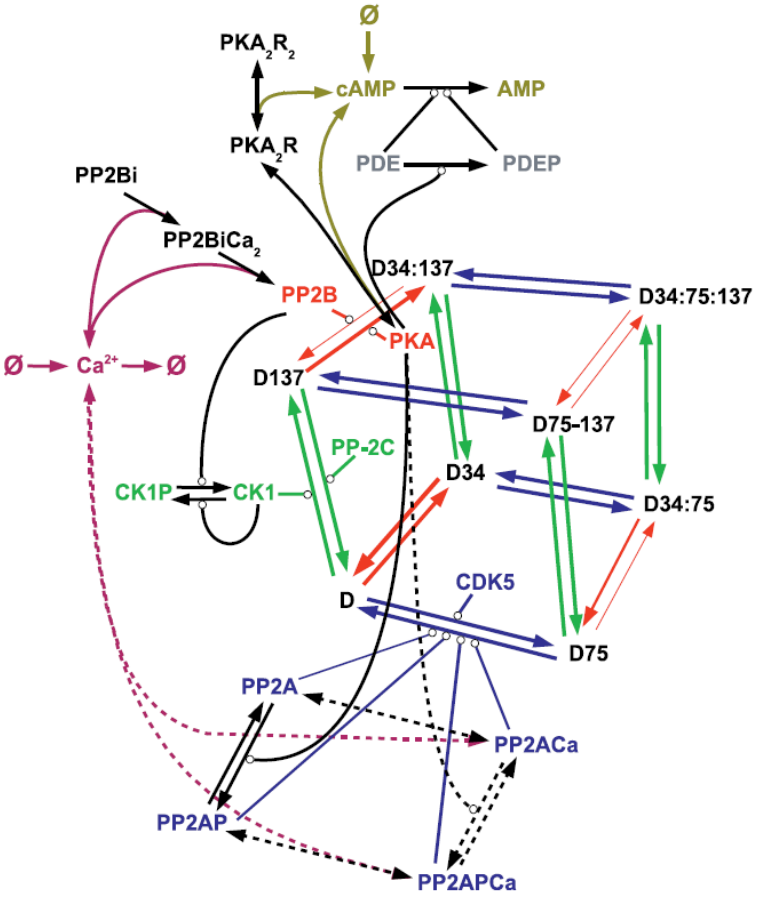
Signalling pathways





Fernandez et al.
PLoS Comput Biol
(2006) 2: e176.

BIOMD0000000153



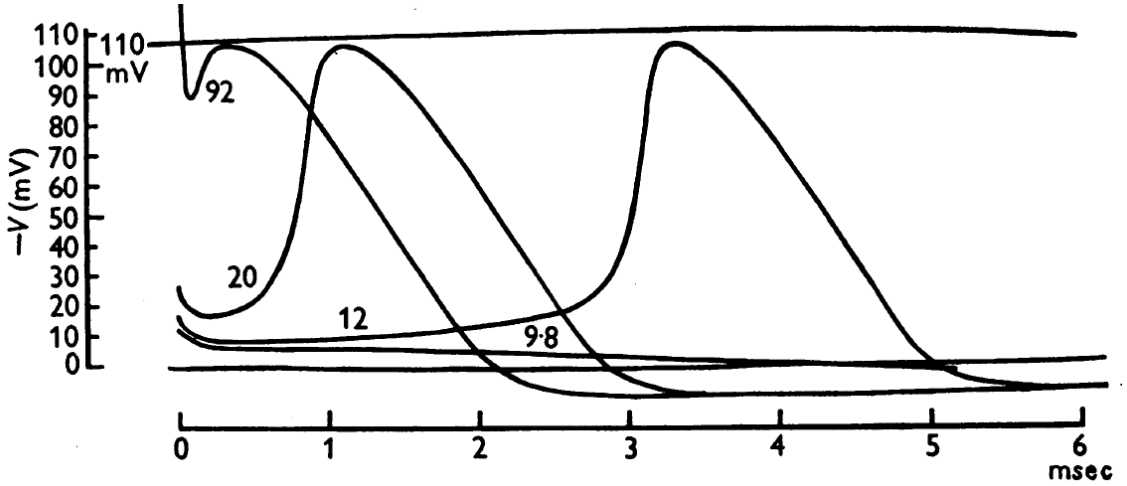
Signalling pathways

```
<reaction metaid="metaid_0000008" id="von1" name="D_CDK5_binding" reversible="false">
  <listOfReactants>
    <speciesReference species="D"/>
    <speciesReference species="CDK5"/>
  </listOfReactants>
  <listOfProducts>
    <speciesReference species="D_CDK5"/>
  </listOfProducts>
  <kineticLaw>
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <times/>
        <ci> Spine </ci>
        <ci> kon1 </ci>
        <ci> D </ci>
        <ci> CDK5 </ci>
      </apply>
    </math>
    <listOfParameters>
      <parameter id="kon1" name="kon1" value="5600000"/>
    </listOfParameters>
  </kineticLaw>
</reaction>
```

reaction:

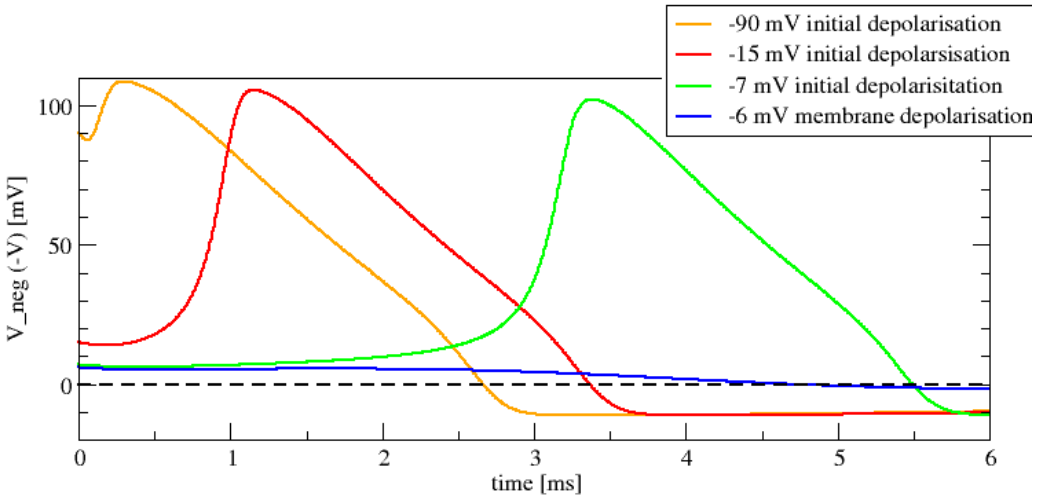
$$v_{on1} = k_{on1} \times [D] \times [CDK5] \times Vol$$

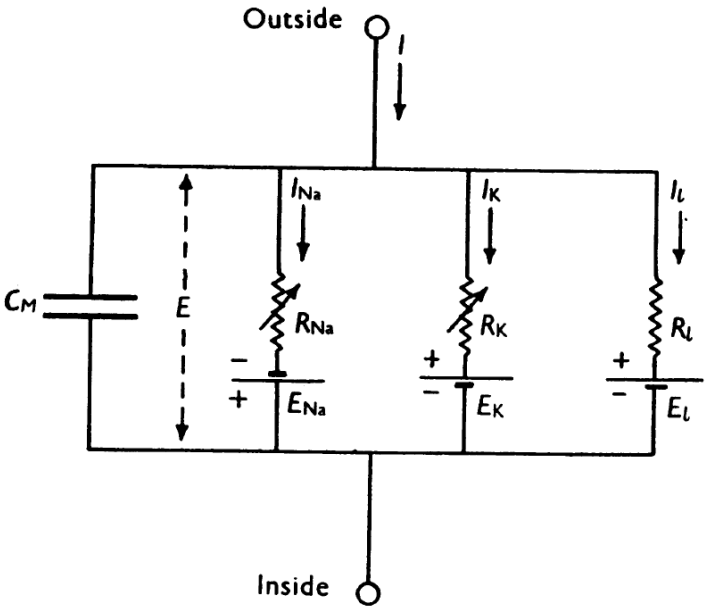
Conductance-based



Hodgkin AL, Huxley AF.
J Physiol
(1952) 117:500-544.

BIOMD0000000020





Conductance-based

```
<rateRule metaid="metaid_0000048" variable="V">
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <divide/>
      <apply>
        <minus/>
        <ci> I </ci>
        <apply>
          <plus/><ci> i_Na </ci><ci> i_K </ci><ci> i_L </ci>
        </apply>
      </apply>
      <ci> Cm </ci>
    </apply>
  </math>
</rateRule>·
<assignmentRule metaid="metaid_0000042" variable="i_Na">
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <times/>
      <ci> g_Na </ci>
      <apply>
        <power/><ci> m </ci><cn> 3.0 </cn>
      </apply>
      <ci> h </ci>
      <apply>
        <minus/><ci> V </ci><ci> E_Na </ci>
      </apply>
    </apply>
  </math>
</assignmentRule>
```

rate rule:

$$\frac{dv}{dt} = \frac{I - (i_{Na} + i_K + i_L)}{C_m}$$

assignment rule:

$$i_{Na} = g_{Na} \times m^3 \times h \times (V - E_{Na})$$

Single-compartment neurons

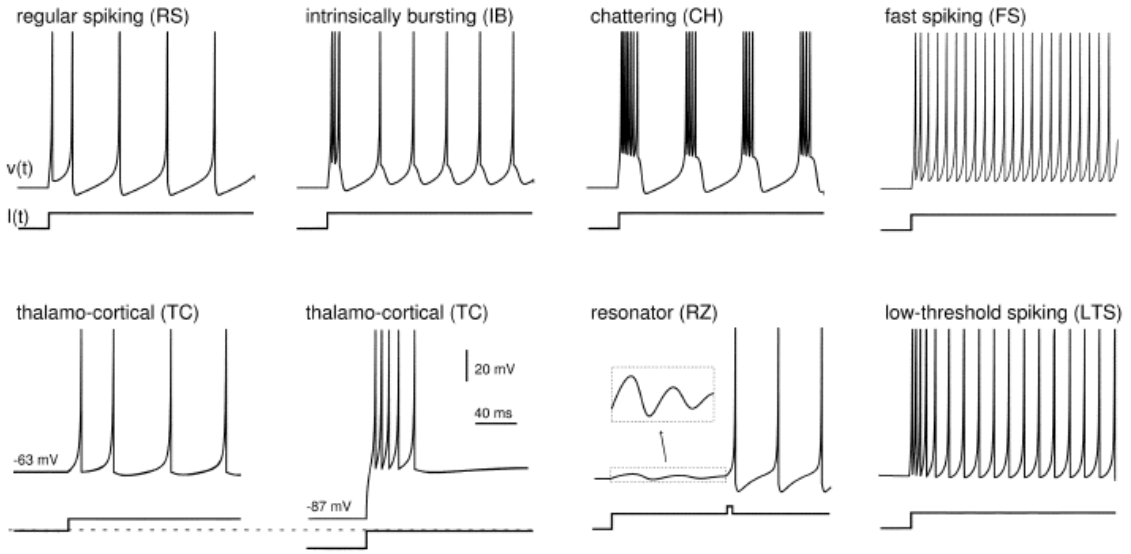
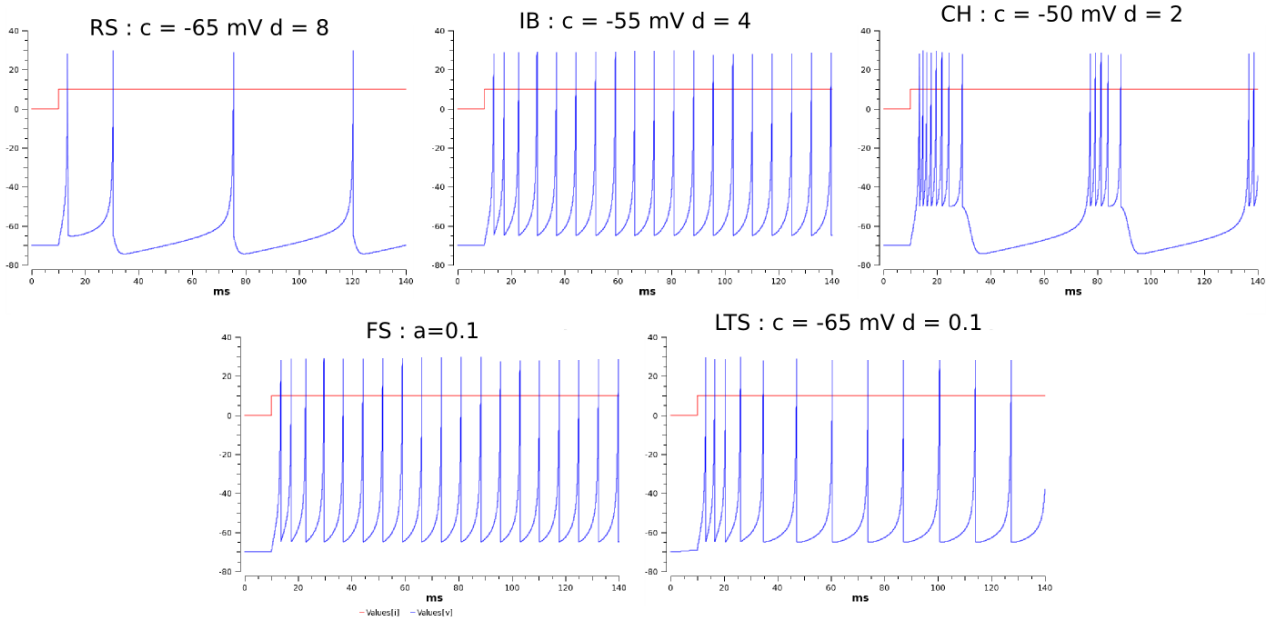


Fig. 2. Known types of neurons correspond to different values of the parameters a, b, c, d in the model described by the (1), (2). RS, IB, and CH are cortical excitatory neurons. FS and LTS are cortical inhibitory interneurons. Each inset shows a voltage response of the model neuron to a step of dc-current $I = 10$ (bottom). Time resolution is 0.1 ms. This figure is reproduced with permission from www.izhikevich.com. (Electronic version of the figure and reproduction permissions are freely available at www.izhikevich.com.)

Izhikevich EM.
IEEE Trans Neural Netw
(2003) 14(6):1569-1572.



BIOMD0000000127

Single-compartment neurons

```
<rateRule metaid="metaid_0000048" variable="V">
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <plus/>
      <apply>
        <minus/>
        <apply>
          <plus/>
          <apply>
            <times/>
            <cn> 0.04 </cn>
            <apply>
              <power/>
              <ci> v </ci>
              <cn type="integer"> 2 </cn>
            </apply>
          </apply>
          <apply>
            <times/>
            <cn type="integer"> 5 </cn>
            <ci> v </ci>
          </apply>
          <cn type="integer"> 140 </cn>
        </apply>
        <ci> U </ci>
      </apply>
      <ci> i </ci>
    </apply>
  </math>
</rateRule>
```

```
<event metaid="metaid_0000012" id="event_0000001">
  <trigger>
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <gt/>
        <ci> v </ci>
        <ci> Vthresh </ci>
      </apply>
    </math>
  </trigger>
  <listOfEventAssignments>
    <eventAssignment variable="v">
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> c </ci>
      </math>
    </eventAssignment>
    <eventAssignment variable="U">
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
          <plus/>
          <ci> U </ci>
          <ci> d </ci>
        </apply>
      </math>
    </eventAssignment>
  </listOfEventAssignments>
</event>
```

rate rule:

$$\frac{dv}{dt} = 0.04^2 + 5 \times V + 140 - U + i$$

event:

$$\text{when } v > V_{thresh} \qquad \begin{matrix} v = c \\ U = U + d \end{matrix}$$

Difference between SBML L1, L2 and L3

L1	L2	L3
predefined functions	function definitions	function definitions
proprietary infix math notation	all math in MathML	all math in MathML
reserved namespaces for annotation	no reserved namespaces for annotations	no reserved namespaces for annotations
no controlled annotation	controlled RDF annotation	controlled RDF annotation
no discrete events	discrete events	discrete events
monolithic	monolithic	modular
default values	default values	no default values

Progressive simplification, generalisation and externalisation

SBML Level 3 packages

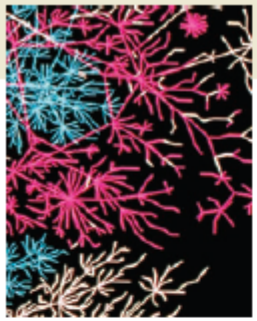
- Core package – Release candidate
- Graph Layout – specification finalised
- Complex species – specification finalised
- Groups - specification finalised
- Model composition – specification under discussion
- Qualitative models – specification under discussion
- Distributions and ranges - specification under discussion
- Graph rendering – specification proposed
- Arrays and sets – specifications proposed
- Geometry - specification proposed
- Spatial diffusion – specification proposed
- Dynamic structures - needed

???

Simulation description

	Models	Simulation	Results
Minimal requirements	MIRIAM	MIASE	
Data-models	SBML SBGN	SED ML	SBRML
Ontologies	SBO	KISAO	TEDDY

Born in Okinawa



_computational BIOLOGY

PERSPECTIVE

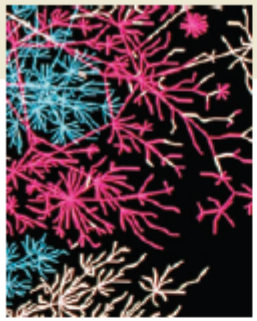
Publishing Group http://www.nature.com/naturebiotechnology

Minimum information requested in the annotation of biochemical models (MIRIAM)

Nicolas Le Novère[1,15], Andrew Finney[2,15], Michael Hucka[3], Upinder S Bhalla[4], Fabien Campagne[5], Julio Collado-Vides[6], Edmund J Crampin[7], Matt Halstead[7], Edda Klipp[8], Pedro Mendes[9], Poul Nielsen[7], Herbert Sauro[10], Bruce Shapiro[11], Jacky L Snoep[12], Hugh D Spence[13] & Barry L Wanner[14]

Most of the published quantitative models in biology are lost for the community because they are either not made available or they are insufficiently characterized to allow them to be reused. The lack of a standard description format, lack of stringent reviewing and authors' carelessness are the main causes for incomplete model descriptions. With today's increased interest in detailed biochemical models, it is necessary to define a minimum quality standard for the encoding of those models. We propose a set of rules for curating quantitative models of biological systems. These rules define procedures for encoding and annotating models represented in machine-readable form. We believe their

During the genomic era we have witnessed a vast increase in availability of large amounts of quantitative data. This is motivating a shift in the focus of molecular and cellular research from qualitative descriptions of biochemical interactions towards the quantification of such interactions and their dynamics. One of the tenets of systems biology is the use of quantitative models (see **Box 1** for definitions) as a mechanism for capturing precise hypotheses and making predictions[1,2]. Many specialized models exist that attempt to explain aspects of the cellular machinery. However, as has happened with other types of biological information, such as sequences, macromolecular structures or



PERSPECTIVE

6. The model, when instantiated within a suitable simulation environment, must be able to reproduce all relevant results given in the reference description that can readily be simulated. Not only does the simulation have to provide results qualitatively similar to the reference description, such as oscillation, bistability, chaos, but the quantitative values of variables, and their relationships (e.g., the shape of the phase portrait) must be reproduced within some epsilon, the difference being attributable to the algorithms used to run the simulation, and the

Minimum … tion of biochem…

Nicolas Le Novère[1], Julio Collado-Vide[2], Herbert Sauro[10], B… n[7],

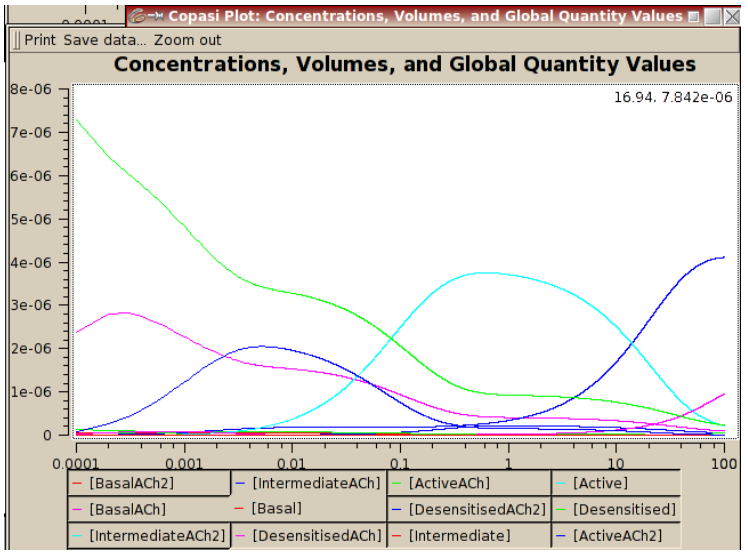
Most of the published quantitative models in biology are lost for the community because they are either not made available or they are insufficiently characterized to allow them to be reused. The lack of a standard description format, lack of stringent reviewing and authors' carelessness are the main causes for incomplete model descriptions. With today's increased interest in detailed biochemical models, it is necessary to define a minimum quality standard for the encoding of those models. We propose a set of rules for curating quantitative models of biological systems. These rules define procedures for encoding and annotating models represented in machine-readable form. We believe their

During the genomic era we have witnessed a vast increase in availability of large amounts of quantitative data. This is motivating a shift in the focus of molecular and cellular research from qualitative descriptions of biochemical interactions towards the quantification of such interactions and their dynamics. One of the tenets of systems biology is the use of quantitative models (see **Box 1** for definitions) as a mechanism for capturing precise hypotheses and making predictions[1,2]. Many specialized models exist that attempt to explain aspects of the cellular machinery. However, as has happened with other types of biological information, such as sequences, macromolecular structures or

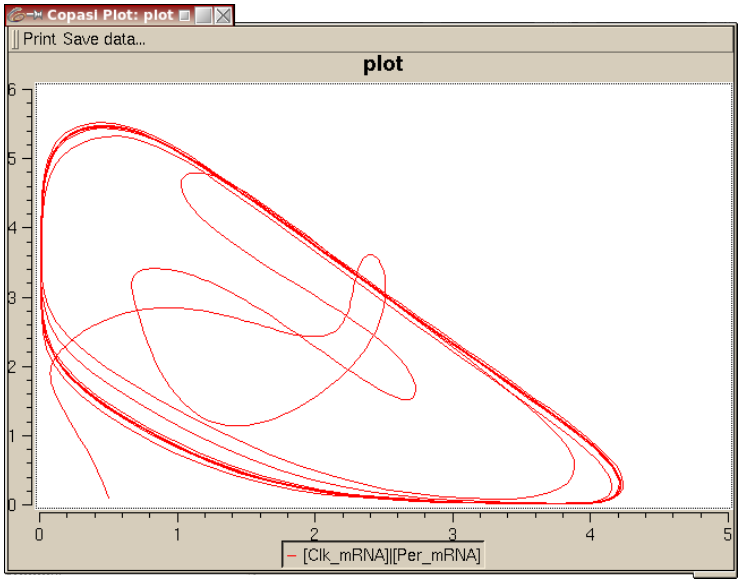
Publishing Group http://www.nature.com/naturebiotechnology

Reproduction of published simulation results

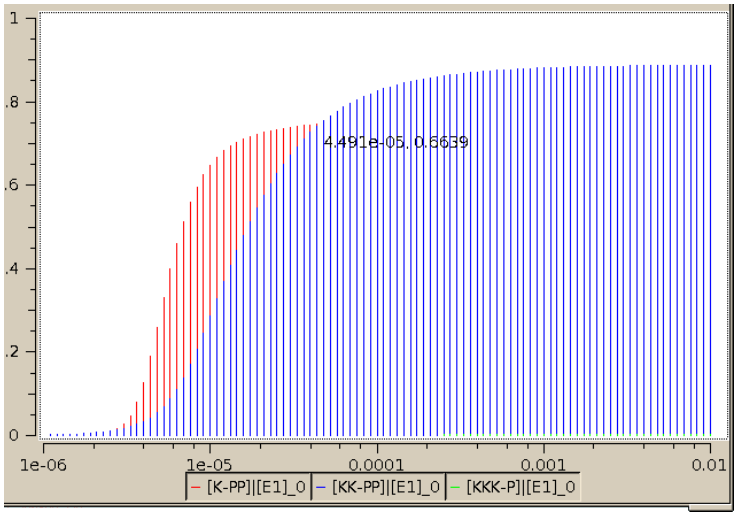
Edelstein et al 1996 (BIOMD0000000002)



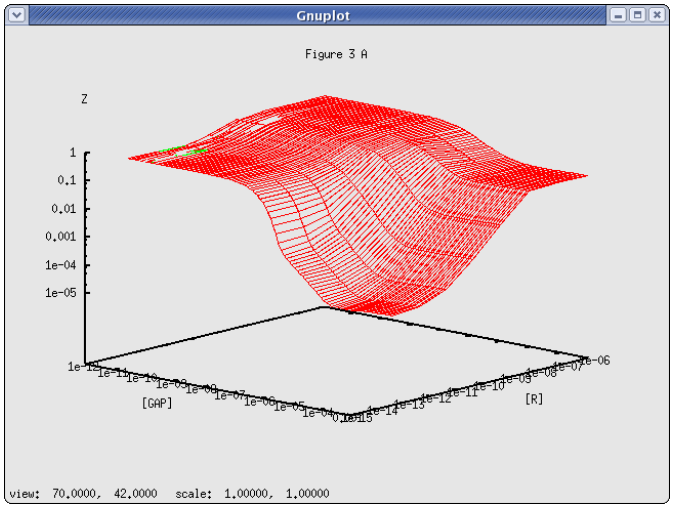
Ueda, Hagiwara, Kitanol 2001 (BIOMD0000000022)

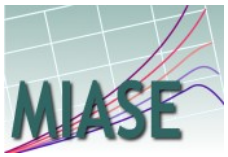


Huang & Ferrell (BIOMD0000000009)



Bornheimer et al 2004 (BIOMD0000000086)





Waltemath D., Adams R., Beard D.A., Bergmann F.T., Bhalla U.S, Britten R., Chelliah V., Cooling M.T., Cooper J., Crampin E., Garny A., Hoops S., Hucka M., Hunter P., Klipp E., Laibe C., Miller A., Moraru i., Nickerson D., Nielsen P., Nikolski M., Sahle S., Sauro H., Schmidt H., Snoep J.L., Tolle D., Wolkenhauer O., Le Novère N.

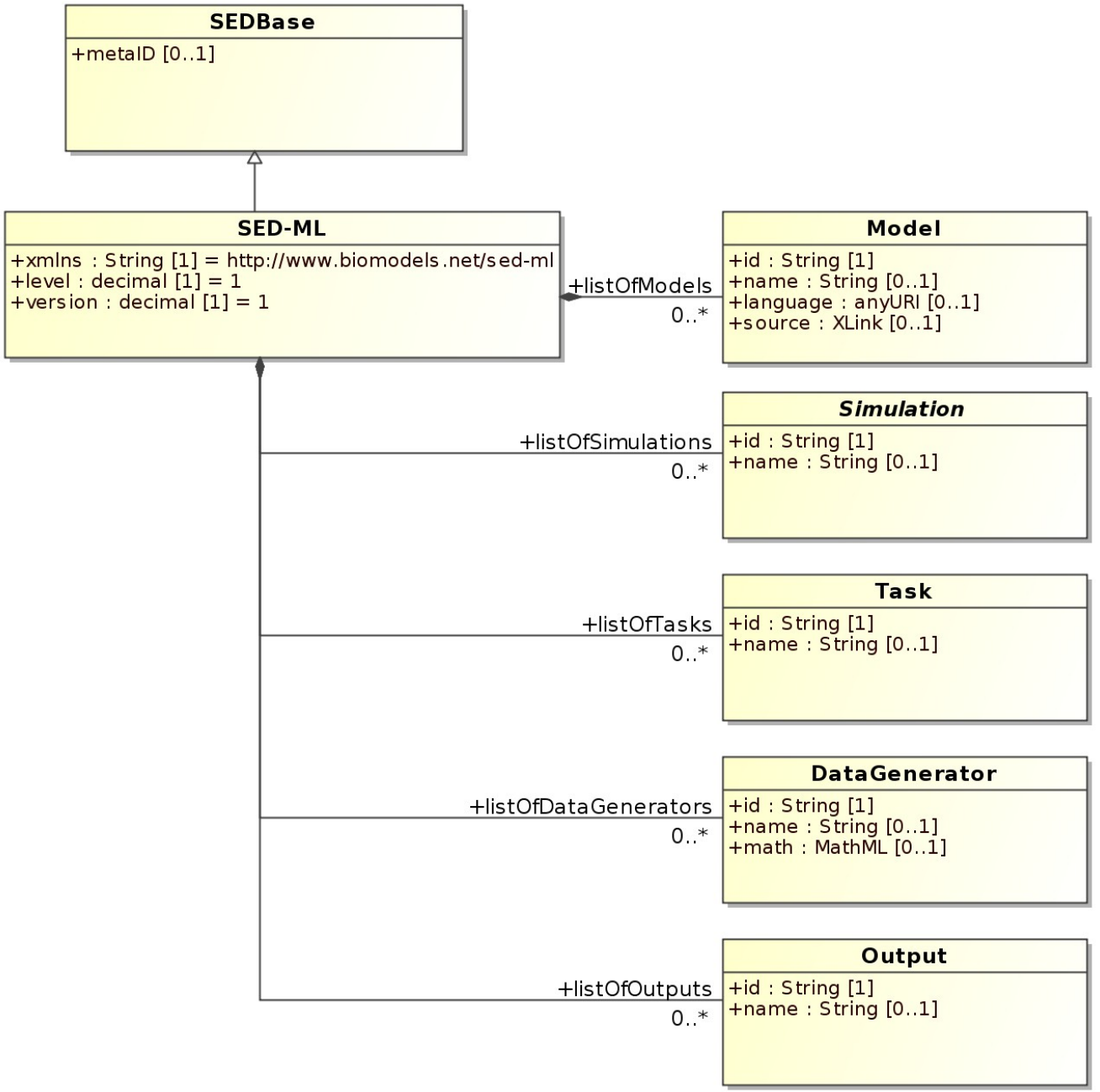
Minimum Information About a Simulation Experiment (MIASE) *In Revision*

Köhn D.,Le Novère N. SED-ML

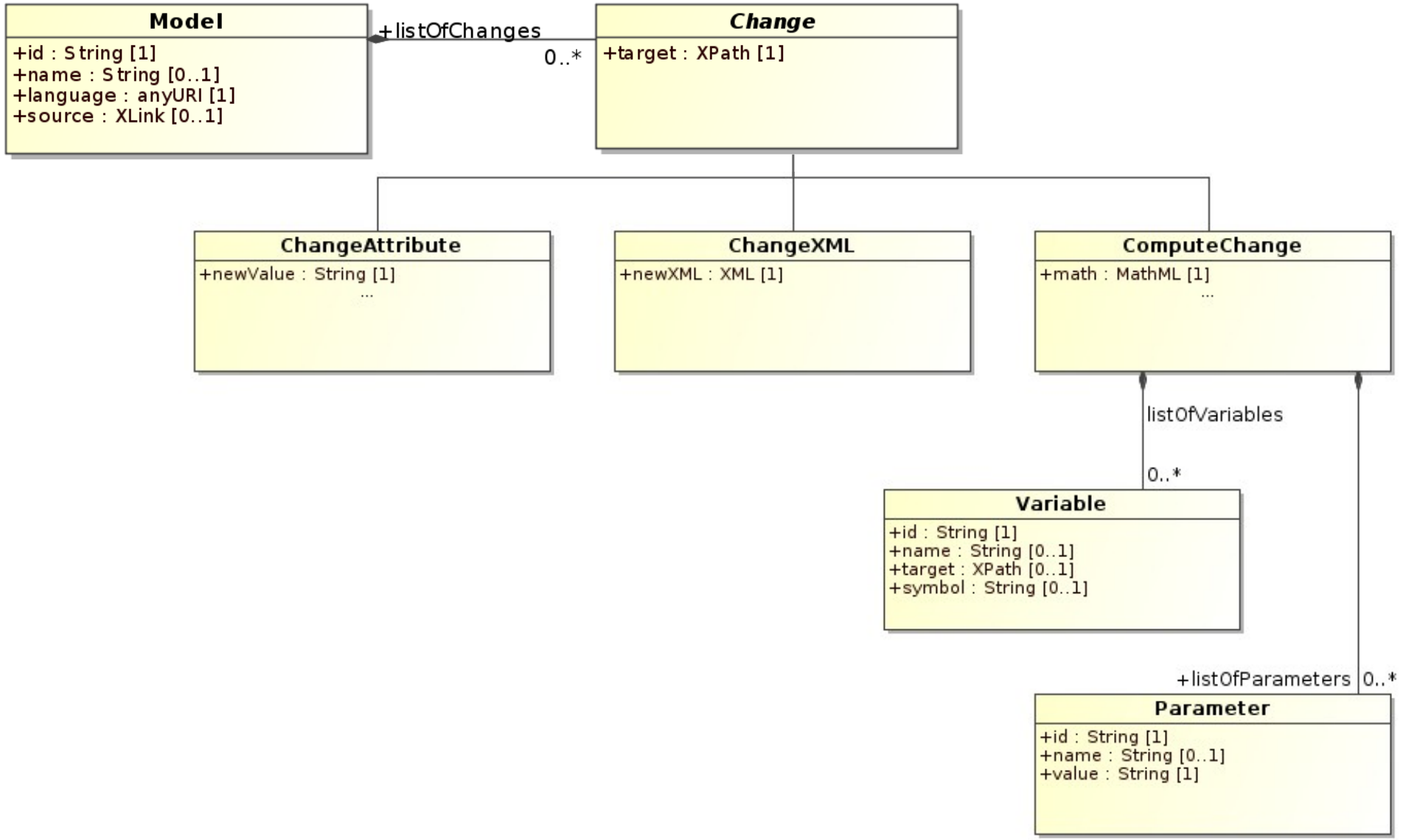
An XML Format for the Implementation of the MIASE Guidelines.

Proc 6th Conf Comput Meth Syst Biol (2008), Heiner M and Uhrmacher AM eds, *Lecture Notes in Bioinformatics*, 5307: 176-190.

General structure of SED-ML



Description of models



Description of models

```
<listOfModels>
  <model id="model1"
         name="Regular_Spiking"
         language="urn:sedml:language:sbml"
         source="urn:miriam:biomodels.db:BIOMD0000000127" />
  <model id="model2"
         name="chattering"
         source="model1">
    <listOfChanges>
      <changeAttribute target=
           "/sbml/model/listOfParameters/parameter[@id='c']/@value" newValue="-50">
      </changeAttribute>
      <changeAttribute target=
           "/sbml/model/listOfParameters/parameter[@id='d']/@value" newValue="42">
      </changeAttribute>
    </listOfChanges>
  </model>
</listOfModels>
```

Description of models

```
<listOfModels>
  <model id="model1"
         name="Regular_Spiking"
         language="urn:sedml:language:sbml"
         source="urn:miriam:biomodels.db:BIOMD0000000127" />
  <model id="model2"
         name="chattering"
         source="model1">
    <listOfChanges>
      <changeAttribute target=
          "/sbml/model/listOfParameters/parameter[@id='c']/@value" newValue="-50">
      </changeAttribute>
      <changeAttribute target=
          "/sbml/model/listOfParameters/parameter[@id='d']/@value" newValue="42">
      </changeAttribute>
    </listOfChanges>
  </model>
</listOfModels>
```

Any model description
in XML such as SBML, CellML,
NeuroML, VCML, NineML etc.

Description of models

```
<listOfModels>
  <model id="model1"
         name="Regular_Spiking"
         language="urn:sedml:language:sbml"
         source="urn:miriam:biomodels.db:BIOMD0000000127" />
  <model id="model2"
         name="chattering"
         source="model1">
    <listOfChanges>
      <changeAttribute target=
          "/sbml/model/listOfParameters/parameter[@id='c']/@value" newValue="-50">
      </changeAttribute>
      <changeAttribute target=
          "/sbml/model/listOfParameters/parameter[@id='d']/@value" newValue="42">
      </changeAttribute>
    </listOfChanges>
  </model>
</listOfModels>
```

Retrieving models

MIRIAM Resources

Data type: *BioModels Database*

General | Tags | Annotation

General information about the data type

Name		
Identifier		MIR:00000007
Name		BioModels Database
Synonyms		BioModels
URIs		
Official URN		urn:miriam:biomodels.db
Deprecated		http://www.ebi.ac.uk/biomodels/
Information		
Definition		BioModels Database is a data resource that allows biologists to store, search and retrieve published mathematical models of biological interests.
Identifier Pattern		^(BIOMD|MODEL)\d{10}$
Physica		
Resource #1	**Data Entry**	http://www.ebi.ac.uk/biomodels-m
	Data Resource	http://www.ebi.ac.uk/biomodels/
	Information	BioModels, a Database of Annotat
	Institution	European Bioinformatics Institute,
Resource #2	**Data Entry**	http://biomodels.caltech.edu/**$id** [
	Data Resource	http://biomodels.caltech.edu/
	Information	Mirror of BioModels Database
	Institution	California Institute of Technology,
Docu		
URL(s)		⊞ http://srs.ebi.ac.uk/srsbin/cgi-b
Misce		
Date of creation		2006-08-14 19:38:06 GMT
Date of last modification		2009-06-05 17:43:08 GMT

Go back to the list of data types

BioModels Home | Models | Submit | Sign in | Support | About BioModels | Search

BIOMD0000000127 - Izhikevich2003_SpikingNeuron

SBML formats | Other formats (auto-generated) | Actions | Submit Model Comment/Bug

Model | Overview | Math | Physical entities | Parameters | Curation

Reference Publication

Publication ID: 18244602

IEEE Trans Neural Netw 2003;14(6):1569-72.
Simple model of spiking neurons.
Izhikevich EM.
The Neurosciences Inst., San Diego, CA, USA. [more]

Model

Original Model: *BIOMD0000000127.xml.origin*

Submitter: Enuo He

Submission ID: MODEL4880479792

Submission Date: 27 Jul 2007 20:22:14 UTC

Last Modification Date: 21 Apr 2009 16:46:12 UTC

Creation Date: 16 Jul 2007 09:41:14 UTC

Encoders: Enuo He

set #1	bqbiol:isVersionOf	Gene Ontology regulation of action potential in neuron Gene Ontology regulation of membrane potential Gene Ontology regulation of action potential
set #2	bqmodel:isDescribedBy	DOI 10.1109/TNN.2003.820440
set #3	bqbiol:is	Taxonomy Mammalia

Notes

model is according to the paper *Simple Model of Spiking Neurons* In this paper, a simple spiking model is presented that is as biologically plausible as the Hodgkin-Huxley model, yet as computationally efficient as the parameters a,b,c,d in the model. Figure2RS,IB,CH,FS,LTS have been simulated by MathSBML.

65, d=8.

35,d=4

02,b=0.2,c=-50,d=2

FS:a=0.1b=0.2c=-65,d=2

LTS:a=0.02,b=0.25,c=-65,d=2

This model originates from BioModels Database: A Database of Annotated Published Models. It is copyright (c) 2005-2010 The BioModels Team.
For more information see the terms of use.
To cite BioModels Database, please use Le Novère N., Bornstein B., Broicher A., Courtot M., Donizelli M., Dharuri H., Li L., Sauro H., Schilstra M., Shapiro B., Snoep J.L., Hucka M. (2006) BioModels Database: A Free, Cen
Biochemical and Cellular Systems Nucleic Acids Res., 34: D689-D691.

Computational Systems Neurobiology Group, European Bioinformatics Institute. | Terms of Use | Contact Us | Developed by the BioModels.net Team

Modifying models

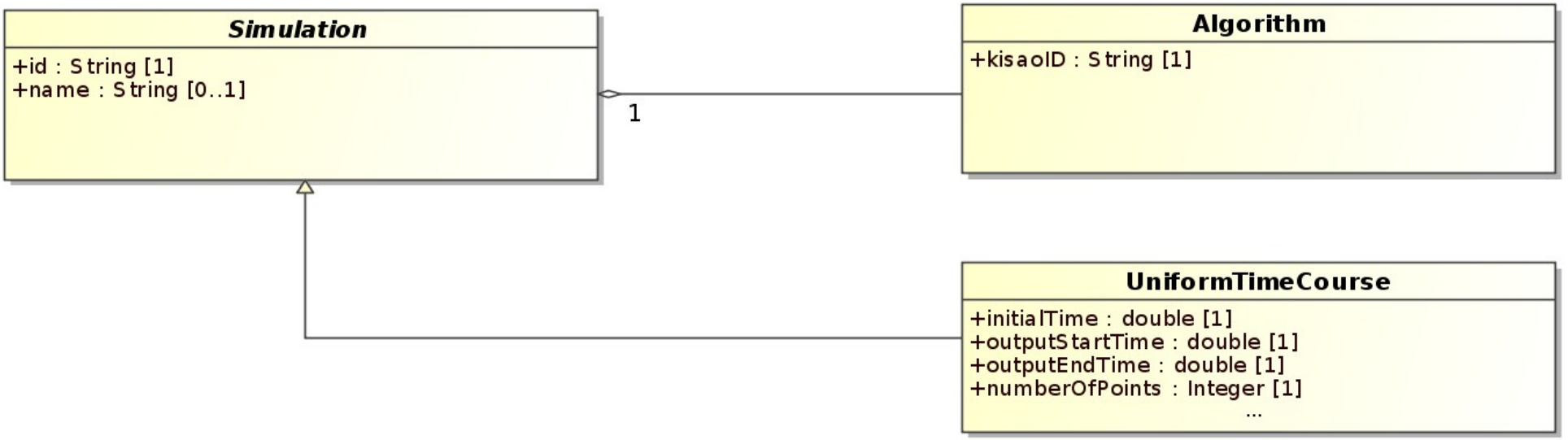
```
<listOfModels>
  <model id="model1"
         name="Regular_Spiking"
         language="urn:sedml:language:sbml"
         source="urn:miriam:biomodels.db:BIOMD0000000127" />
  <model id="model2"
         name="chattering"
         source="model1">
    <listOfChanges>
      <changeAttribute target=
          "/sbml/model/listOfParameters/parameter[@id='c']/@value" newValue="-50">
      </changeAttribute>
      <changeAttribute target=
          "/sbml/model/listOfParameters/parameter[@id='d']/@value" newValue="42">
      </changeAttribute>
    </listOfChanges>
  </model>
</listOfModels>
```

Modifying models

```
<listOfModels>
  <model id="model1"
         name="Regular_Spiking"
         language="urn:sedml:language:sbml"
         source="urn:miriam:biomodels.db:BIOMD0000000127" />
  <model id="model2"
         name="chattering"
         source="model1">
    <listOfChanges>
      <changeAttribute target=
           "/sbml/model/listOfParameters/parameter[@id='c']/@value" newValue="-50">
      </changeAttribute>
      <changeAttribute target=
           "/sbml/model/listOfParameters/parameter[@id='d']/@value" newValue="42">
      </changeAttribute>
    </listOfChanges>
  </model>
</listOfModels>
```

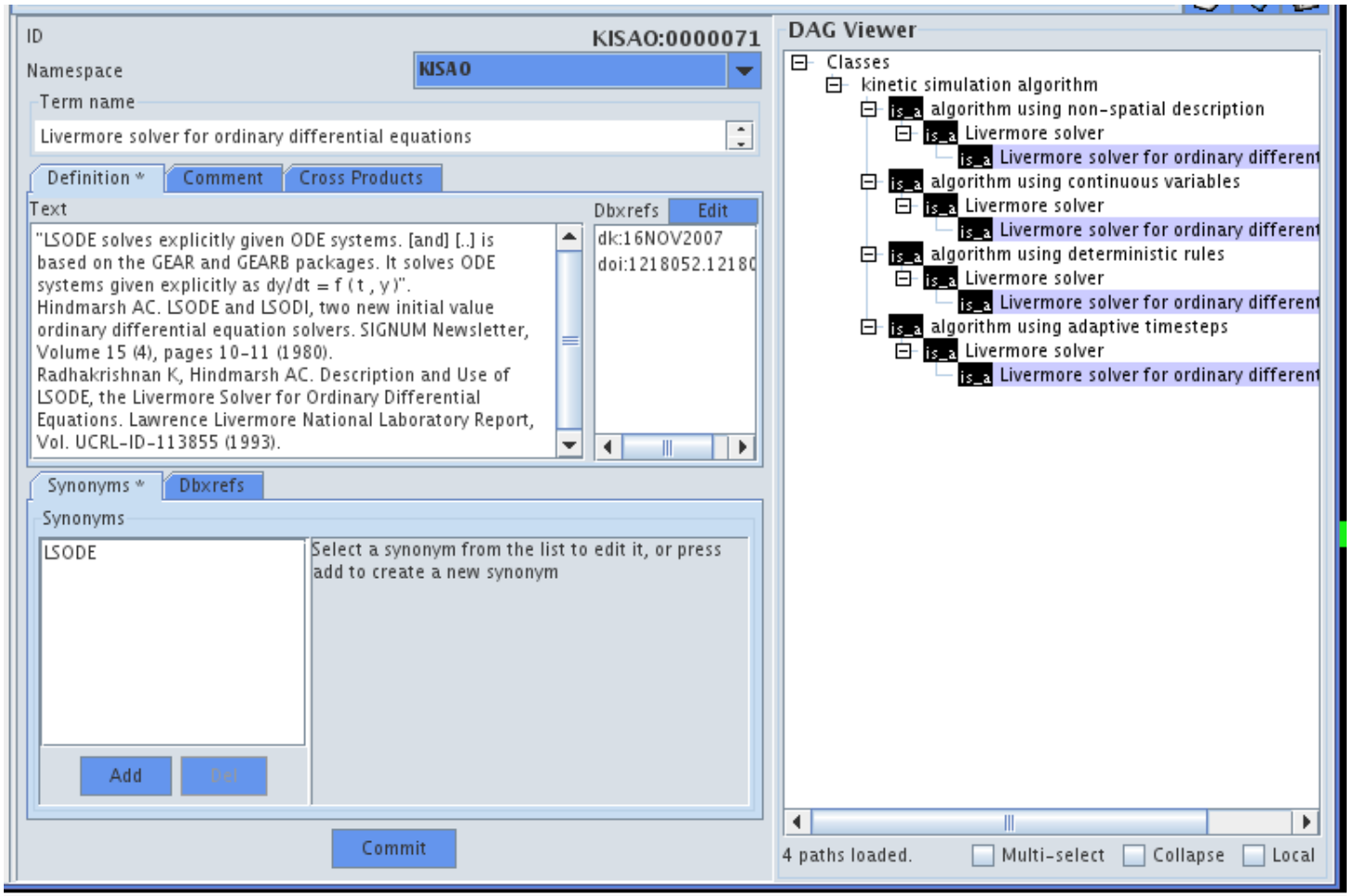
Simulation approach

```
<listOfSimulations>
  <uniformTimeCourse id="simulation1"
                     initialTime="0"
                     outputStartTime="0"
                     outputEndTime="140"
                     numberOfPoints="1000">
    <algorithm kisaoID="KiSAO:0000030"/>
  </uniformTimeCourse>
</listOfSimulations>
```



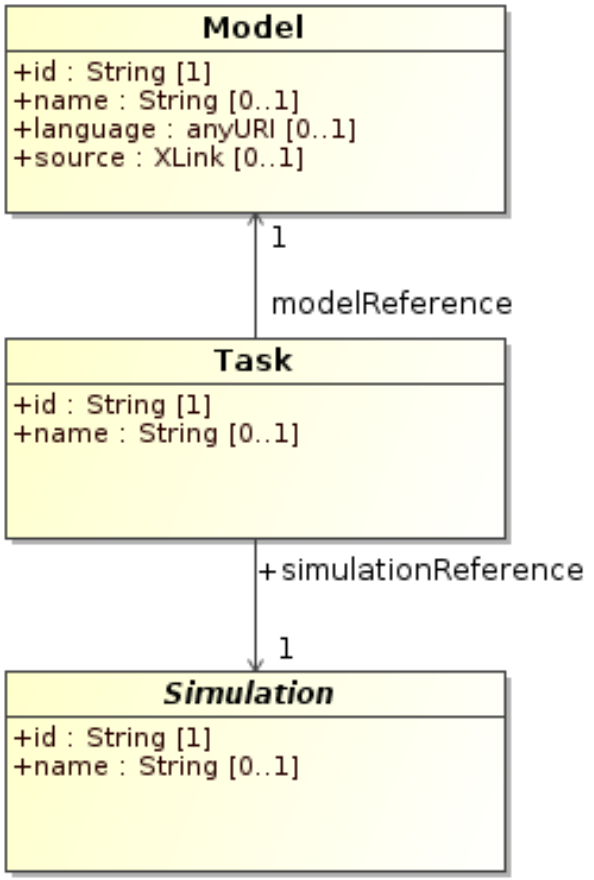
Simulation approach

```
<listOfSimulations>
  <uniformTimeCourse id="simulation1"
                     initialTime="0"
                     outputStartTime="0"
                     outputEndTime="140"
                     numberOfPoints="1000">
    <algorithm kisaoID="KiSAO:0000030"/>
  </uniformTimeCourse>
</listOfSimulations>
```

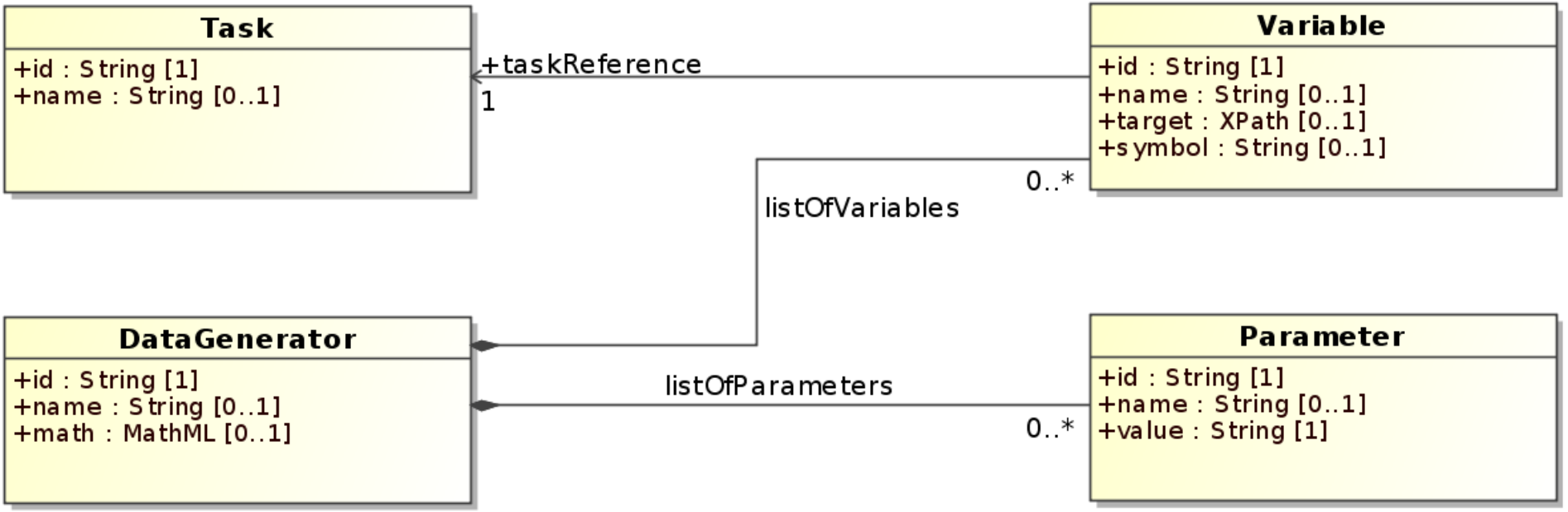


Simulation task

```
<listOfTasks>
  <task id="task1"
        name="regular spiking"
        modelReference="model1"
        simulationReference="simulation1">
  </task>
  <task id="task2"
        name="chattering"
        modelReference="model2"
        simulationReference="simulation1">
  </task>
</listOfTasks>
```



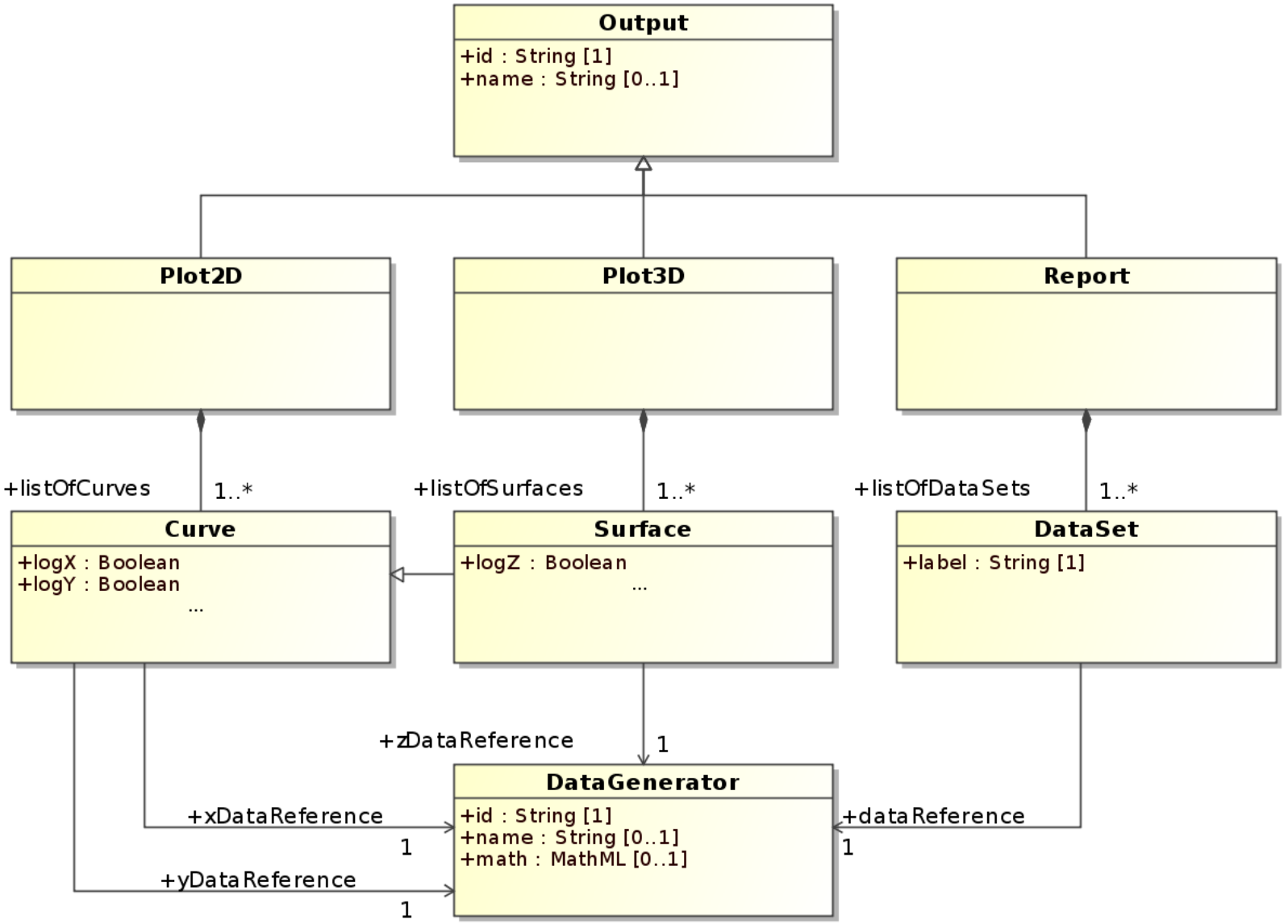
Data generation



Data generation

```
<listOfDatGenerators >
  <dataGenerator id="d1" name="time">
    <listOfVariables >
      <variable id="time" taskReference="task1" symbol="urn:sedml:symbol:time" />
    </listOfVariables>
    <math xmlns="http://www.w3.org /1998/Math/MathML">
      <ci> time </ci>
    </math>
  </dataGenerator>
  <dataGenerator id="d2" name="voltage">
    <listOfVariables>
      <variable id="v" taskReference="task1"
        target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='v']" />
    </listOfVariables>
    <math xmlns="http://www.w3.org /1998/Math/MathML">
      <ci>v</ci>
    </math>
  </dataGenerator>
 <dataGenerator id="d3" name="current">
    <listOfVariables>
      <variable id="i" taskReference="task1"
        target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='i']" />
    </listOfVariables>
    <math xmlns="http://www.w3.org /1998/Math/MathML">
      <ci>i</ci>
    </math>
  </dataGenerator>
</listOfDataGenerators>
```

Production of results

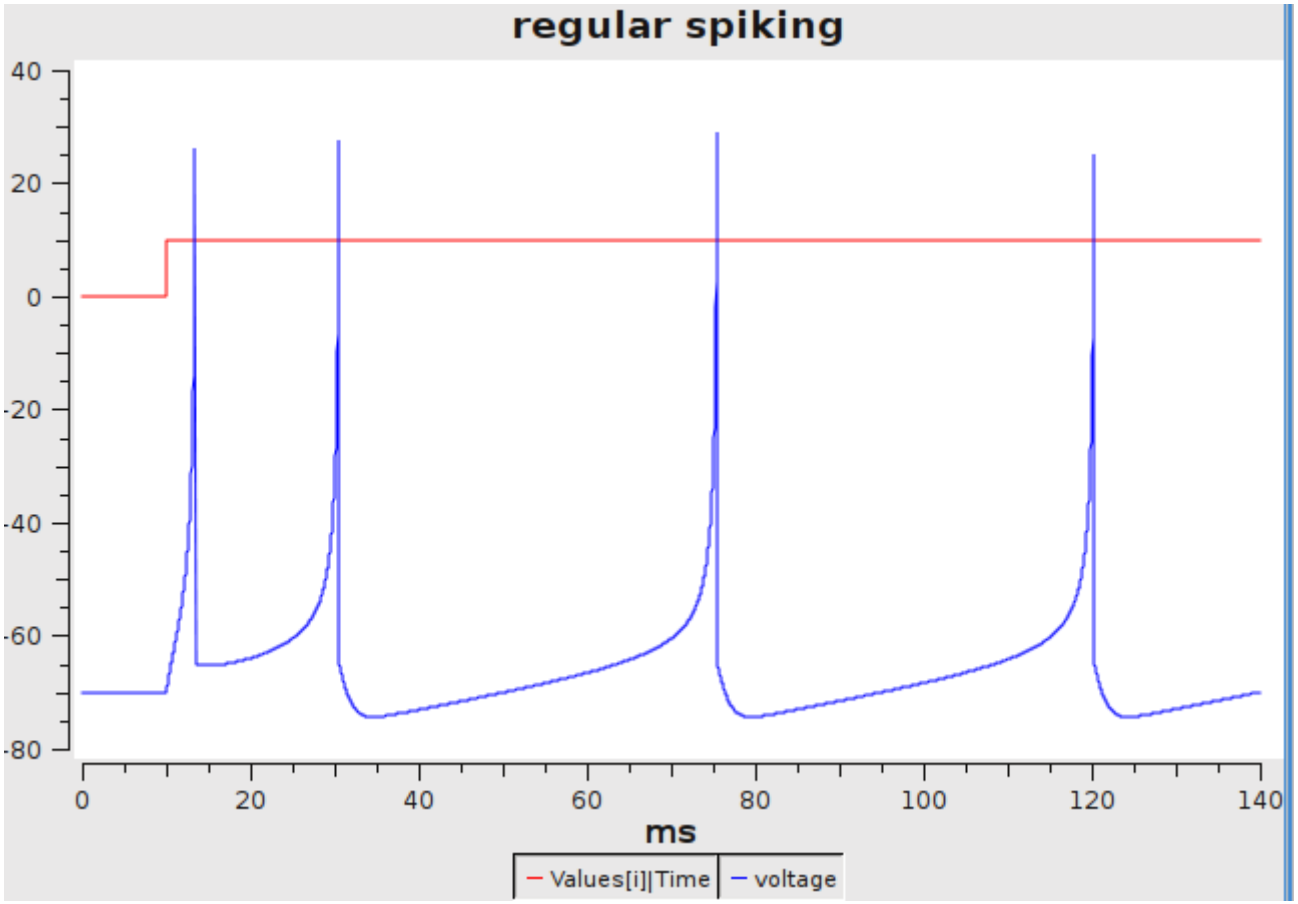


Production of results

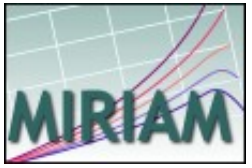
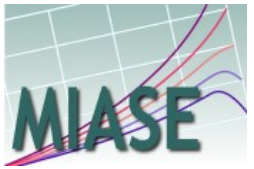
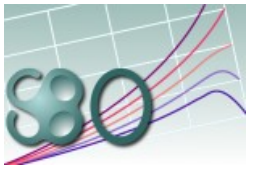
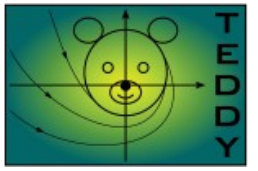
```
<listOfOutputs>
  <plot2D id="plot1" name="current and voltage of a ">
    <listOfCurves>
      <curve logX="false"
             logY="false"
             xDataReference="time"
             yDataReference="v" />
      <curve logX="false"
             logY="false"
             xDataReference="time"
             yDataReference="i" />
    </listOfCurves>
  </plot2D>
</listOfOutputs>
```

Production of results

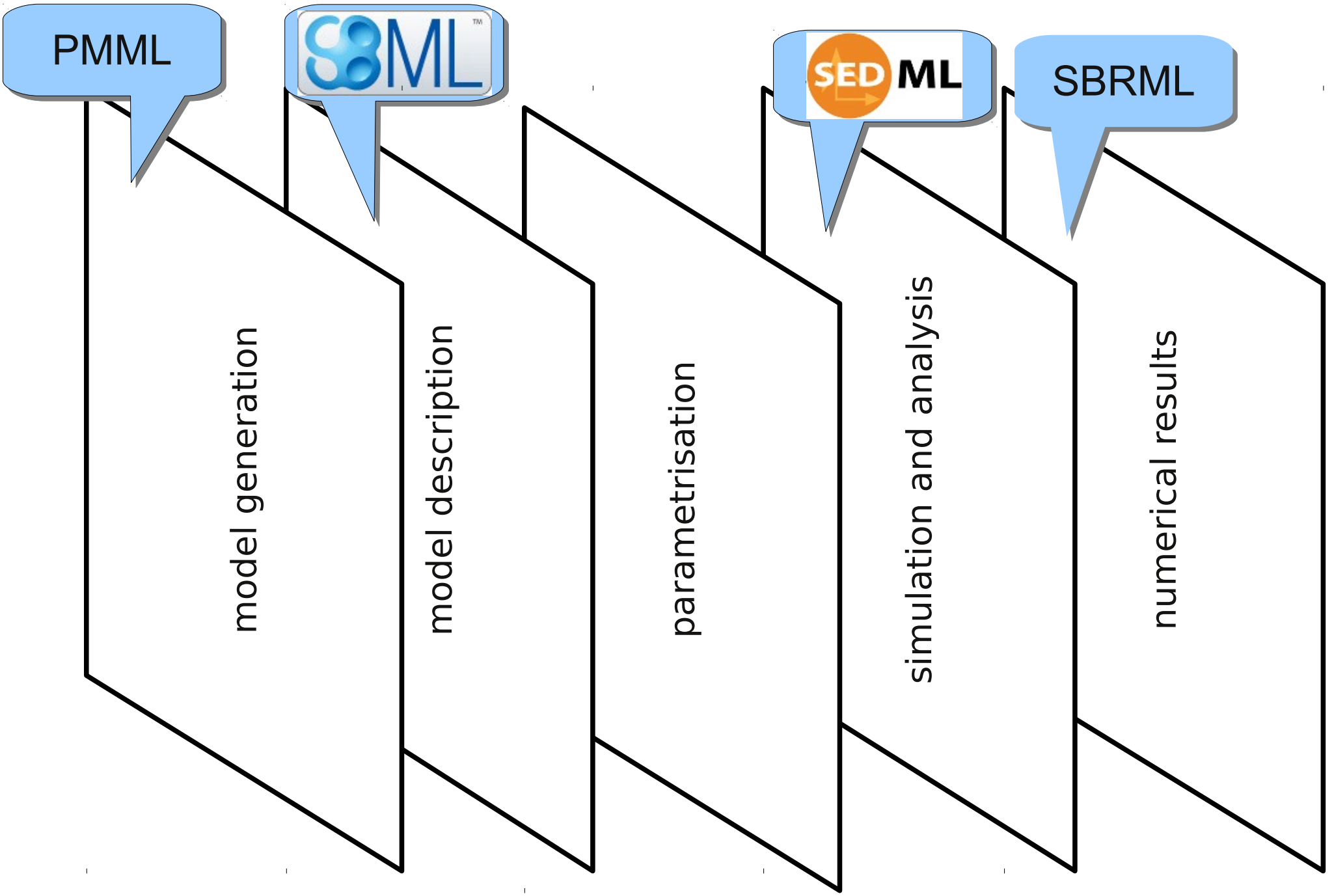
```
<listOfOutputs>
  <plot2D id="plot1" name="current and voltage of a ">
    <listOfCurves>
      <curve logX="false"
             logY="false"
             xDataReference="time"
             yDataReference="v" />
      <curve logX="false"
             logY="false"
             xDataReference="time"
             yDataReference="i" />
    </listOfCurves>
  </plot2D>
</listOfOutputs>
```



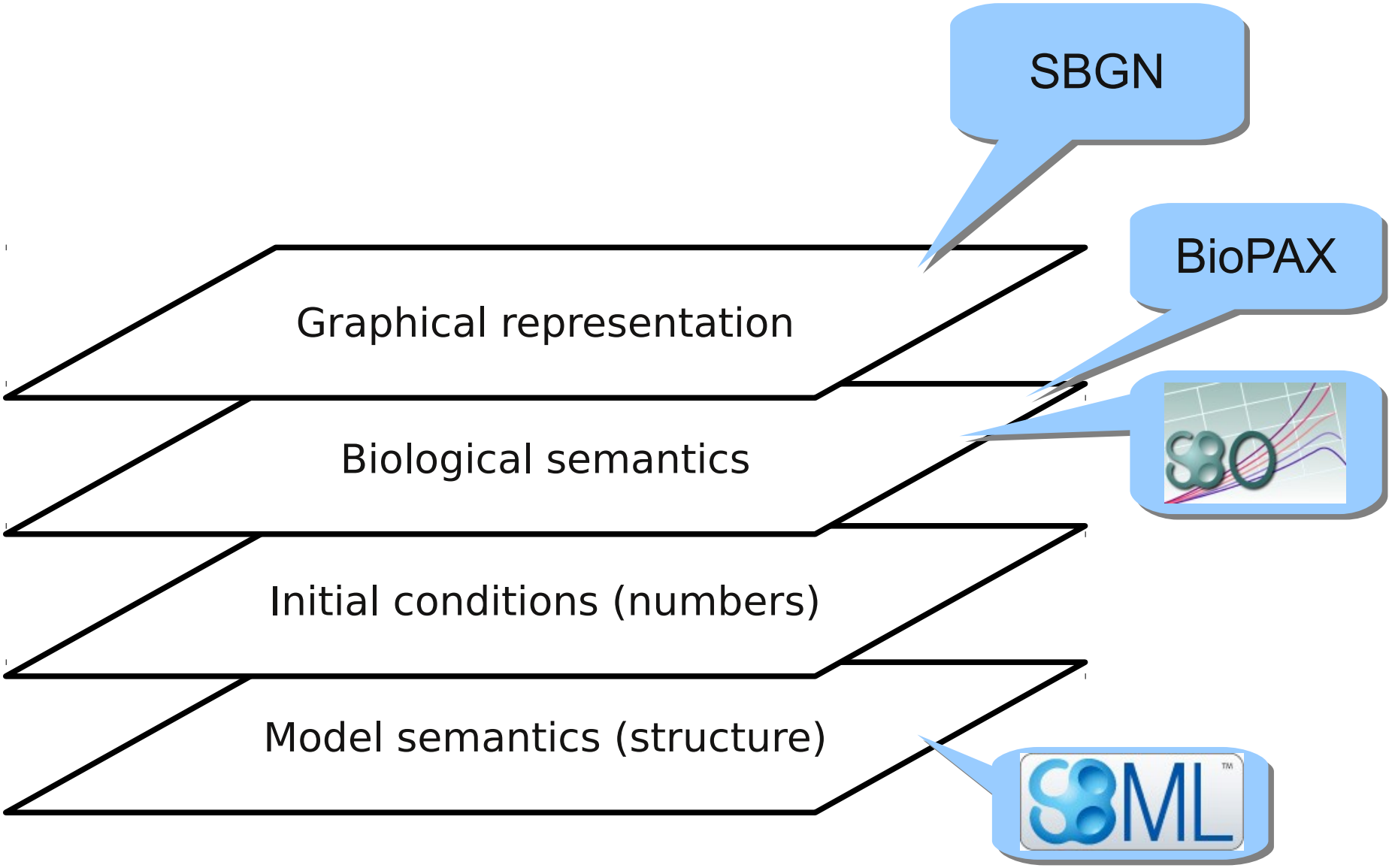
Is the mosaic of standards complete?

	Models	Simulation	Results
Minimal requirements			
Data-models			SBRML
Ontologies			

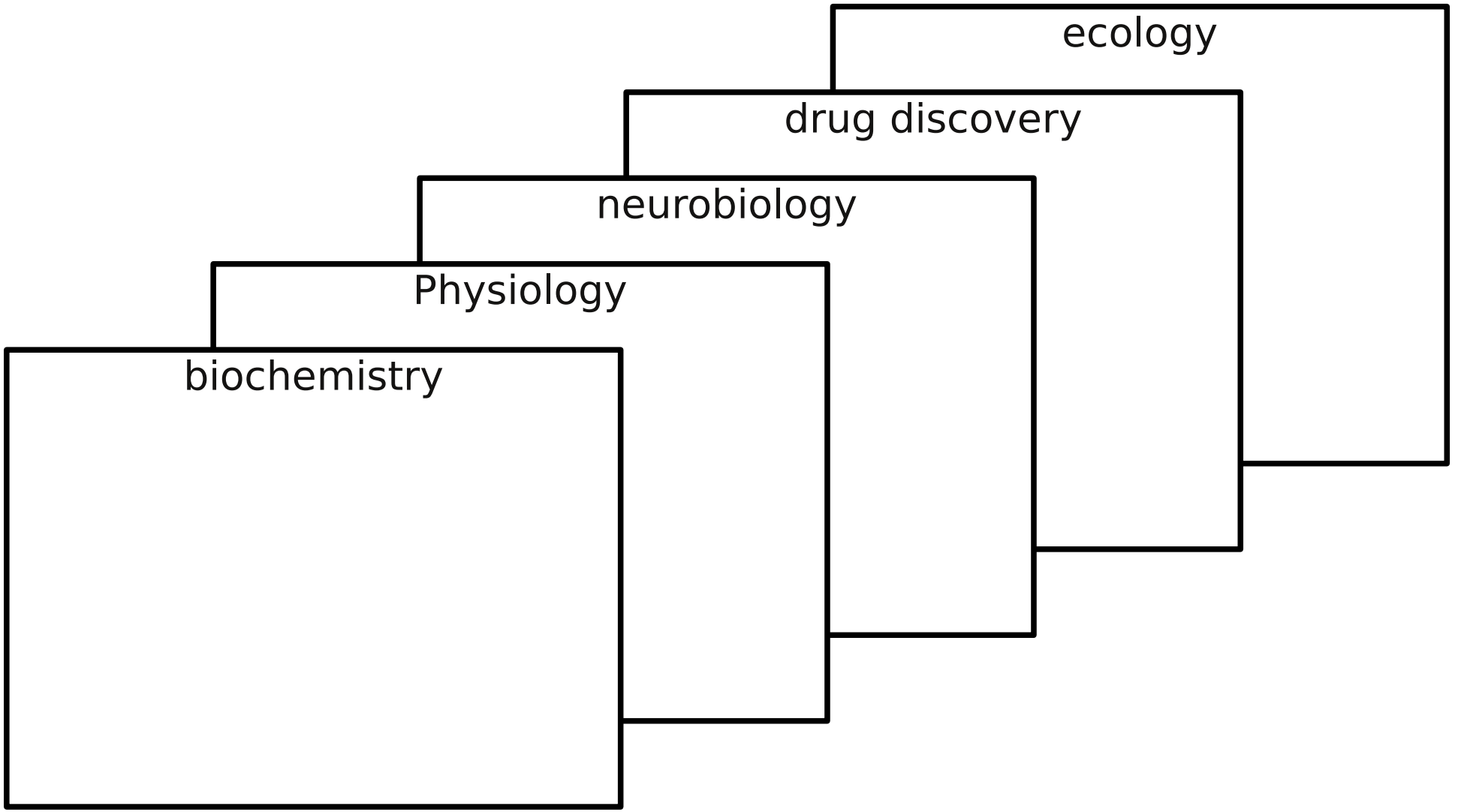
Disentangling the model life-cycle



Disentangling the level of discourse

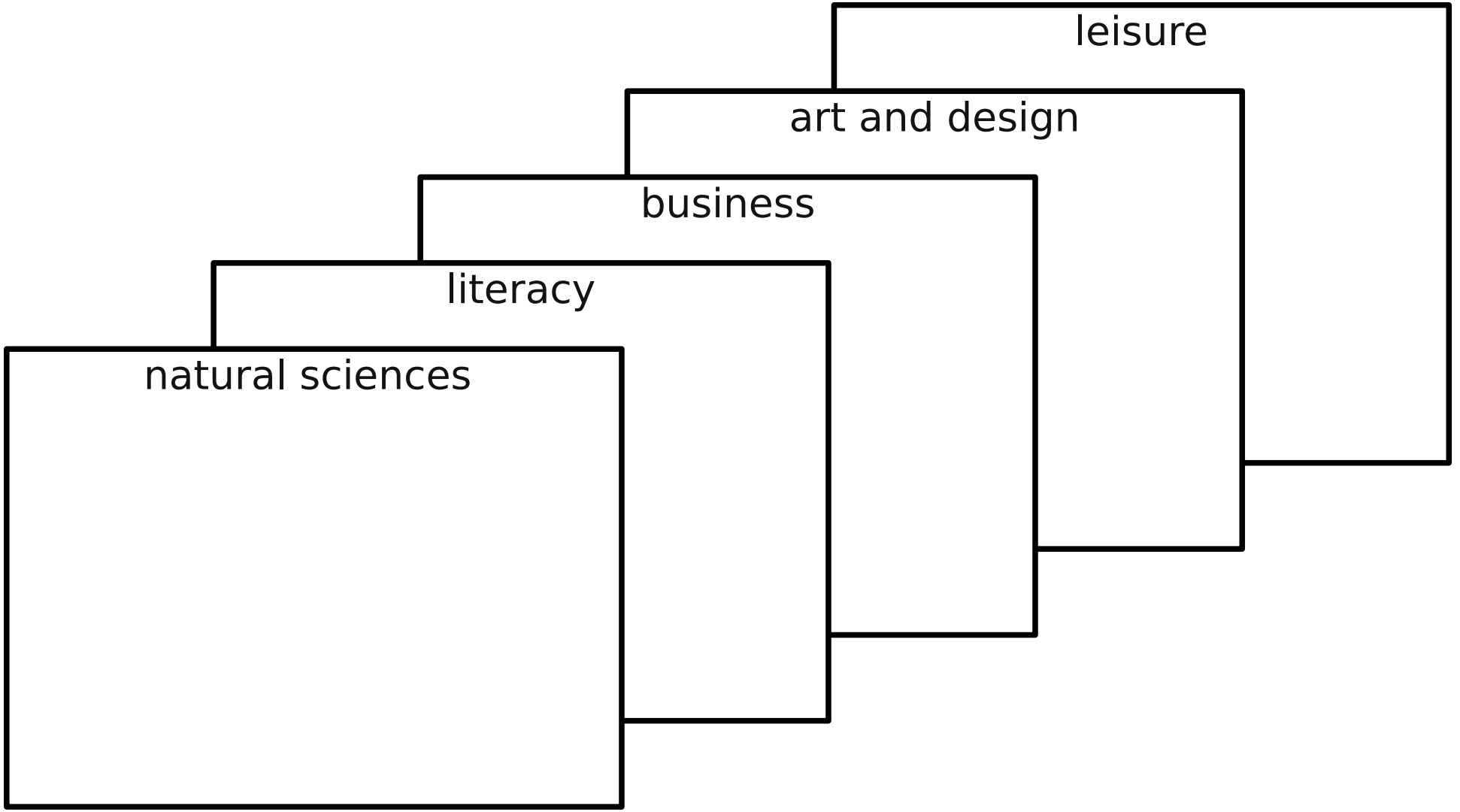


Parallel and redundant efforts

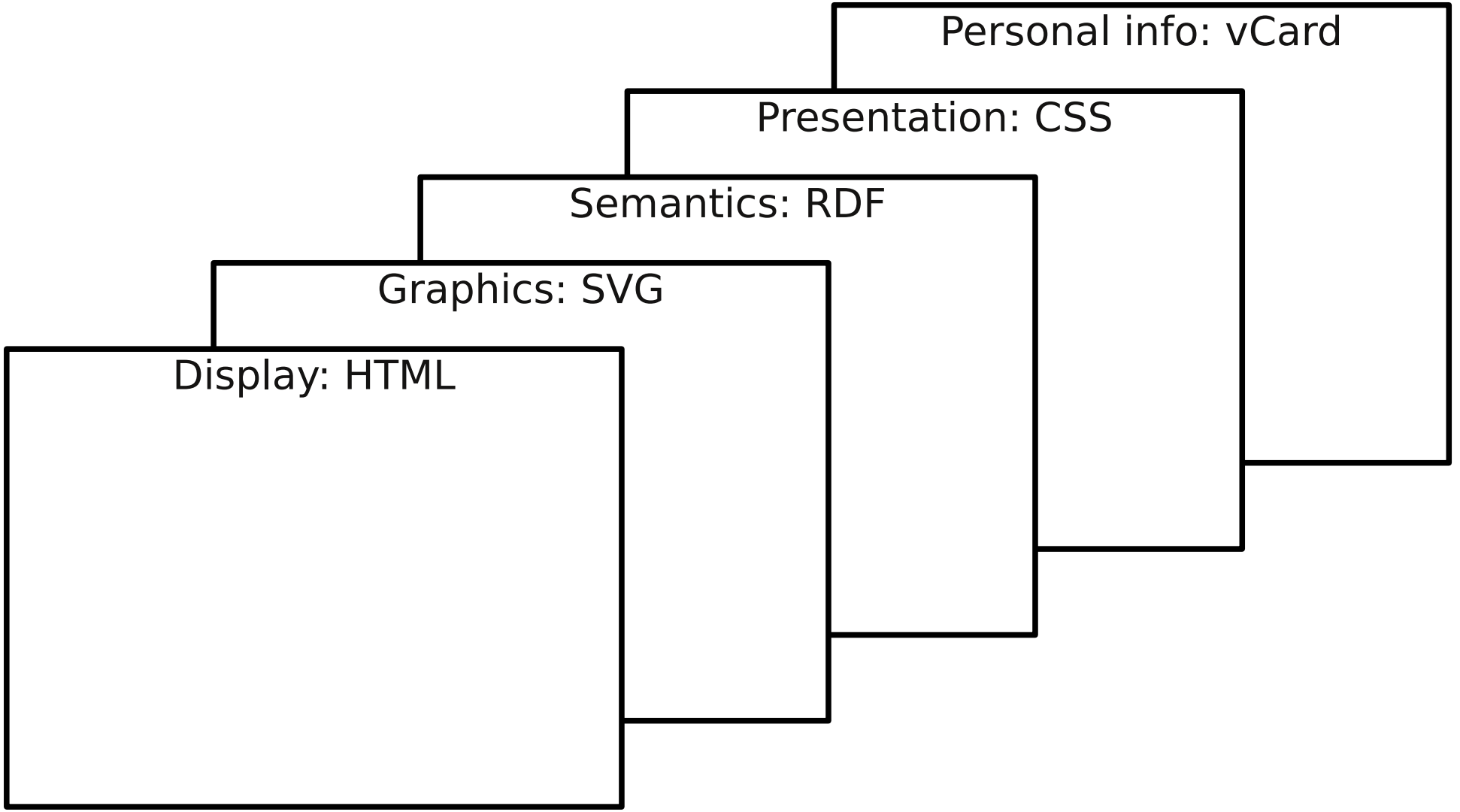


Large-scale efforts to extend the spectrum of standards

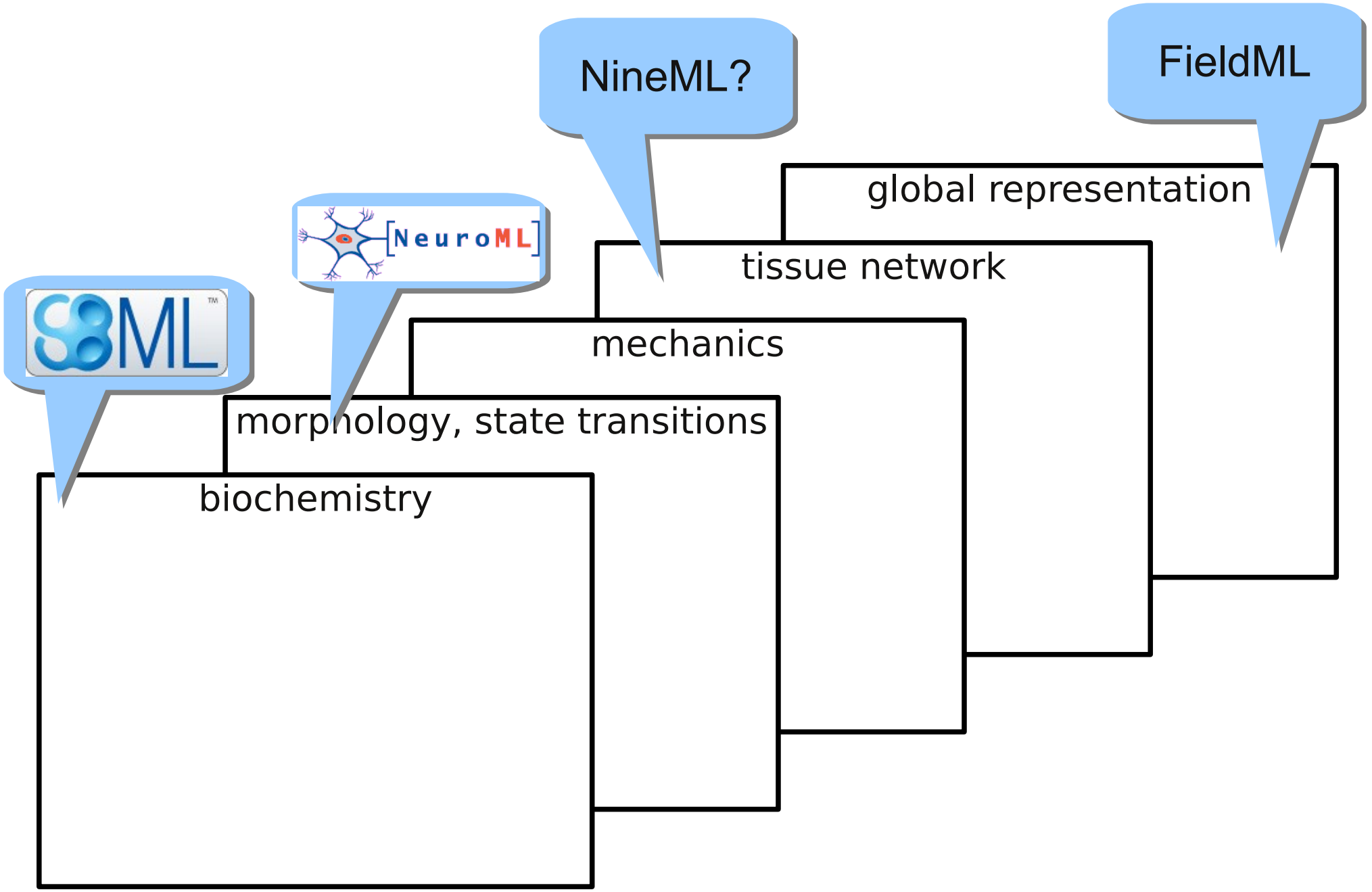
What if the world-wide web was built like this?



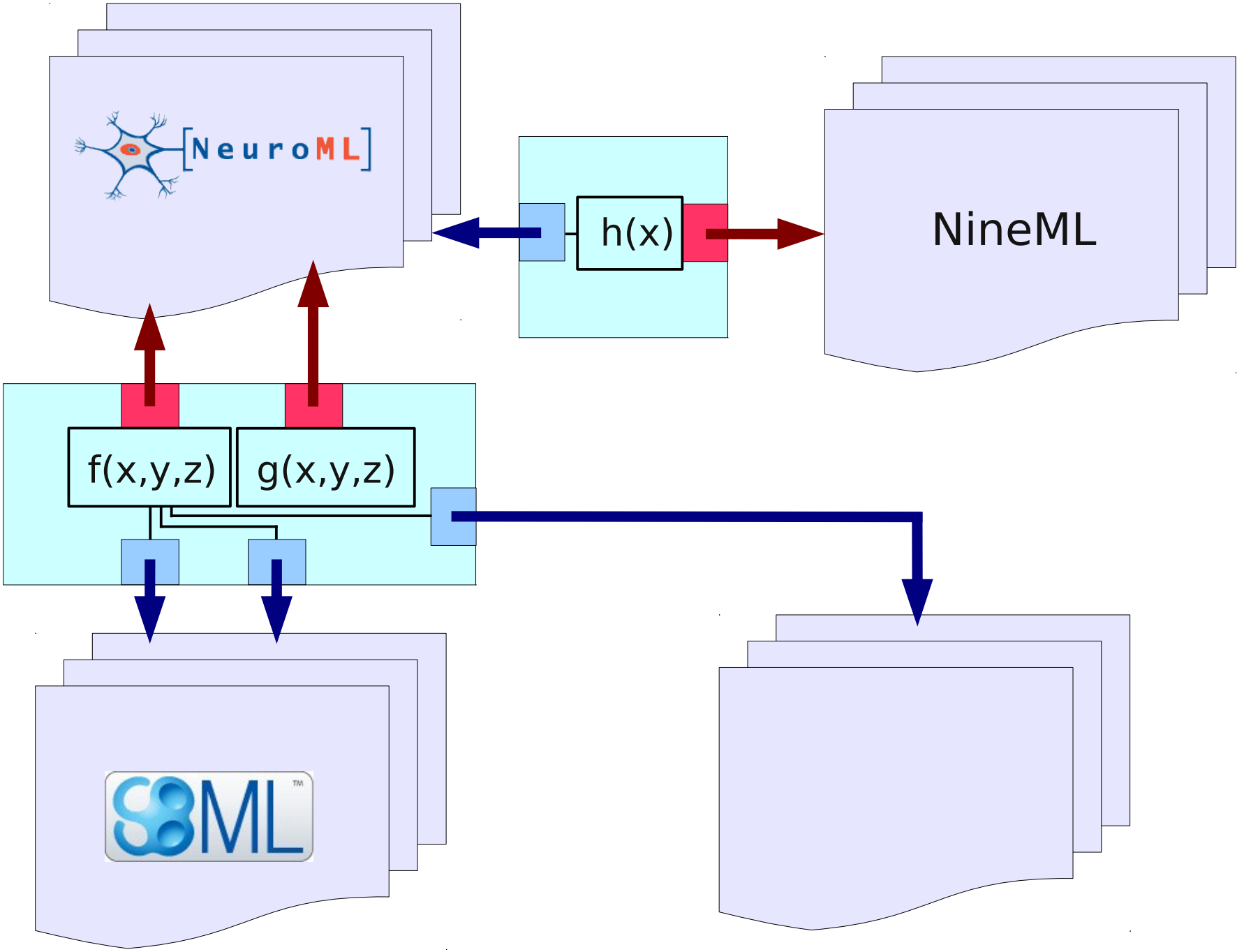
The correct way to do it



Non-overlapping languages



Multi-scale representation using adapters



Standards interoperability along the three dimensions

- SBML to BioPAX: conversion using metadata (MIRIAM annotations and SBO terms), e.g.
  - mapping between Species and PhysicalEntity
  - mapping between Reactions and PhysicalInteraction
- Conversion of SBML or BioPAX descriptions to SBGN map
- Usage of SBML descriptions (or CellML or VCML) in SED-ML: Identification of variables using XPath
- Descriptions using SBML and NeuroML: Interface based on XPath

Requirements for a overarching standardisation structure

- What?
  - Set of interoperable description languages
  - Cover all aspects of modelling and simulation
  - Cover all type of descriptions / views of the real
  - Role of community-maintained ontologies.
- How?
  - Independence towards Institutions, funders and individuals
  - Able to receive funds, to employ staff
  - Role of European Research Infrastructures? (ELIXIR, ISBE)
- Who?
  - Communities developing their standards: Systems Biology, Physiology (VPH), Neuroscience (INCF), Drug discovery (DDMoRe)
  - Other players in knowledge-representation (W3C, ...)
  - Academic and corporate users: Modeling platforms (MatWorks ...), Pharma (Pistoia alliance) ...

Requirements for a overarching standardisation structure

- What?
  - Set of interoperable description languages
  - Cover all aspects of modelling and simulation
  - Cover all type of descriptions / views of the real
  - Role of community-maintained ontologies.
- How?
  - Independence towards Institutions, funders and individuals
  - Able to receive funds, to employ staff
  - Role of European Research Infrastructures? (ELIXIR, ISBE)
- Who?
  - Communities developing their standards: Systems Biology, Physiology (VPH), Neuroscience (INCF), Drug discovery (DDMoRe)
  - Other players in knowledge-representation (W3C, ...)
  - Academic and corporate users: Modeling platforms (MatWorks ...), Pharma (Pistoia alliance) ...

COmputational Modeling in Biology NEtwork (COMBINE) forthcoming: http://co.mbine.org

A first step: common meetings

- January 2008: SBGN hackathon; BioModels DB; MIRIAM; SBO
- March 2009: SBML hackathon; BioModels DB; MIRIAM; SBO
- April 2009: CellML; SED-ML; SBGN hackathon
- May 2010: SBML hackathon; BioModels DB; MIRIAM; SBO; SED-ML
- October 2010: 1st ***COMBINE*** MEETING with SBML; SBGN; BioPAX, CellML
- From now on, two grouped annual meetings
  - ***COMBINE*** forum: presentation of support, discussion about future developments and collaboration etc.
  - ***HARMONY*** hackathon: developing support, writing specifications, tinkering with interoperability etc.

COMBINE 2010

- 6 to 9 October 2010, Edinburgh, before the ICSB
- 75 registrations so far (forecast was 50 max ...)
- 14 sessions, plus breakouts, 42 presentations, 30 posters

Physiome standards
SED-ML
SBGN languages
libSBGN and SBGN support

Encoding graph layouts
Interactions and reactions
Semantics and metadata resources
Encoding and using semantics

Format conversion
Software support
BioPAX levels
What is not covered yet

SBML Level 3
libSBML and SBML support

followed by:

SBML 10th anniversary

Acknowledgements

Visionary: **Hiroaki Kitano**

SBML editors: Frank Bergmann, *Andrew Finney, Stefan Hoops*, ***Michael Hucka***, *Nicolas Le Novère, Sarah Keating*, Sven Sahle, *Herbert Sauro*, Jim Schaff, Lucian Smith, Darren Wilkinson

SED-ML/MIASE: Richard Adams, Frank Bergmann, Dagmar Köhn/Waltemath, Nicolas Le Novère

The EBI group Computational Systems Neurobiology

The whole community of Computational Systems Biology