A brief tutorial on
SBML (the Systems Biology Markup Language)

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ICSB 2013, Copenhagen, September 2013

Outline

General background and motivations

Core features of SBML

A few additional details about SBML

Packages in SBML Level 3

A selection of resources for the SBML-oriented modeler

Closing

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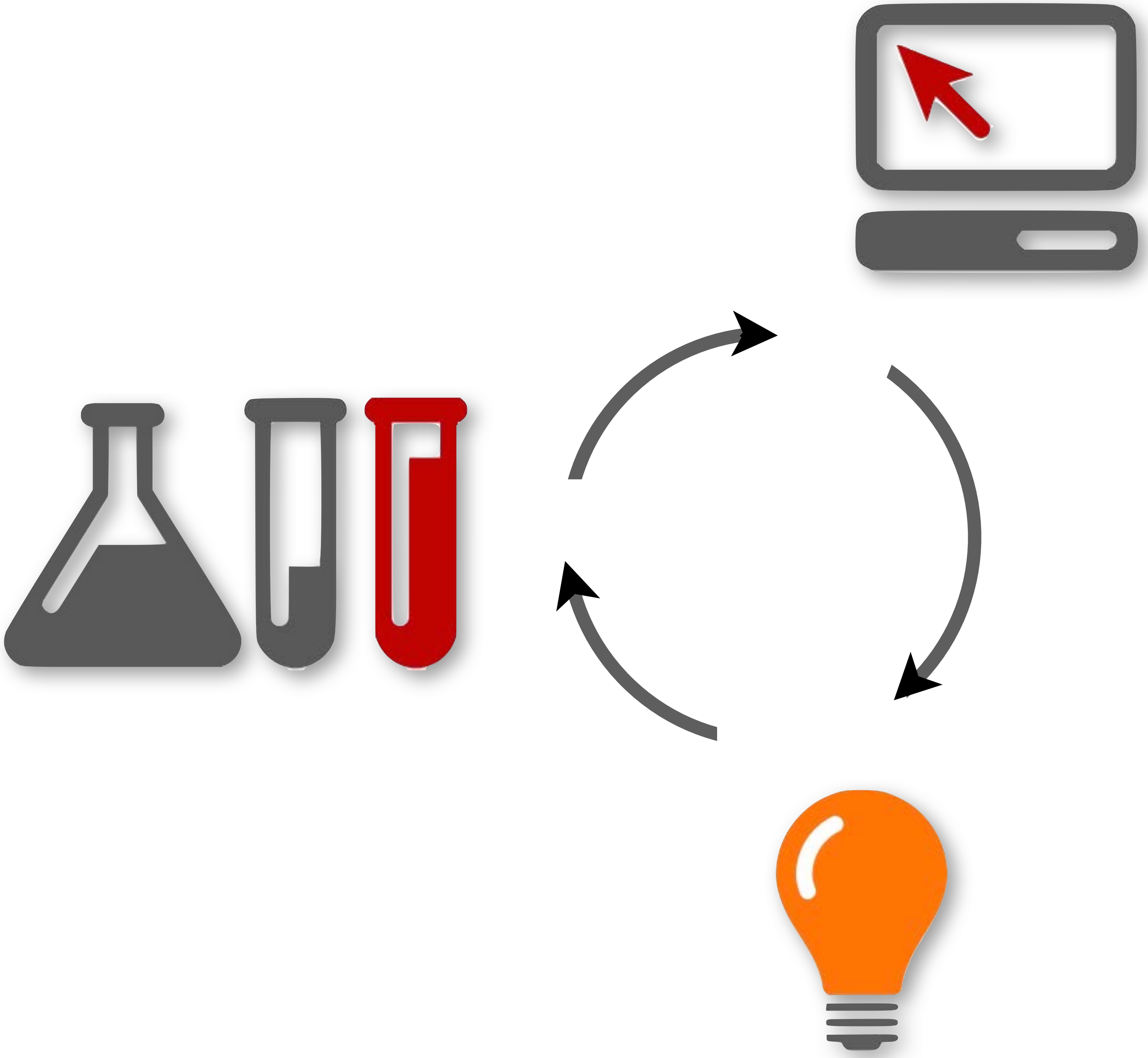
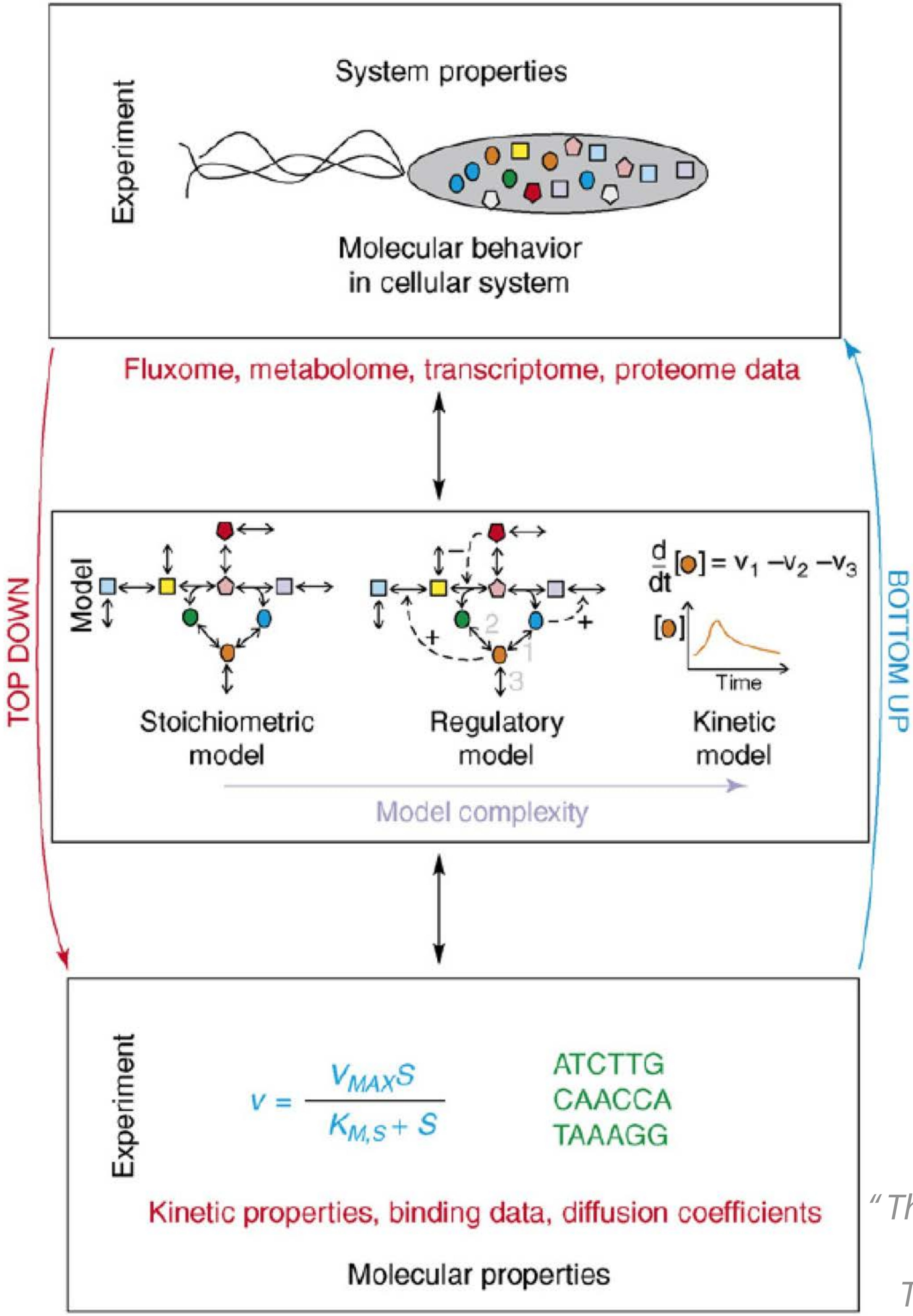


Research today: experimentation, computation, cogitation



" The nature of systems biology"
Bruggeman & Westerhoff,
Trends Microbiol. 15 (2007).

Is it enough to communicate the model in a paper?

Traditional method of dissemination in the recent past

Problems:

- Errors in printing
- Missing information
- Dependencies on implementation
- Outright errors
- Larger model
  ⇒ more time & effort

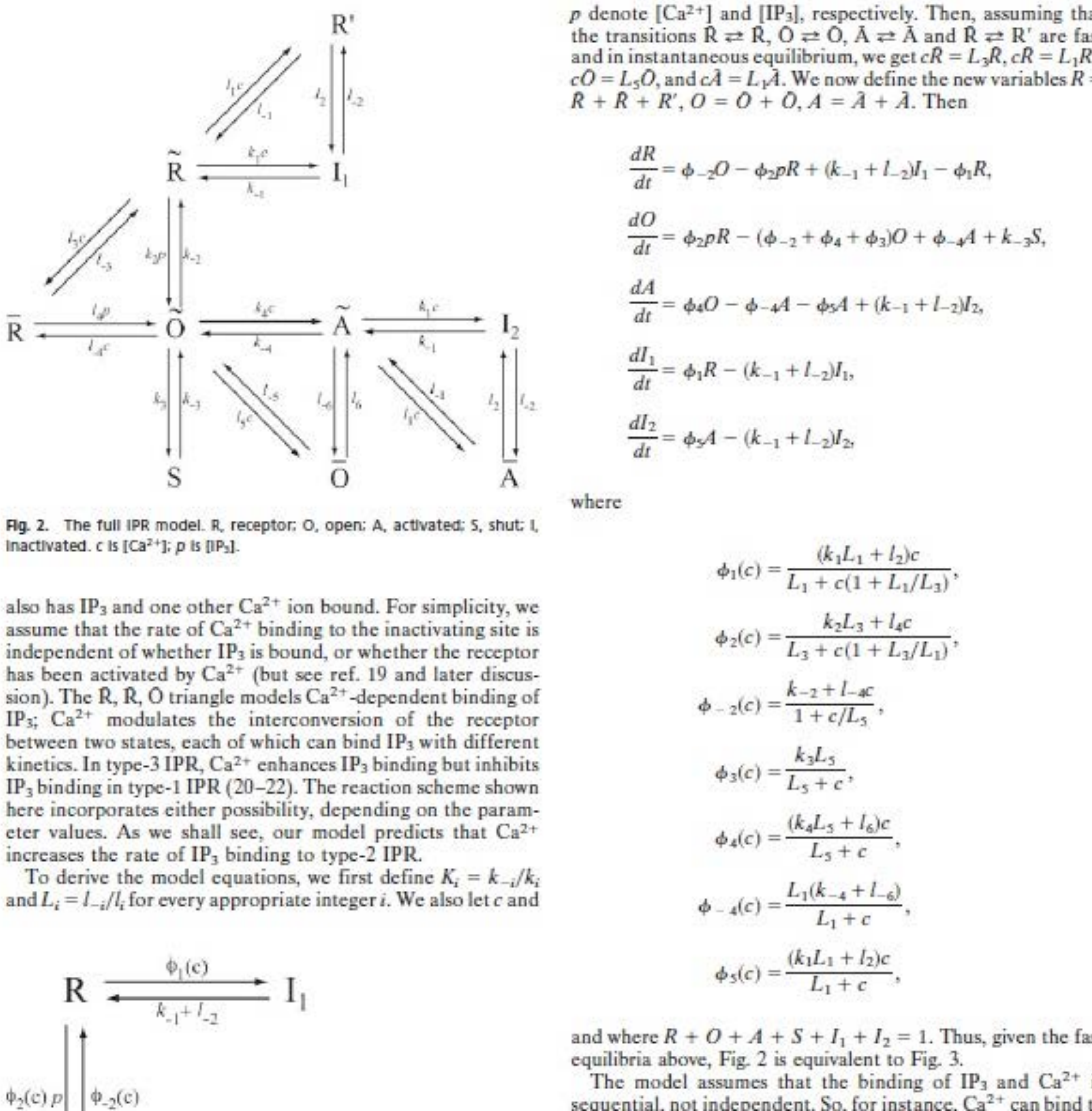


Fig. 2. The full IPR model. R, receptor; O, open; A, activated; S, shut; I, inactivated. c is $[Ca^{2+}]$; p is $[IP_3]$.

also has IP_3 and one other Ca^{2+} ion bound. For simplicity, we assume that the rate of Ca^{2+} binding to the inactivating site is independent of whether IP_3 is bound, or whether the receptor has been activated by Ca^{2+} (but see ref. 19 and later discussion). The $\bar{R}$, $\tilde{R}$, $\tilde{O}$ triangle models Ca^{2+}-dependent binding of IP_3; Ca^{2+} modulates the interconversion of the receptor between two states, each of which can bind IP_3 with different kinetics. In type-3 IPR, Ca^{2+} enhances IP_3 binding but inhibits IP_3 binding in type-1 IPR (20–22). The reaction scheme shown here incorporates either possibility, depending on the parameter values. As we shall see, our model predicts that Ca^{2+} increases the rate of IP_3 binding to type-2 IPR.

To derive the model equations, we first define $K_i = k_{-i}/k_i$ and $L_i = l_{-i}/l_i$ for every appropriate integer i. We also let c and

p denote $[Ca^{2+}]$ and $[IP_3]$, respectively. Then, assuming tha the transitions $\bar{R} \rightleftarrows \tilde{R}$, $\bar{O} \rightleftarrows \tilde{O}$, $\bar{A} \rightleftarrows \tilde{A}$ and $\tilde{R} \rightleftarrows R'$ are fa and in instantaneous equilibrium, we get $c\tilde{R} = L_3\bar{R}$, $cR' = L_1\tilde{R}$ $c\tilde{O} = L_5\bar{O}$, and $c\bar{A} = L_1\tilde{A}$. We now define the new variables R $\bar{R} + \tilde{R} + R'$, $O = \bar{O} + \tilde{O}$, $A = \bar{A} + \tilde{A}$. Then

$$\frac{dR}{dt} = \phi_{-2}O - \phi_2 pR + (k_{-1} + l_{-2})I_1 - \phi_1 R,$$

$$\frac{dO}{dt} = \phi_2 pR - (\phi_{-2} + \phi_4 + \phi_3)O + \phi_{-4}A + k_{-3}S,$$

$$\frac{dA}{dt} = \phi_4 O - \phi_{-4}A - \phi_5 A + (k_{-1} + l_{-2})I_2,$$

$$\frac{dI_1}{dt} = \phi_1 R - (k_{-1} + l_{-2})I_1,$$

$$\frac{dI_2}{dt} = \phi_5 A - (k_{-1} + l_{-2})I_2,$$

where

$$\phi_1(c) = \frac{(k_1 L_1 + l_2)c}{L_1 + c(1 + L_1/L_3)},$$

$$\phi_2(c) = \frac{k_2 L_3 + l_4 c}{L_3 + c(1 + L_3/L_1)},$$

$$\phi_{-2}(c) = \frac{k_{-2} + l_{-4}c}{1 + c/L_5},$$

$$\phi_3(c) = \frac{k_3 L_5}{L_5 + c},$$

$$\phi_4(c) = \frac{(k_4 L_5 + l_6)c}{L_5 + c},$$

$$\phi_{-4}(c) = \frac{L_1(k_{-4} + l_{-6})}{L_1 + c},$$

$$\phi_5(c) = \frac{(k_1 L_1 + l_2)c}{L_1 + c},$$

and where $R + O + A + S + I_1 + I_2 = 1$. Thus, given the fa equilibria above, Fig. 2 is equivalent to Fig. 3.

The model assumes that the binding of IP_3 and Ca^{2+} sequential, not independent. So, for instance, Ca^{2+} can bind

Is it enough to make your (software X) code available?

It’s vital for good science:

- Someone with access to the same software can try to run it, understand it, verify the computational results, build on them, etc.
- Opinion: you should **always do this** in any case

Is it enough to make your (software X) code available?

It's vital for good science—

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- Opinion: you should **always do this** in any case

But it's still not ideal for communication of scientific results:

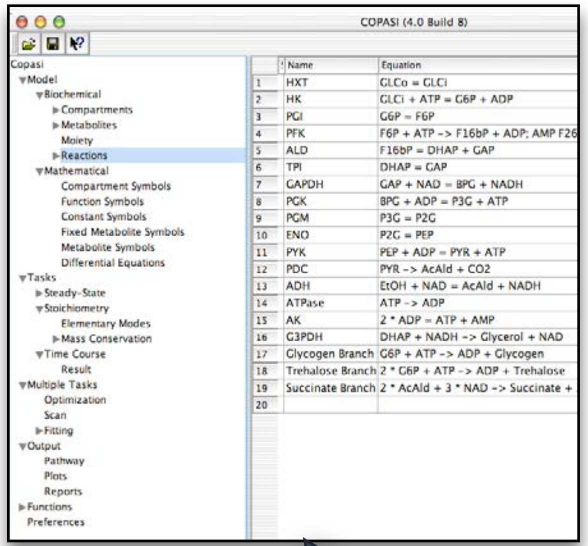
- **Doesn't necessarily encode biological semantics of the model**
- What if they don't have access to the same software?
- What if they don't want to use that software?
- What if they want to use a different conceptual framework?
- And how will people be able to relate the model to other work?

Different tools ⇒ different interfaces & languages

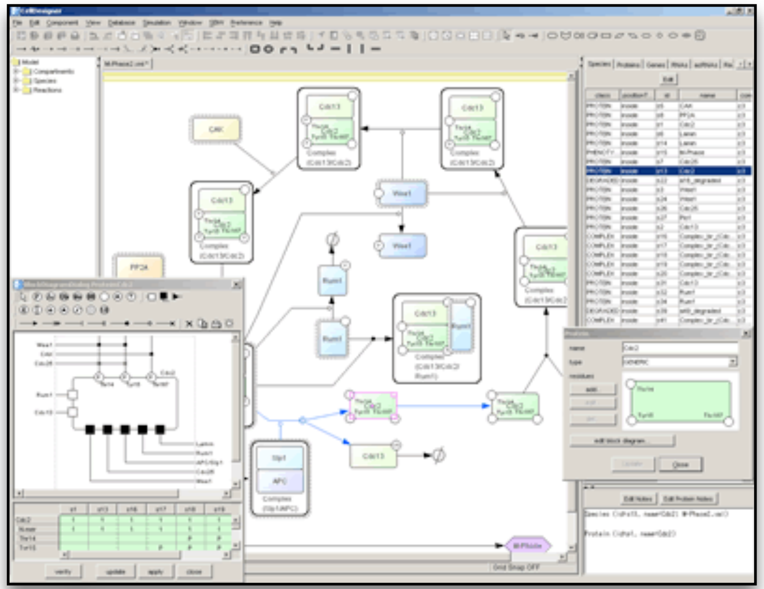
Outline

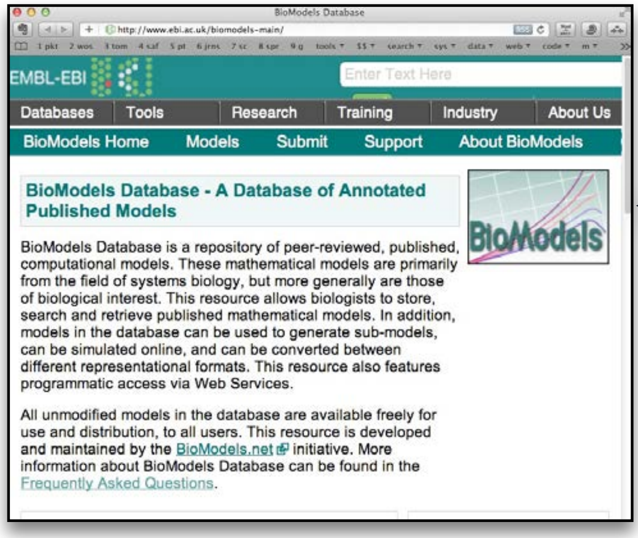
- General background and motivations
- Core features of SBML
- A few additional details about SBML
- Packages in SBML Level 3
- A selection of resources for the SBML-oriented modeler
- Closing

SBML: a lingua franca for software



	Name	Equation
1	HXT	GLCo = GLCi
2	HK	GLCi + ATP = G6P + ADP
3	PGI	G6P = F6P
4	PFK	F6P + ATP -> F16bP + ADP; AMP F26
5	ALD	F16bP = DHAP + GAP
6	TPI	DHAP = GAP
7	GAPDH	GAP + NAD = BPG + NADH
8	PGK	BPG + ADP = P3G + ATP
9	PGM	P3G = P2G
10	ENO	P2G = PEP
11	PYK	PEP + ADP = PYR + ATP
12	PDC	PYR -> AcAld + CO2
13	ADH	EtOH + NAD = AcAld + NADH
14	ATPase	ATP -> ADP
15	AK	2 * ADP = ATP + AMP
16	G3PDH	DHAP + NADH -> Glycerol + NAD
17	Glycogen Branch	G6P + ATP -> ADP + Glycogen
18	Trehalose Branch	2 * G6P + ATP -> ADP + Trehalose
19	Succinate Branch	2 * AcAld + 3 * NAD -> Succinate +
20		

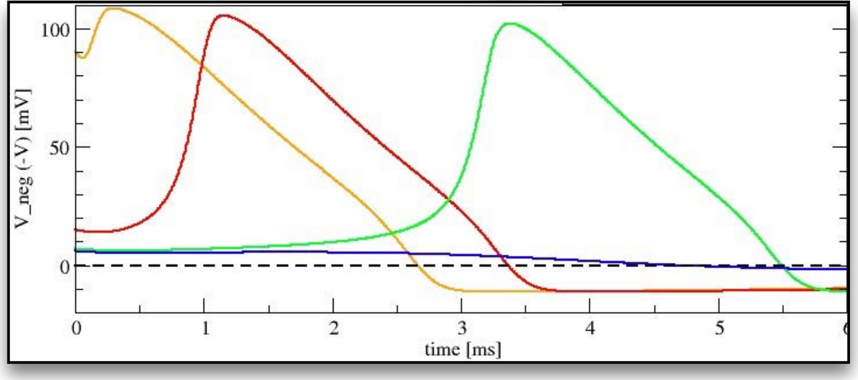


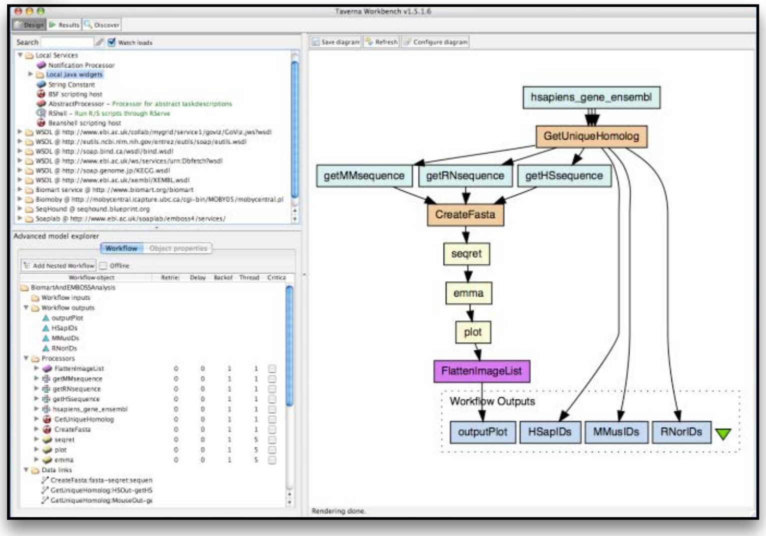


BioModels Database - A Database of Annotated Published Models

BioModels Database is a repository of peer-reviewed, published, computational models. These mathematical models are primarily from the field of systems biology, but more generally are those of biological interest. This resource allows biologists to store, search and retrieve published mathematical models. In addition, models in the database can be used to generate sub-models, can be simulated online, and can be converted between different representational formats. This resource also features programmatic access via Web Services.

All unmodified models in the database are available freely for use and distribution, to all users. This resource is developed and maintained by the BioModels.net initiative. More information about BioModels Database can be found in the Frequently Asked Questions.





SBML = Systems Biology Markup Language

Format for **representing** computational models of biological processes

- Data structures + usage principles + serialization to XML
- (Mostly) Declarative, not procedural—not a scripting language

Neutral with respect to modeling framework

- E.g., ODE, stochastic systems, etc.

Important: **software** reads/writes SBML, **not humans**

The raw SBML (as XML)

```
<listOfSpecies>
    <species compartment="cytosol" id="ES" initialAmount="0"     name="ES"/>
    <species compartment="cytosol" id="P"  initialAmount="0"     name="P"/>
    <species compartment="cytosol" id="S"  initialAmount="1e-20" name="S"/>
    <species compartment="cytosol" id="E"  initialAmount="5e-21" name="E"/>
</listOfSpecies>
<listOfReactions>
    <reaction id="veq">
        <listOfReactants>
            <speciesReference species="E"/>
            <speciesReference species="S"/>
        </listOfReactants>
        <listOfProducts>
            <speciesReference species="ES"/>
        </listOfProducts>
        <kineticLaw>
            <math xmlns="http://www.w3.org/1998/Math/MathML">
                <apply>
                    <times/>
                    <ci>cytosol</ci>
                    <apply>
                        <minus/>
                        <apply>
                            <times/>
                            <ci>kon</ci>
                            <ci>E</ci>
                            <ci>S</ci>
                        </apply>
                        <apply>
                            <times/>
                            <ci>koff</ci>
                            <ci>ES</ci>
                        </apply>
                    </apply>
                </apply>
```

The process is central

- Literally called a "**reaction**" in SBML
- Participants are pools of entities (biochemical **species**)

$$n_a A + n_b B \xrightarrow{f([A],[B],[P],\ldots)} n_p P$$

$$n_c C \xrightarrow{f(\ldots)} n_d D + n_e E + n_f F$$

$$\vdots$$

Models can further include:

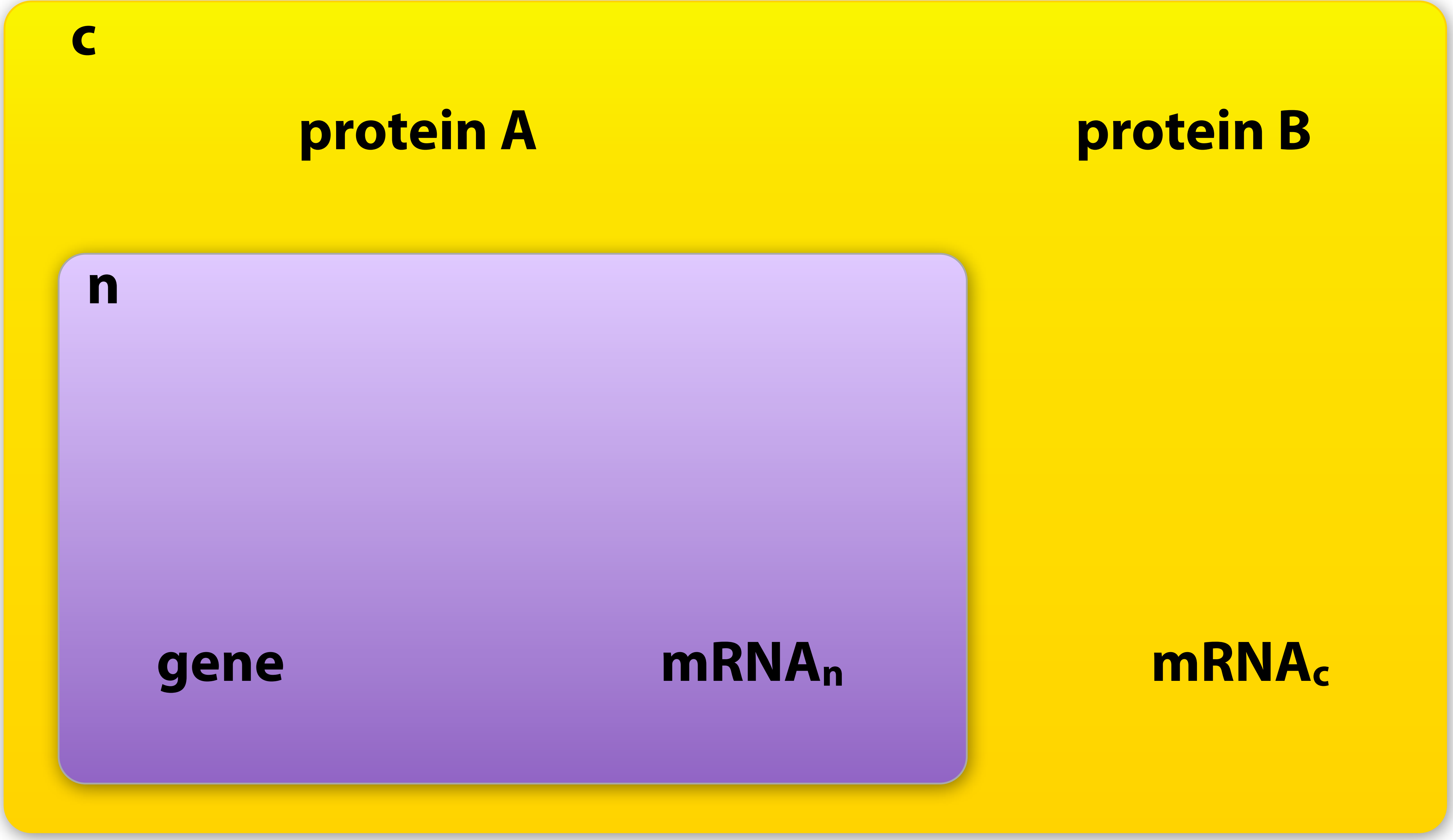
- **Compartments**
- Other constants & variables
- Discontinuous **events**
- **Other, explicit math**
- Unit definitions
- Annotations

Core SBML concepts are fairly simple

Some basics of SBML core model encoding

Well-stirred compartments

Species pools are located in compartments



c

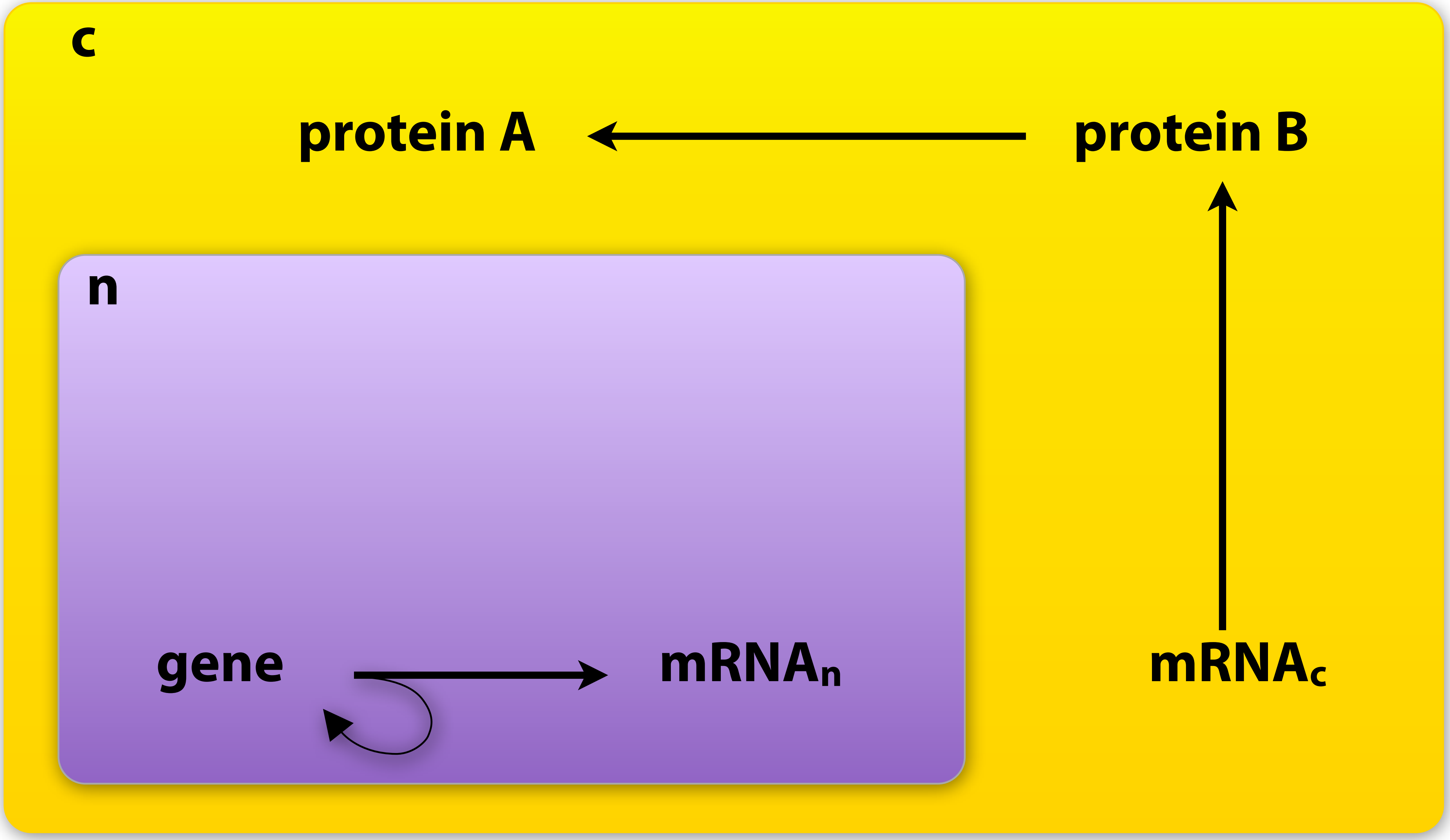
protein A **protein B**

n

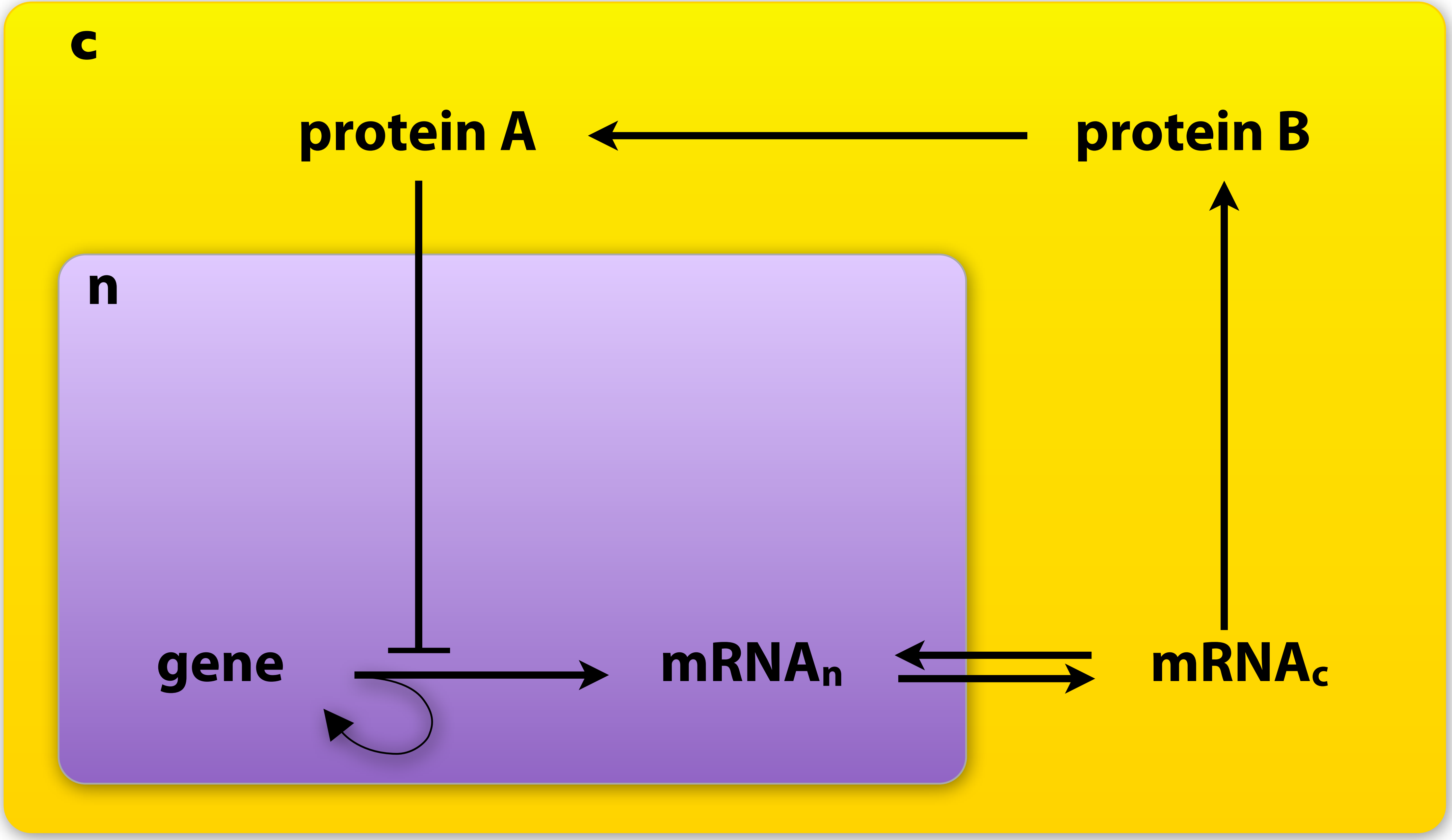
gene **mRNA_n**

mRNA_c

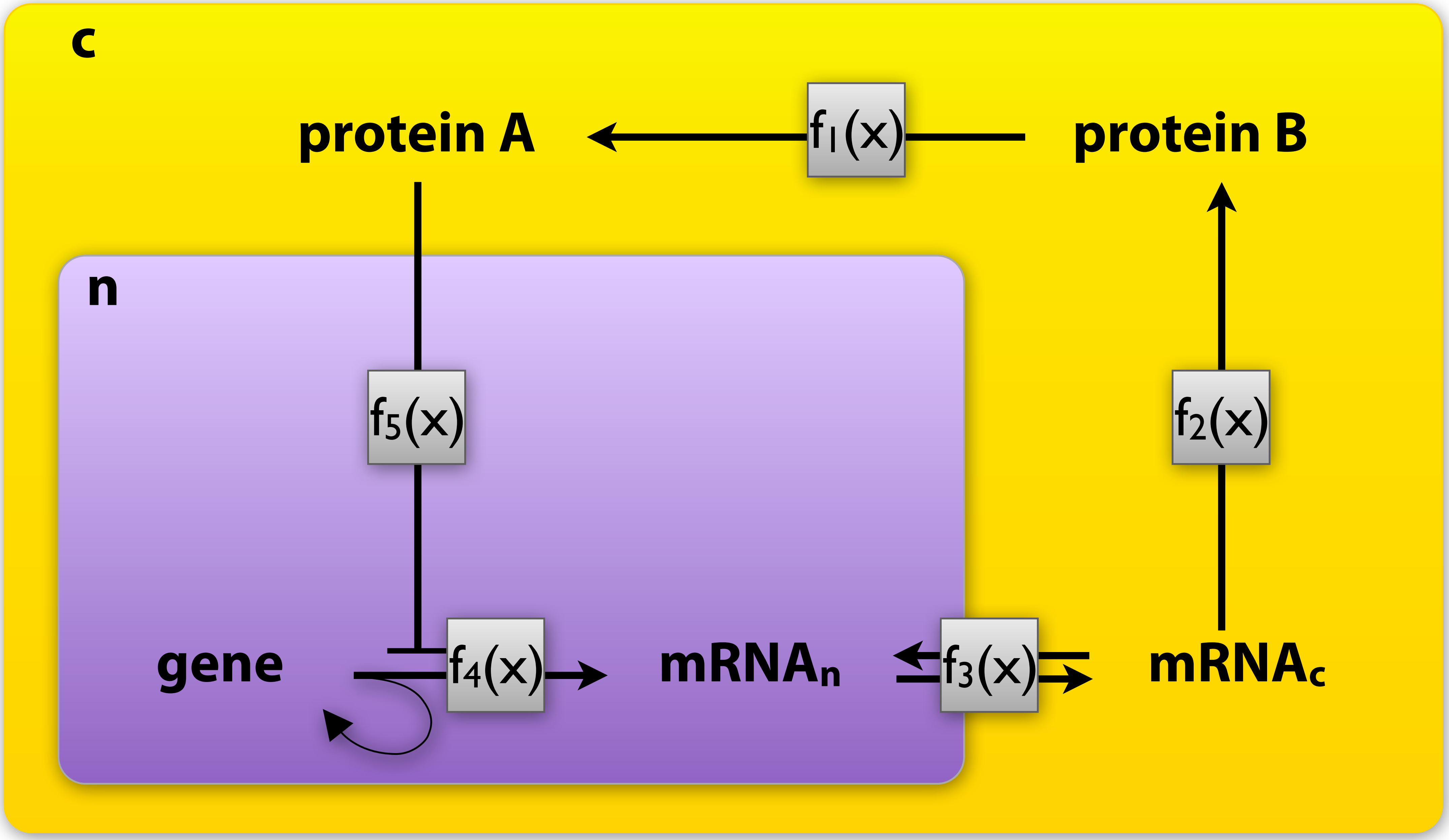
Reactions can involve any species anywhere



Reactions can cross compartment boundaries



Reaction/process rates can be (almost) arbitrary formulas



“Rules”: equations expressing relationships in addition to reaction sys.

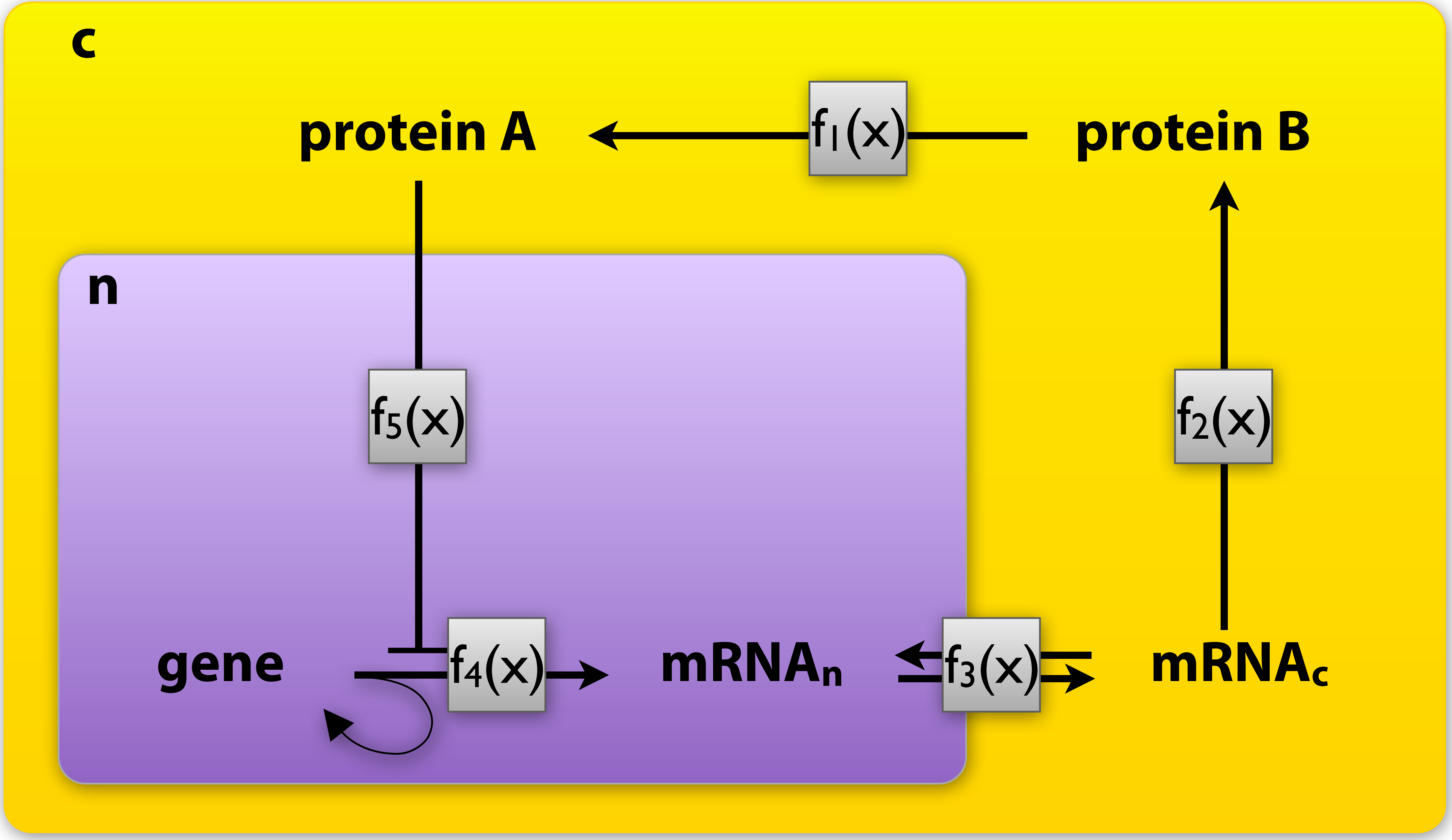
$g_1(x)$

$g_2(x)$

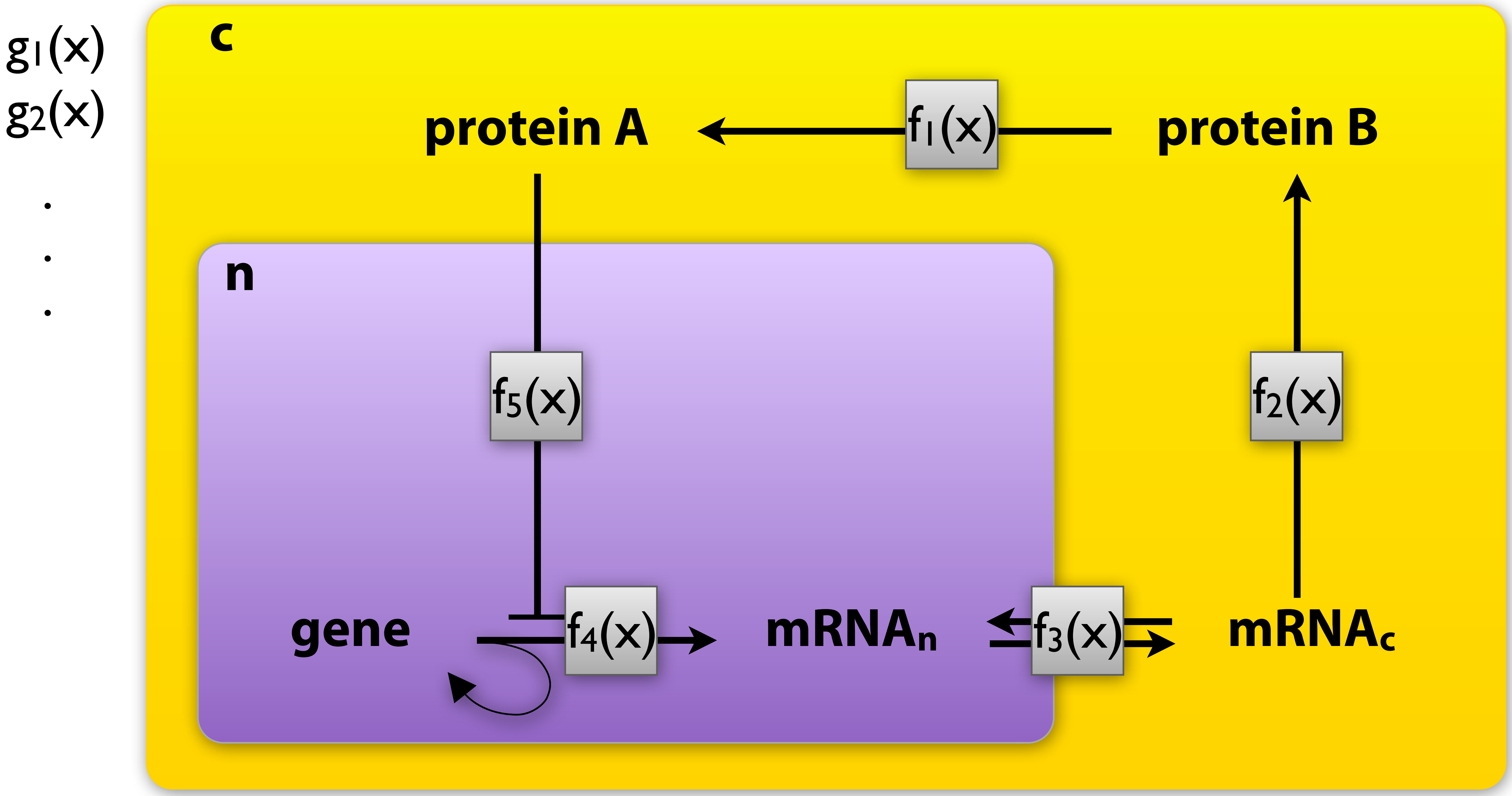
.

.

.

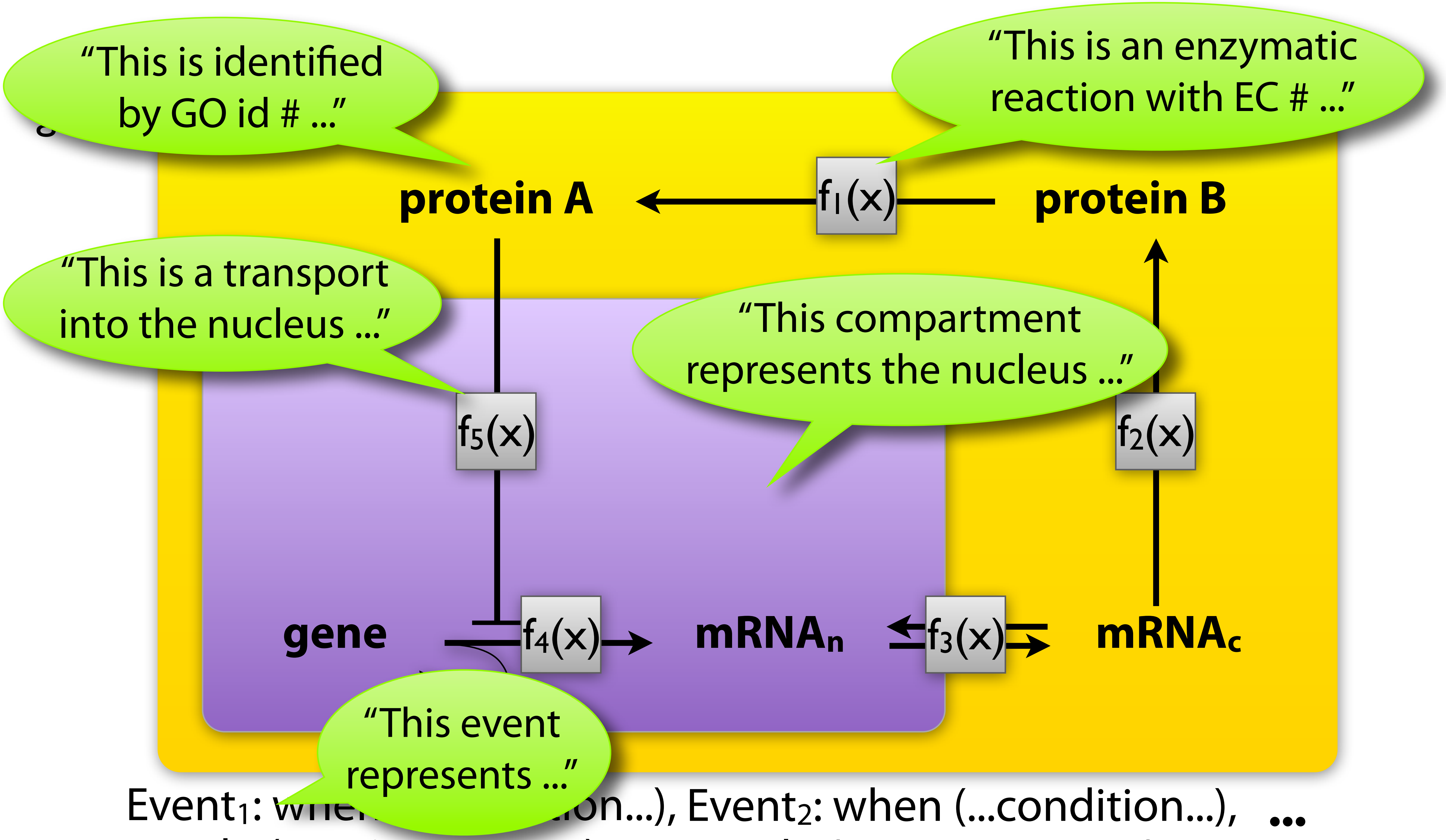


“Events”: discontinuous actions triggered by system conditions



$Event_1$: when (...condition...), $Event_2$: when (...condition...), ...
do (...assignments...) do (...assignments...)

Annotations: machine-readable semantics and links to other resources



"This is identified by GO id # ..."

"This is an enzymatic reaction with EC # ..."

protein A

$f_1(x)$

protein B

"This is a transport into the nucleus ..."

"This compartment represents the nucleus ..."

$f_5(x)$

$f_2(x)$

gene

$f_4(x)$

mRNA$_n$

$f_3(x)$

mRNA$_c$

"This event represents ..."

Event$_1$: whe on...), Event$_2$: when (...condition...), ...
do (...assignments...) do (...assignments...)

Scope of SBML encompasses many types of models

Many types of models can be encoded just using core SBML features

- Metabolic network models
- Signaling pathway models
- Conductance-based models
- Neural models
- Pharmacokinetic/dynamics models
- Infectious diseases

Find examples in BioModels Database

http://biomodels.net/biomodels

SBML Level 3 *packages* extend the core to support other types

- E.g.: Spatially inhomogeneous models, also qualitative/logical

SBML funding sources over the past 13+ years

National Institute of General Medical Sciences (USA)

European Molecular Biology Laboratory (EMBL)

JST ERATO Kitano Symbiotic Systems Project (Japan) (to 2003)

JST ERATO-SORST Program (Japan)

ELIXIR (UK)

Beckman Institute, Caltech (USA)

Keio University (Japan)

International Joint Research Program of NEDO (Japan)

Japanese Ministry of Agriculture

Japanese Ministry of Educ., Culture, Sports, Science and Tech.

BBSRC (UK)

National Science Foundation (USA)

DARPA IPTO Bio-SPICE Bio-Computation Program (USA)

Air Force Office of Scientific Research (USA)

STRI, University of Hertfordshire (UK)

Molecular Sciences Institute (USA)

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SBML Files

Format: text (technically UTF-8)

Extension: usually **.xml** (not .sbml)

Does **not** store experimental data, or simulation descriptions

- But software may write proprietary metadata (annotations) in SBML

Applications usually have their own native format

- Import/export SBML

Models exist in different "Levels and Versions" of SBML

- Indicated at top of file

SBML identifiers and names

Most elements have both an "id" and a "name" field

- Identifier field has restricted syntax: **`abc123`** or **`_abc123`**, etc.
  - This "id" field value is what you use in expressions
- Value of "name" field is almost completely unrestricted
  - Names with spaces, **`$tr@nge`** and **`Fμηηγ`** characters!
- **Must assign a value to "id"**, but "name" is optional

Some tools let you use the names and ignore id's (e.g., COPASI)—they generate the id's automatically

- But some (especially those w/ script language features) expose id's

SBML "rules"

"Rules" in SBML define extra mathematical expressions

- E.g.: if need to express additional mathematical relationships beyond what is implied by the system of reactions

3 subtypes:

Rule type	General form	Example
algebraic	$0 = f(\mathbf{W})$	0 = S1 + S2
assignment	$x = f(\mathbf{V})$	x = y + z
rate	$dx/dt = f(\mathbf{W})$	dS/dt = 10.5

Rules define relationships that hold at all times

$$
\begin{aligned}
dS_1/dt &= r_1 + r_2 + r_3 + \ldots \\
dS_2/dt &= -r_1 + r_5 + \ldots \\
\ldots \\
0 &= f_1(\mathbf{W}) \\
0 &= f_2(\mathbf{W}) \\
\ldots \\
x &= g_1(\mathbf{W}) \\
y &= g_2(\mathbf{W}) \\
\ldots \\
dm/dt &= h_1(\mathbf{W}) \\
dq/dt &= h_2(\mathbf{W}) \\
\ldots
\end{aligned}
$$

Rules in the context of the overall model

Rules in the context of the overall model

Equations derived from reaction definitions

$$
\begin{aligned}
dS_1/dt &= r_1 + r_2 + r_3 + \ldots \\
dS_2/dt &= -r_1 + r_5 + \ldots \\
&\ldots \\
0 &= f_1(\mathbf{W}) \\
0 &= f_2(\mathbf{W}) \\
&\ldots \\
x &= g_1(\mathbf{W}) \\
y &= g_2(\mathbf{W}) \\
&\ldots \\
dm/dt &= h_1(\mathbf{W}) \\
dq/dt &= h_2(\mathbf{W}) \\
&\ldots
\end{aligned}
$$

Rules in the context of the overall model

$$dS_1/dt = r_1 + r_2 + r_3 + \dots$$

$$dS_2/dt = -r_1 + r_5 + \dots$$

$$\dots$$

Algebraic rules

$$0 = f_1(\mathbf{W})$$

$$0 = f_2(\mathbf{W})$$

$$\dots$$

$$x = g_1(\mathbf{W})$$

$$y = g_2(\mathbf{W})$$

$$\dots$$

$$dm/dt = h_1(\mathbf{W})$$

$$dq/dt = h_2(\mathbf{W})$$

$$\dots$$

Rules in the context of the overall model

$$
\begin{aligned}
dS_1/dt &= r_1 + r_2 + r_3 + \dots \\
dS_2/dt &= -r_1 + r_5 + \dots \\
&\dots \\
0 &= f_1(\mathbf{W}) \\
0 &= f_2(\mathbf{W}) \\
&\dots
\end{aligned}
$$

Assignment rules

$$
\boxed{
\begin{aligned}
x &= g_1(\mathbf{W}) \\
y &= g_2(\mathbf{W})
\end{aligned}
}
$$

$$
\begin{aligned}
&\dots \\
dm/dt &= h_1(\mathbf{W}) \\
dq/dt &= h_2(\mathbf{W}) \\
&\dots
\end{aligned}
$$

$$\begin{aligned}
dS_1/dt &= r_1 + r_2 + r_3 + \ldots \\
dS_2/dt &= -r_1 + r_5 + \ldots \\
&\ldots \\
0 &= f_1(\mathbf{W}) \\
0 &= f_2(\mathbf{W}) \\
&\ldots \\
x &= g_1(\mathbf{W}) \\
y &= g_2(\mathbf{W}) \\
&\ldots \\
dm/dt &= h_1(\mathbf{W}) \\
dq/dt &= h_2(\mathbf{W}) \\
&\ldots
\end{aligned}$$

Rate rules

Rules in the context of the overall model

$$
\begin{aligned}
dS_1/dt &= r_1 + r_2 + r_3 + \ldots \\
dS_2/dt &= -r_1 + r_5 + \ldots \\
&\ldots \\
0 &= f_1(\mathbf{W}) \\
0 &= f_2(\mathbf{W}) \\
&\ldots \\
x &= g_1(\mathbf{W}) \\
y &= g_2(\mathbf{W}) \\
&\ldots \\
dm/dt &= h_1(\mathbf{W}) \\
dq/dt &= h_2(\mathbf{W}) \\
&\ldots
\end{aligned}
$$

Rules and equations from reactions are taken together

Rules in the context of the overall model

SBML supports two annotation schemes

SBO (Systems Biology Ontology)

- For mathematical semantics
- One SBML object ← one SBO term
- Short, compact, tightly coupled but limited scope

MIRIAM (Minimum Information Requested In the Annotation of Models)

- For any kind of annotation
- One SBML object ← multiple MIRIAM annotations
- Larger, more free-form, wider scope

Both are **externalized** and **independent of SBML**

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SBML Level 1	SBML Level 2	SBML Level 3
predefined math functions	user-defined functions	user-defined functions
text-string math notation	MathML subset	MathML subset
reserved namespaces for annotations	no reserved namespaces for annotations	no reserved namespaces for annotations
no controlled annotation scheme	RDF-based controlled annotation scheme	RDF-based controlled annotation scheme
no discrete events	discrete events	discrete events
default values defined	default values defined	no default values
monolithic	monolithic	modular

Evolution of SBML continues

Today: SBML Level 3

- Level 3 Core provides framework for common models
- Level 3 *packages* add additional constructs to the Core

Level 3 package	What it enables	Status
Hierarchical model composition	Models containing submodels	✔
Flux balance constraints	Constraint-based models	✔
Qualitative models	Petri net models, Boolean models	✔
Graph layout	Diagrams of models	✔
Multicomponent/state species	Entities w/ structure; also rule-based models	draft
Spatial	Nonhomogeneous spatial models	draft
Graph rendering	Diagrams of models	draft
Groups	Arbitrary grouping of components	draft
Distributions	Numerical values as statistical distributions	in dev
Arrays & sets	Arrays or sets of entities	in dev
Dynamic structures	Creation & destruction of components	in dev
Annotations	Richer annotation syntax	

SBML Level 3 Qualitative models (released)

Some models use a **discrete logical formalism** – e.g., Boolean net, Petri

- SBML species are quantities, **not states or levels**

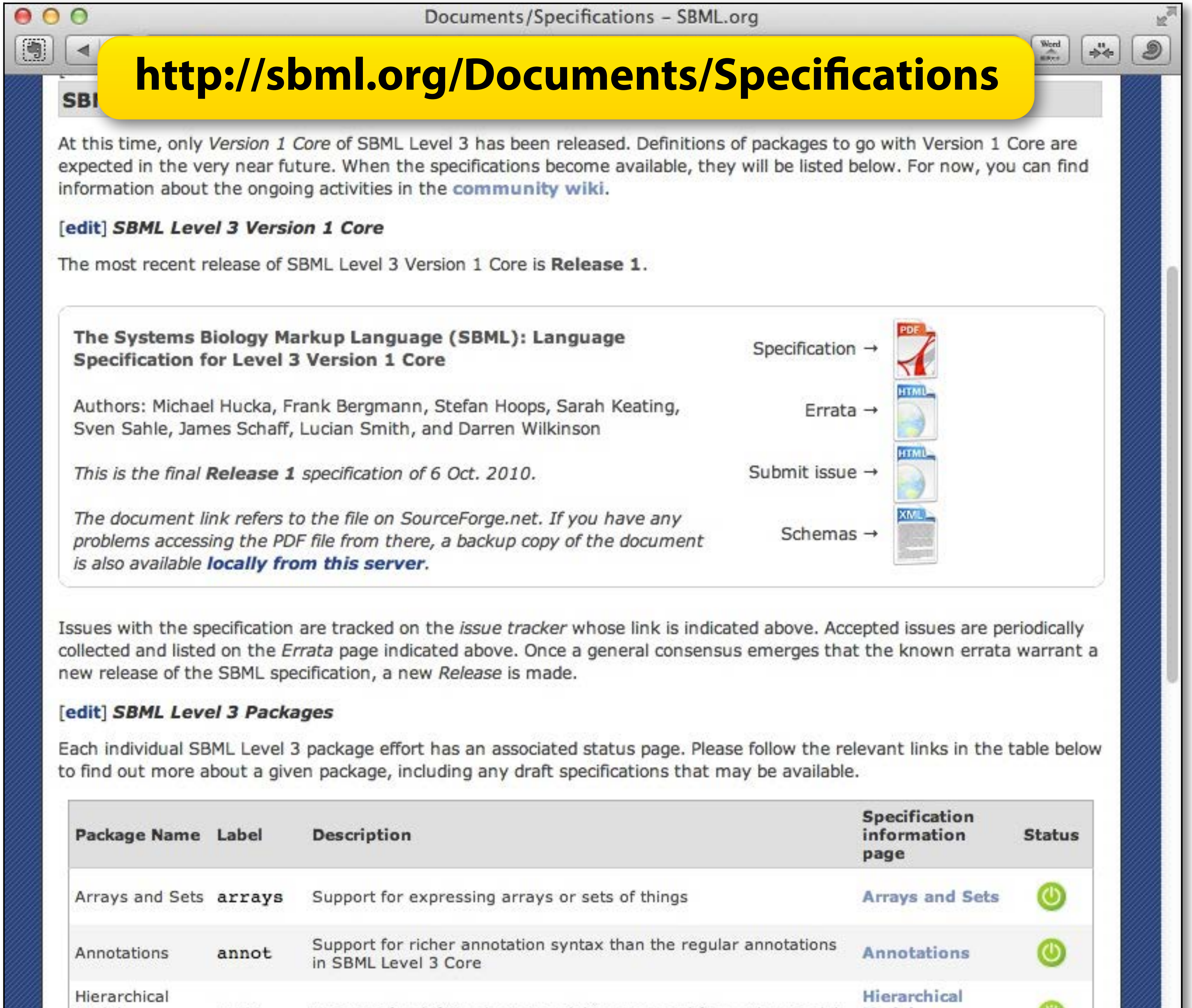
SBML Level 3 *Qualitative Models* package provides proper support

- Adds data structures for:
  - **Qualitative species**, with assume discrete values (e.g., 0 or 1)
  - **Transitions**, with inputs, outputs and function terms
    - At each time step in a simulation, all function terms evaluated
    - Terms evaluating to *true* dictate resulting state changes

Developed by Claudine Chaouiya, Sarah Keating, Duncan Berenguier, Aurélien Naldi, Denis Thieffry, Tomáš Helikar, Martijn van Iersel

Supported in GINsim, CellNOpt, Cell Collective

New table & status pages for package *specifications*



http://sbml.org/Documents/Specifications

SBI

At this time, only *Version 1 Core* of SBML Level 3 has been released. Definitions of packages to go with Version 1 Core are expected in the very near future. When the specifications become available, they will be listed below. For now, you can find information about the ongoing activities in the **community wiki**.

[edit] ***SBML Level 3 Version 1 Core***

The most recent release of SBML Level 3 Version 1 Core is **Release 1**.

The Systems Biology Markup Language (SBML): Language Specification for Level 3 Version 1 Core

Authors: Michael Hucka, Frank Bergmann, Stefan Hoops, Sarah Keating, Sven Sahle, James Schaff, Lucian Smith, and Darren Wilkinson

*This is the final **Release 1** specification of 6 Oct. 2010.*

*The document link refers to the file on SourceForge.net. If you have any problems accessing the PDF file from there, a backup copy of the document is also available **locally from this server**.*

Specification →

Errata →

Submit issue →

Schemas →

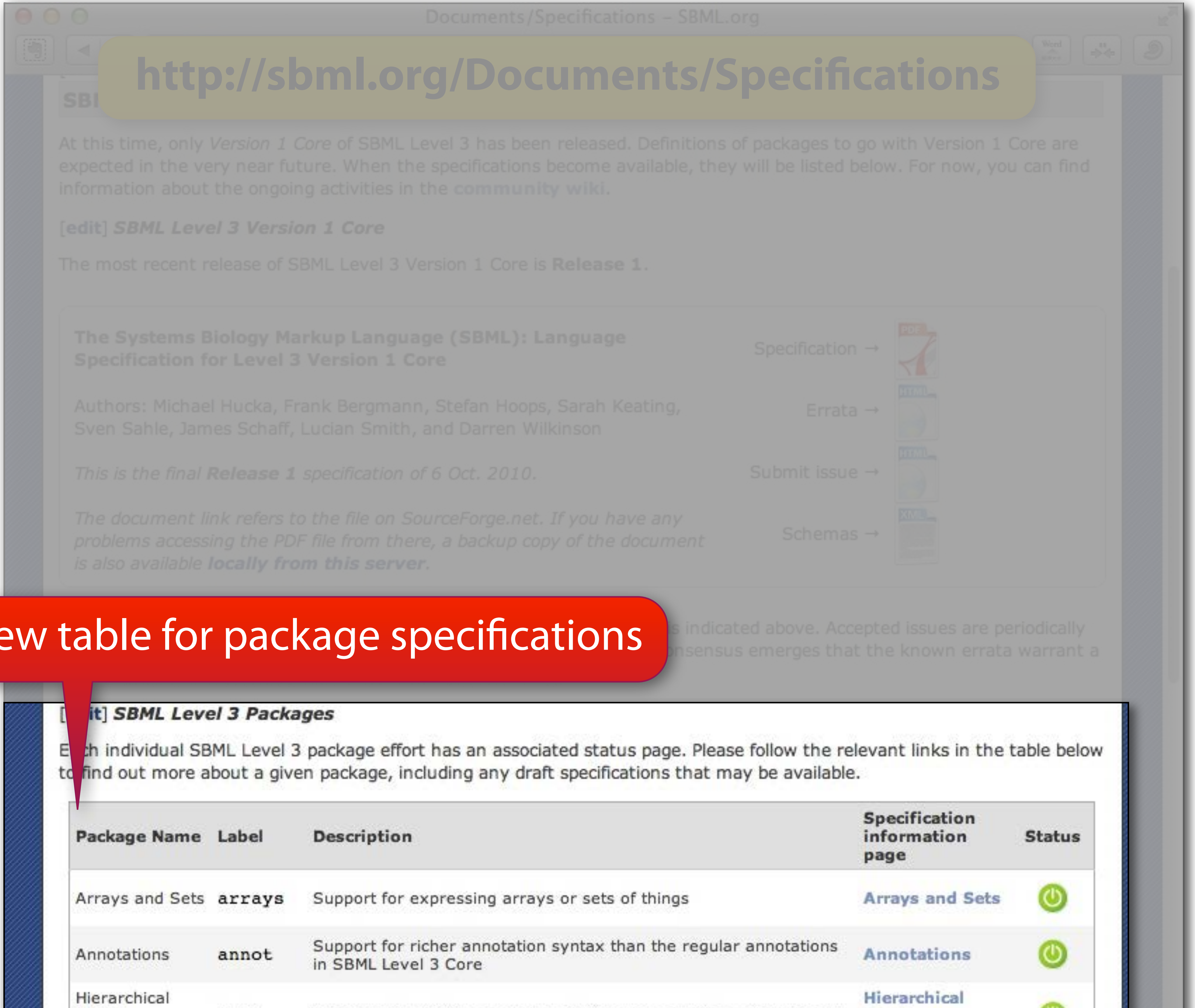
Issues with the specification are tracked on the *issue tracker* whose link is indicated above. Accepted issues are periodically collected and listed on the *Errata* page indicated above. Once a general consensus emerges that the known errata warrant a new release of the SBML specification, a new *Release* is made.

[edit] ***SBML Level 3 Packages***

Each individual SBML Level 3 package effort has an associated status page. Please follow the relevant links in the table below to find out more about a given package, including any draft specifications that may be available.

Package Name	Label	Description	Specification information page	Status
Arrays and Sets	`arrays`	Support for expressing arrays or sets of things	**Arrays and Sets**	⏻
Annotations	`annot`	Support for richer annotation syntax than the regular annotations in SBML Level 3 Core	**Annotations**	⏻
Hierarchical			**Hierarchical**	

New table & status pages for package *specifications*



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The most recent release of SBML Level 3 Version 1 Core is **Release 1**.

The Systems Biology Markup Language (SBML): Language Specification for Level 3 Version 1 Core

Authors: Michael Hucka, Frank Bergmann, Stefan Hoops, Sarah Keating, Sven Sahle, James Schaff, Lucian Smith, and Darren Wilkinson

*This is the final **Release 1** specification of 6 Oct. 2010.*

*The document link refers to the file on SourceForge.net. If you have any problems accessing the PDF file from there, a backup copy of the document is also available **locally from this server**.*

Specification →

Errata →

Submit issue →

Schemas →

s indicated above. Accepted issues are periodically
nsensus emerges that the known errata warrant a

New table for package specifications

[it] ***SBML Level 3 Packages***

E ch individual SBML Level 3 package effort has an associated status page. Please follow the relevant links in the table below to find out more about a given package, including any draft specifications that may be available.

Package Name	Label	Description	Specification information page	Status
Arrays and Sets	`arrays`	Support for expressing arrays or sets of things	**Arrays and Sets**	⏻
Annotations	`annot`	Support for richer annotation syntax than the regular annotations in SBML Level 3 Core	**Annotations**	⏻
Hierarchical			**Hierarchical**	

Outline

General background and motivations

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A few additional details about SBML

Packages in SBML Level 3

A selection of resources for the SBML-oriented modeler

Closing

BioModels Database

Stores & serves quantitative models of biological interest

- **Free**, public resource
- Models must be described in **peer-reviewed publication**(s)

Hundreds of models are **curated by hand**

Imports & exports models in several formats

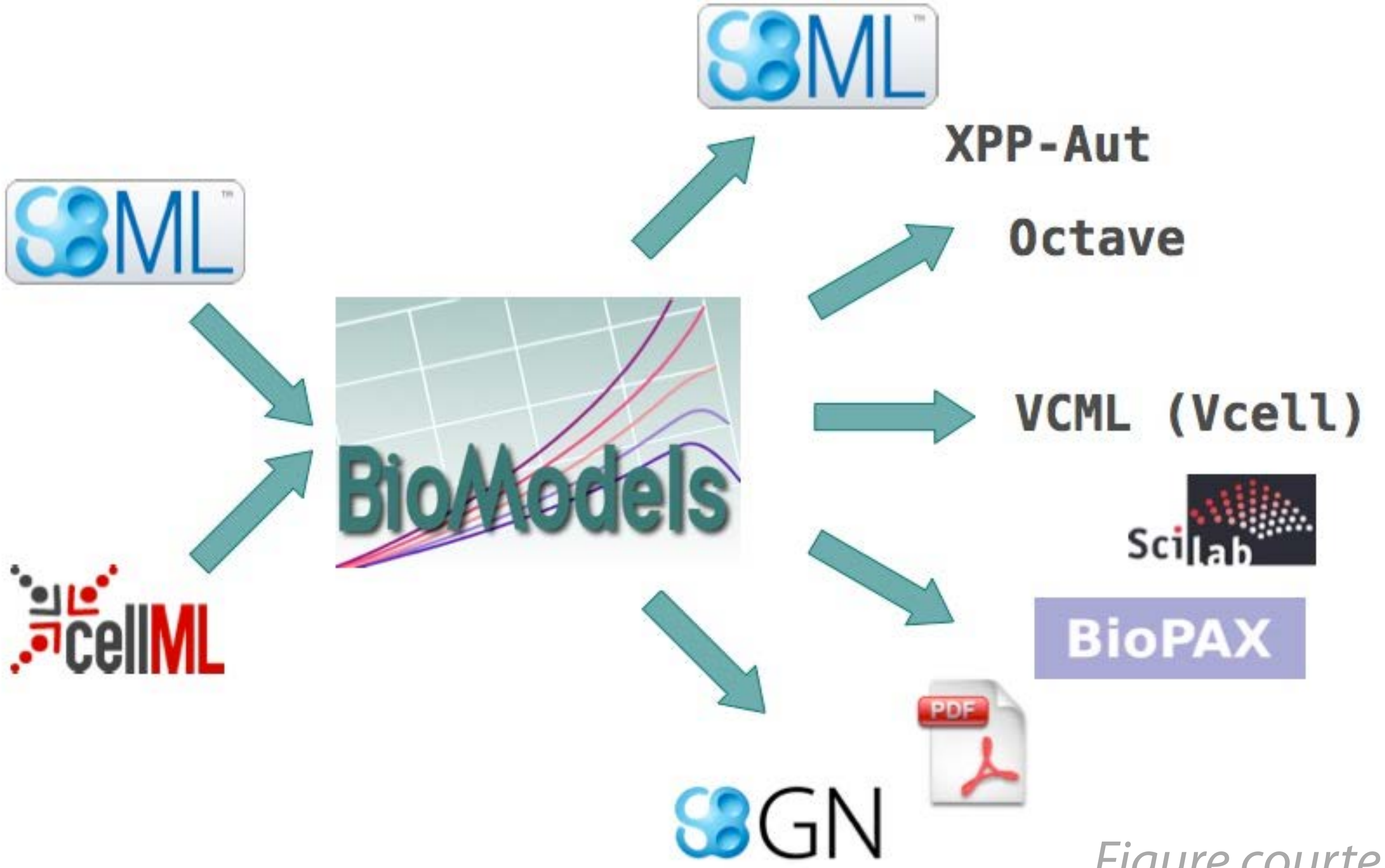
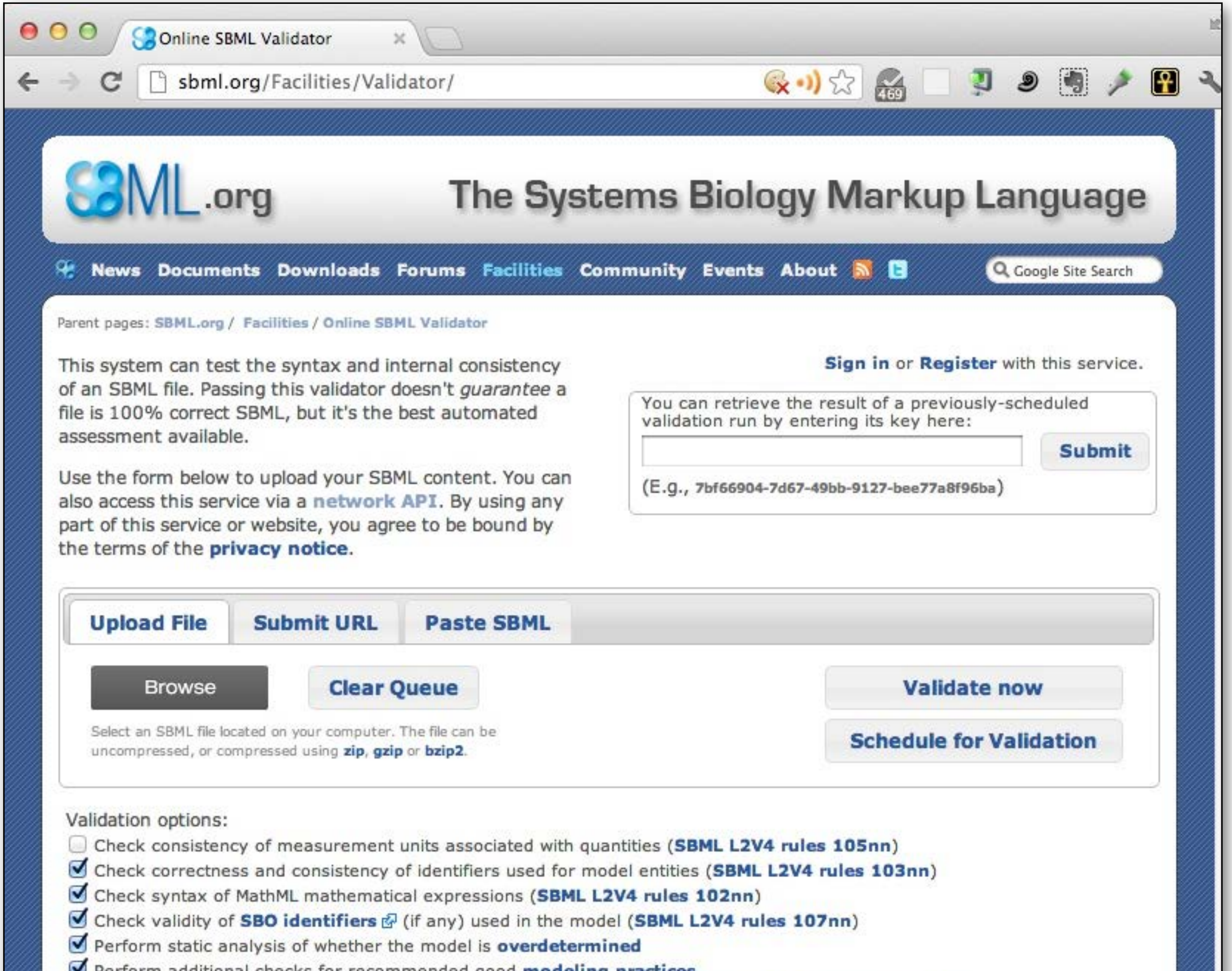


Figure courtesy of Camille Laibe

The Online SBML Validator



Parent pages: SBML.org / Facilities / Online SBML Validator

This system can test the syntax and internal consistency of an SBML file. Passing this validator doesn't *guarantee* a file is 100% correct SBML, 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 or website, you agree to be bound by 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)

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

Validation options:

- ☐ Check consistency of measurement units associated with quantities (**SBML L2V4 rules 105nn**)
- ☑ Check correctness and consistency of identifiers used for model entities (**SBML L2V4 rules 103nn**)
- ☑ Check syntax of MathML mathematical expressions (**SBML L2V4 rules 102nn**)
- ☑ Check validity of **SBO identifiers** (if any) used in the model (**SBML L2V4 rules 107nn**)
- ☑ Perform static analysis of whether the model is **overdetermined**
- ☑ Perform additional checks for recommended good **modeling practices**

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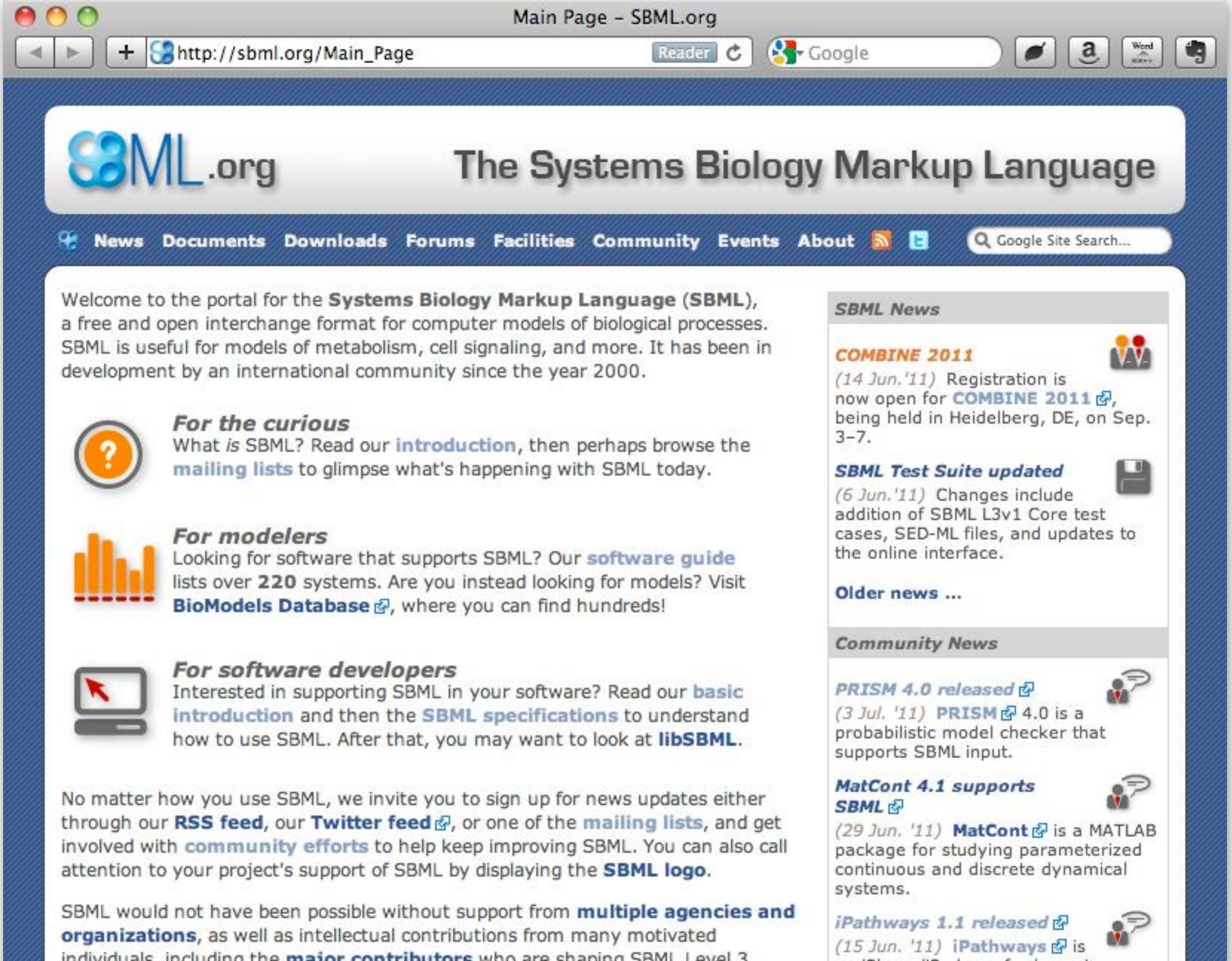
Find it here

http://sbml.org/Facilities/Validator

Find software in the SBML Software Guide



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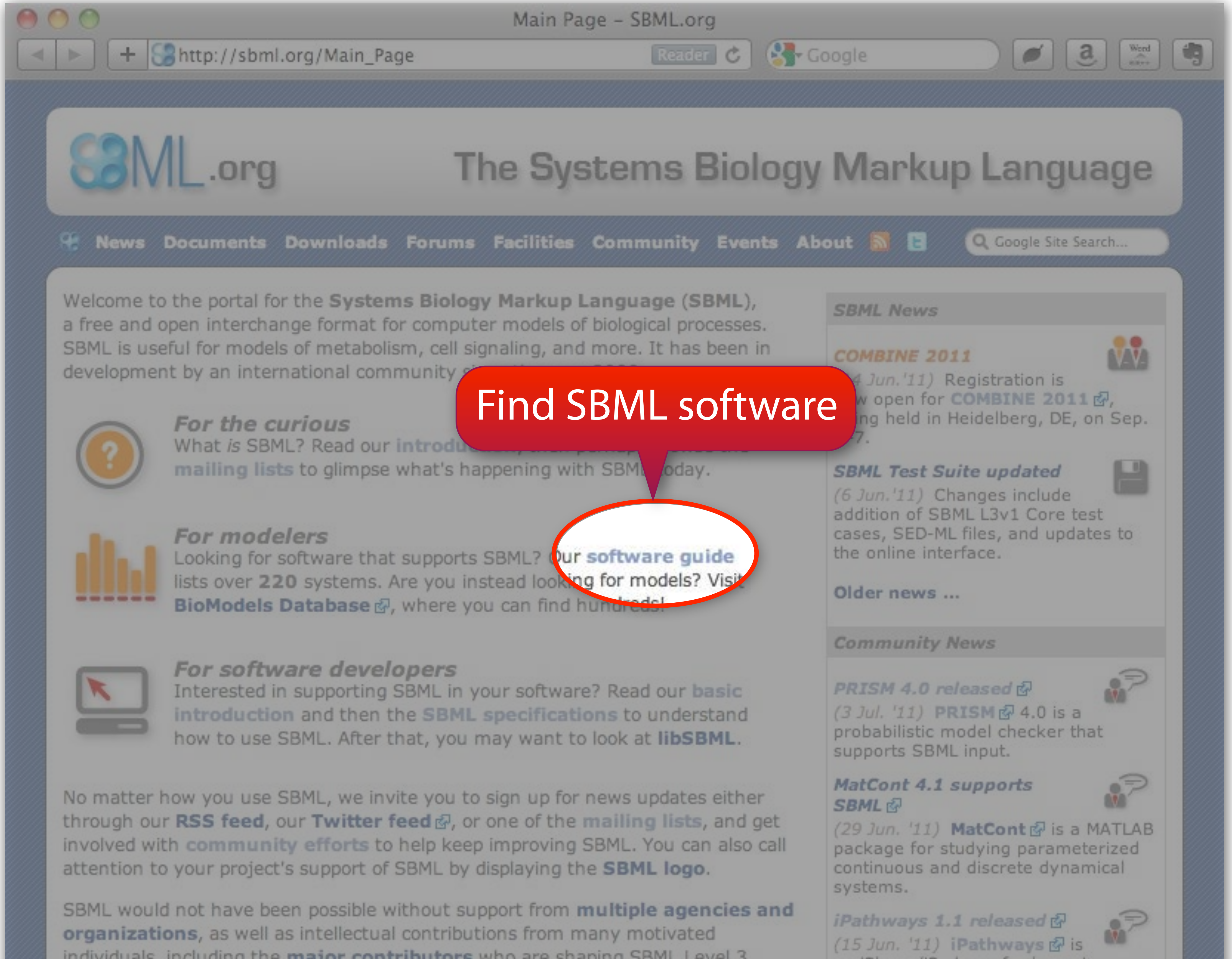

SBML.org The Systems Biology Markup Language

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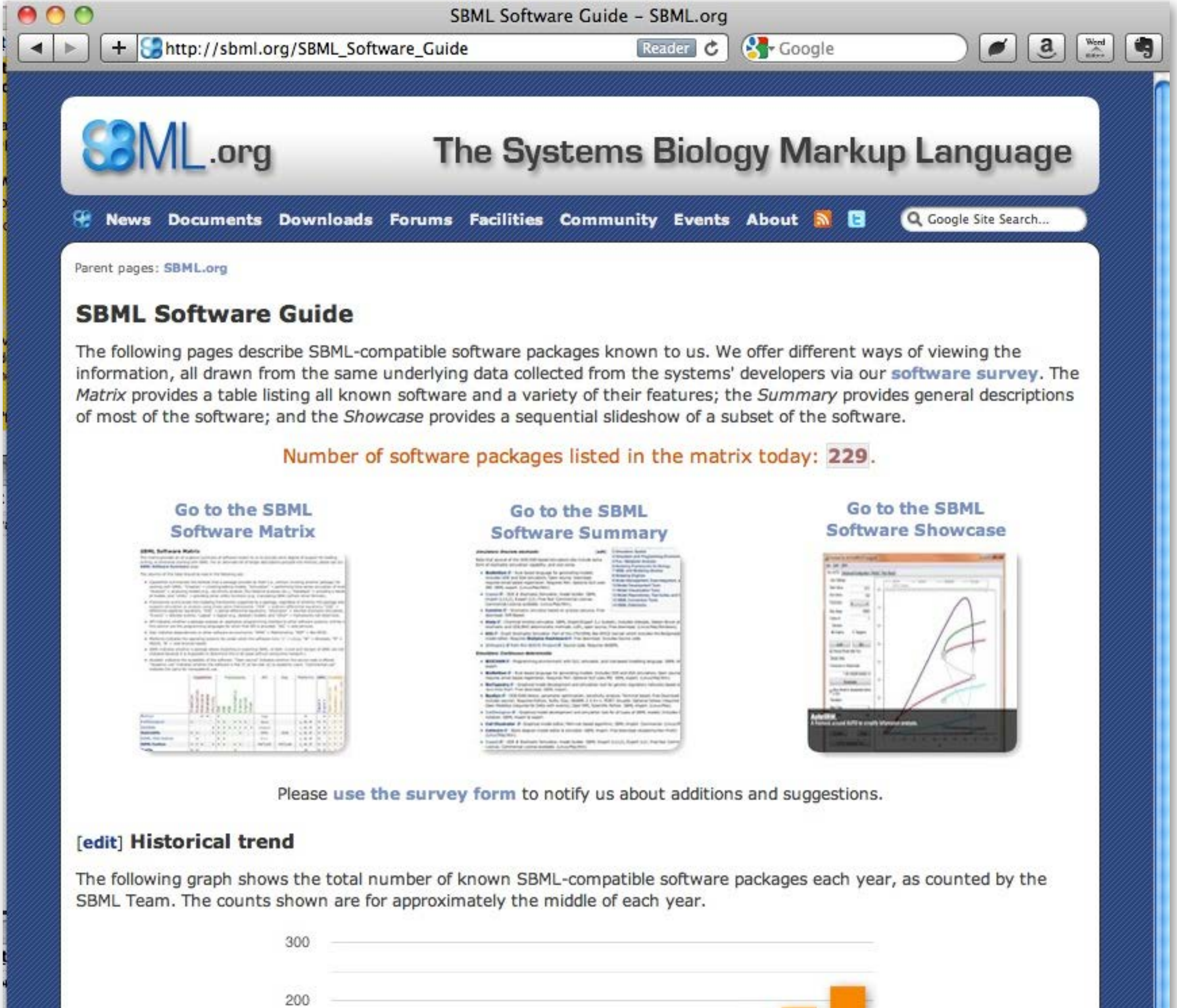


Parent pages: **SBML.org**

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: **229**.

Go to the SBML Software Matrix

Go to the SBML Software Summary

Go to the SBML Software Showcase

Please **use the survey form** to notify us about additions and suggestions.

[edit] Historical trend

The following graph shows the total number of known SBML-compatible software packages each year, as counted by the SBML Team. The counts shown are for approximately the middle of each year.

libSBML

Reads, writes, validates SBML

Can check & convert units

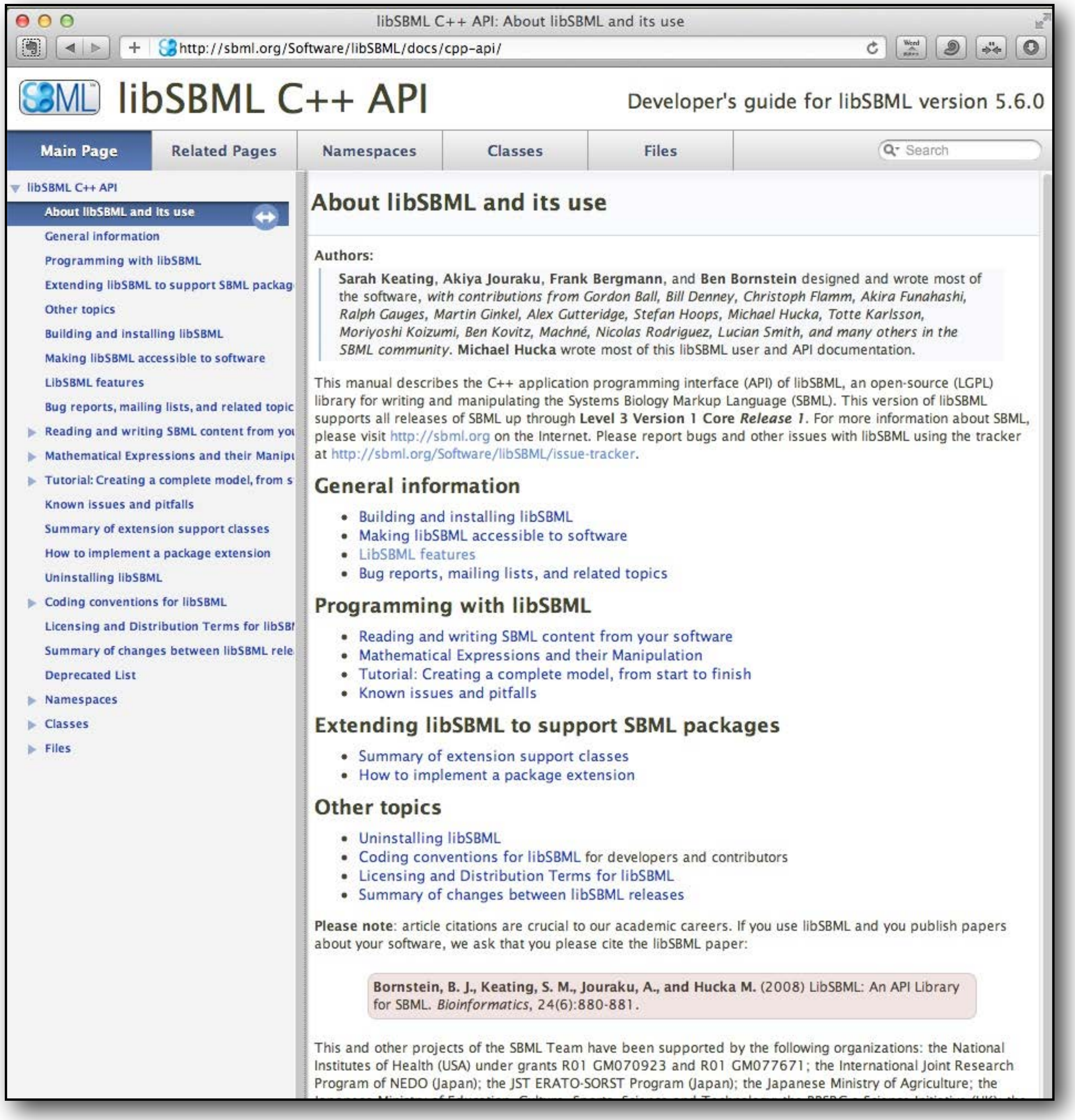
Written in portable C++

Runs on Linux, Mac, Windows

APIs for C, C++, C#, Java, Octave, Perl, Python, R, Ruby, MATLAB

Well documented API

Open-source (LGPL)



libSBML C++ API

Developer's guide for libSBML version 5.6.0

About libSBML and its use

Authors:

> **Sarah Keating**, **Akiya Jouraku**, **Frank Bergmann**, and **Ben Bornstein** designed and wrote most of the software, *with contributions from Gordon Ball, Bill Denney, Christoph Flamm, Akira Funahashi, Ralph Gauges, Martin Ginkel, Alex Gutteridge, Stefan Hoops, Michael Hucka, Totte Karlsson, Moriyoshi Koizumi, Ben Kovitz, Machné, Nicolas Rodriguez, Lucian Smith, and many others in the SBML community*. **Michael Hucka** wrote most of this libSBML user and API documentation.

This manual describes the C++ application programming interface (API) of libSBML, an open-source (LGPL) library for writing and manipulating the Systems Biology Markup Language (SBML). This version of libSBML supports all releases of SBML up through **Level 3 Version 1 Core *Release 1***. For more information about SBML, please visit http://sbml.org on the Internet. Please report bugs and other issues with libSBML using the tracker at http://sbml.org/Software/libSBML/issue-tracker.

General information

- Building and installing libSBML
- Making libSBML accessible to software
- LibSBML features
- Bug reports, mailing lists, and related topics

Programming with libSBML

- Reading and writing SBML content from your software
- Mathematical Expressions and their Manipulation
- Tutorial: Creating a complete model, from start to finish
- Known issues and pitfalls

Extending libSBML to support SBML packages

- Summary of extension support classes
- How to implement a package extension

Other topics

- Uninstalling libSBML
- Coding conventions for libSBML for developers and contributors
- Licensing and Distribution Terms for libSBML
- Summary of changes between libSBML releases

Please note: article citations are crucial to our academic careers. If you use libSBML and you publish papers about your software, we ask that you please cite the libSBML paper:

> **Bornstein, B. J., Keating, S. M., Jouraku, A., and Hucka M.** (2008) LibSBML: An API Library for SBML. *Bioinformatics*, 24(6):880-881.

This and other projects of the SBML Team have been supported by the following organizations: the National Institutes of Health (USA) under grants R01 GM070923 and R01 GM077671; the International Joint Research Program of NEDO (Japan); the JST ERATO-SORST Program (Japan); the Japanese Ministry of Agriculture; the

http://sbml.org/Software/libSBML

JSBML

User Guide for JSBML

Version: 1.0.0 (preview)

Authors:

Andreas Dräger[a]
Alexander Dörr[a]
Florian Mittag[a]

Nicolas Rodriguez[b]
Clemens Wrzodek[a]
Michael Hucka[c]

Marine Dumousseau[b]
Finja Büchel[a]

Principal investigators:

Nicolas Le Novère[b]
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Wellcome Trust Genome Campus
Hinxton, Cambridge, UK

[c] Computing and Mathematical Sciences
California Insitute of Technology
Pasadena, CA, USA

SBML (the Systems Biology Markup Language) is an XML-based format for storing and exchanging computational descriptions of biological processes. To read, write, manipulate, and perform higher-level operations on SBML files and data streams, software applications need to map SBML entities to suitable software objects. JSBML provides a pure Java library for this purpose. It supports all Levels and Versions of SBML, and provides many powerful features, including facilities to help migrate from the use of libSBML (a popular library for SBML that is not written in Java).

This document provides an introduction to JSBML and its use. It is aimed at both developers writing new Java-based applications as well as those who want to adapt libSBML-based applications to using JSBML. This user guide is a companion to the JSBML API documentation.

The JSBML home page is `http://sbml.org/Software/JSBML/`.

Pure Java implementation

API is compatible with libSBML but more Java-like

Functionality is subset of libSBML

Open source (LGPL)

Main developers: Nicolas Rodriguez, Andreas Dräger

http://sbml.org/Software/JSBML

What is the SBML Test Suite?

System for testing SBML support in software

- Currently aimed at simulators (easiest to assess)
- Extensible architecture—easy to add more test cases

Components:

- Test models + simulation run parameters + expected results
  - Each case is labeled with tags that indicate tested features
- Online assessment system
- Standalone test runner – run an application through all tests
- Online database of test results

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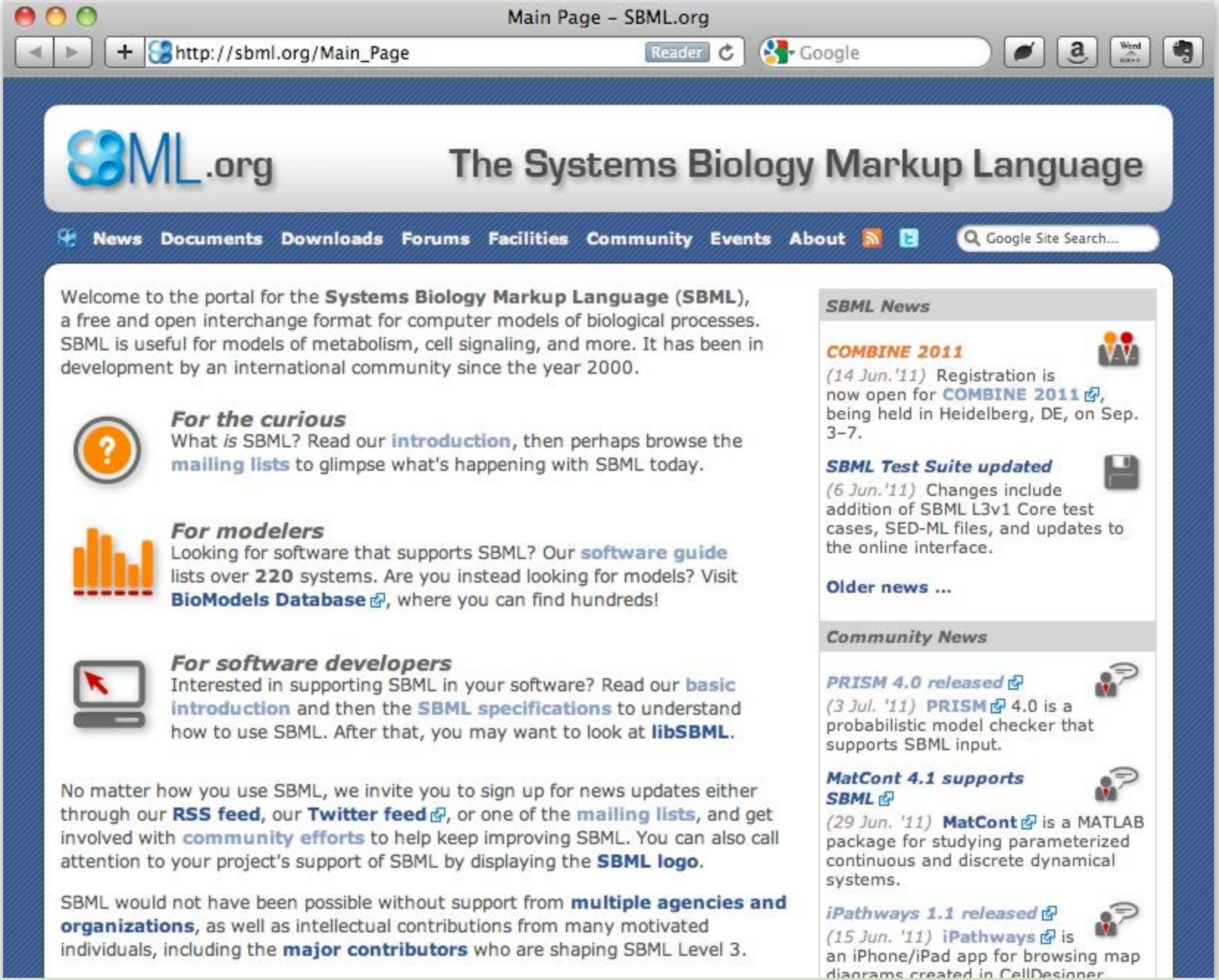
http://sbml.org/Facilities/Online_SBML_Test_Suite



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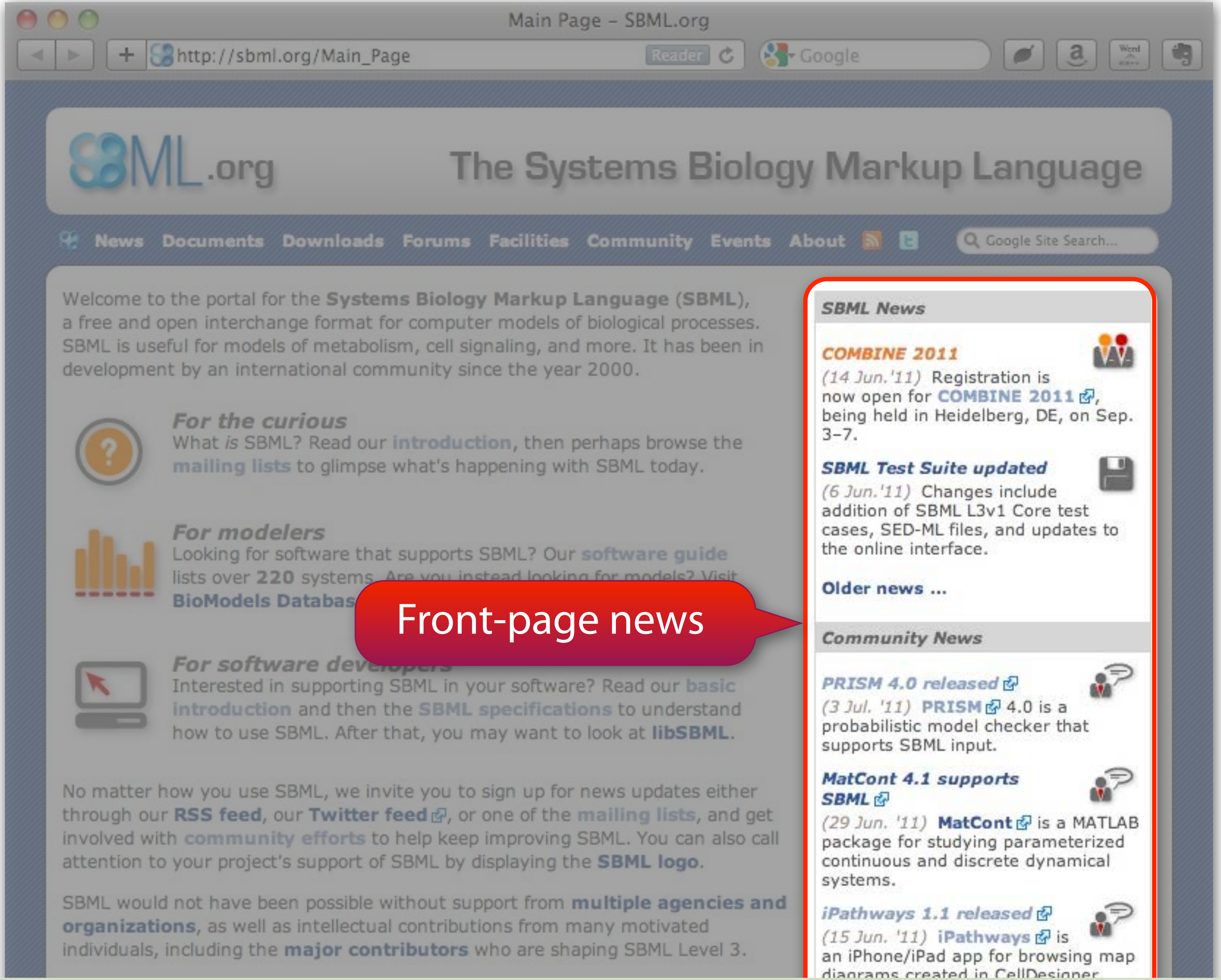

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Front-page news

Twitter & RSS feeds

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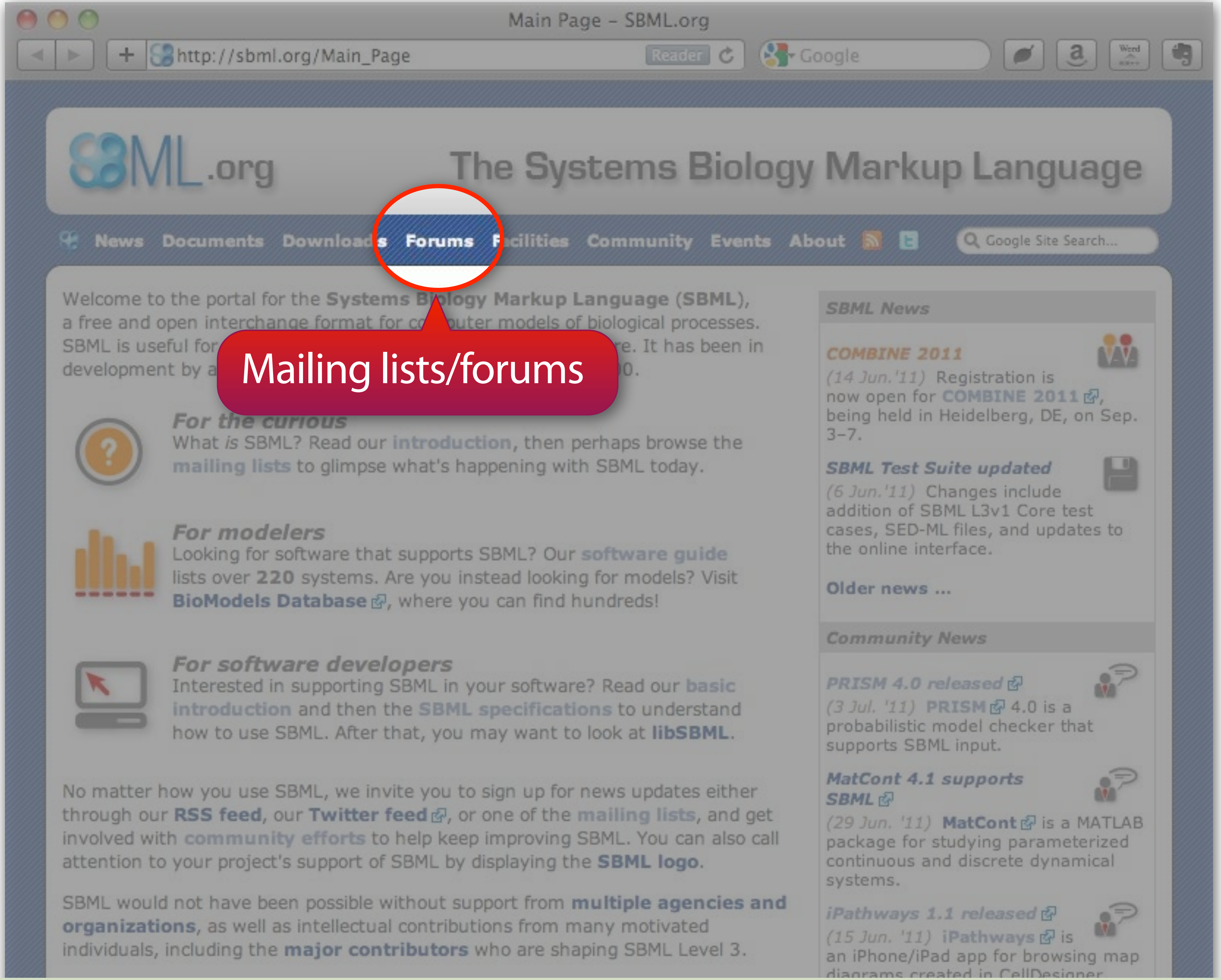

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SBML Editors: Mike Hucka, Nicolas Le Novère, Sarah Keating, Frank Bergmann, Lucian Smith, Chris Myers, Stefan Hoops, Sven Sahle, James Schaff, Darren Wilkinson

BioModels DB: Nicolas Le Novère, Henning Hermjakob, Camille Laibe, Chen Li, Lukas Endler, Nico Rodriguez, Marco Donizelli, Viji Chelliah, Mélanie Courtot, Harish Dharuri

Original PI's: John C. Doyle, Hiroaki Kitano

And a huge thanks to many others in the COMBINE community

Attendees at SBML 10th Anniversary Symposium, Edinburgh, 2010

This work was made possible thanks to a great community

URLs

SBML	http://sbml.org
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MIRIAM	http://biomodels.net/miriam
identifiers.org	http://identifiers.org
SED-ML	http://biomodels.net/sed-ml
SBO	http://biomodels.net/sbo
SBGN	http://sbgn.org
COMBINE	http://co.mbine.org

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