An SBML Overview

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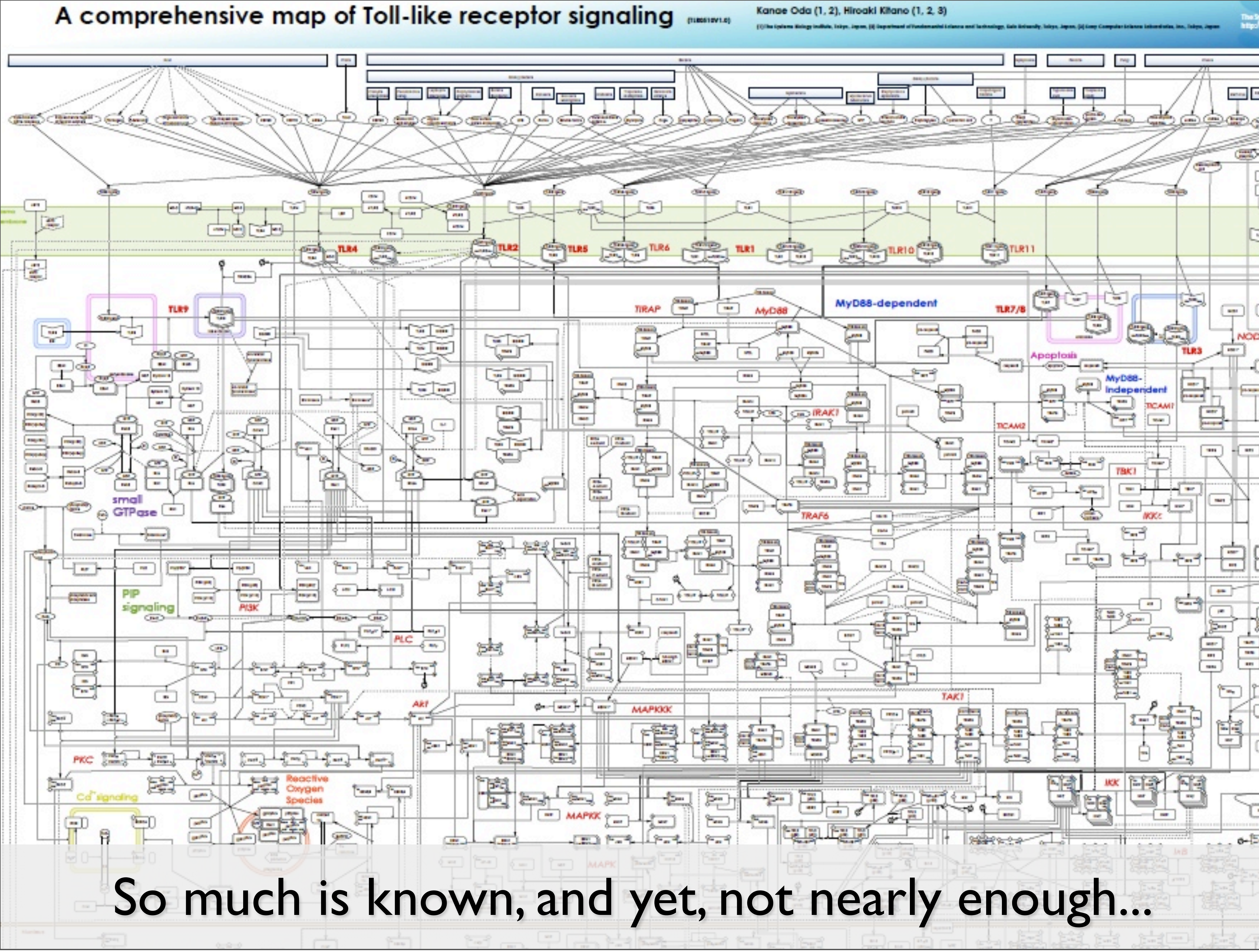
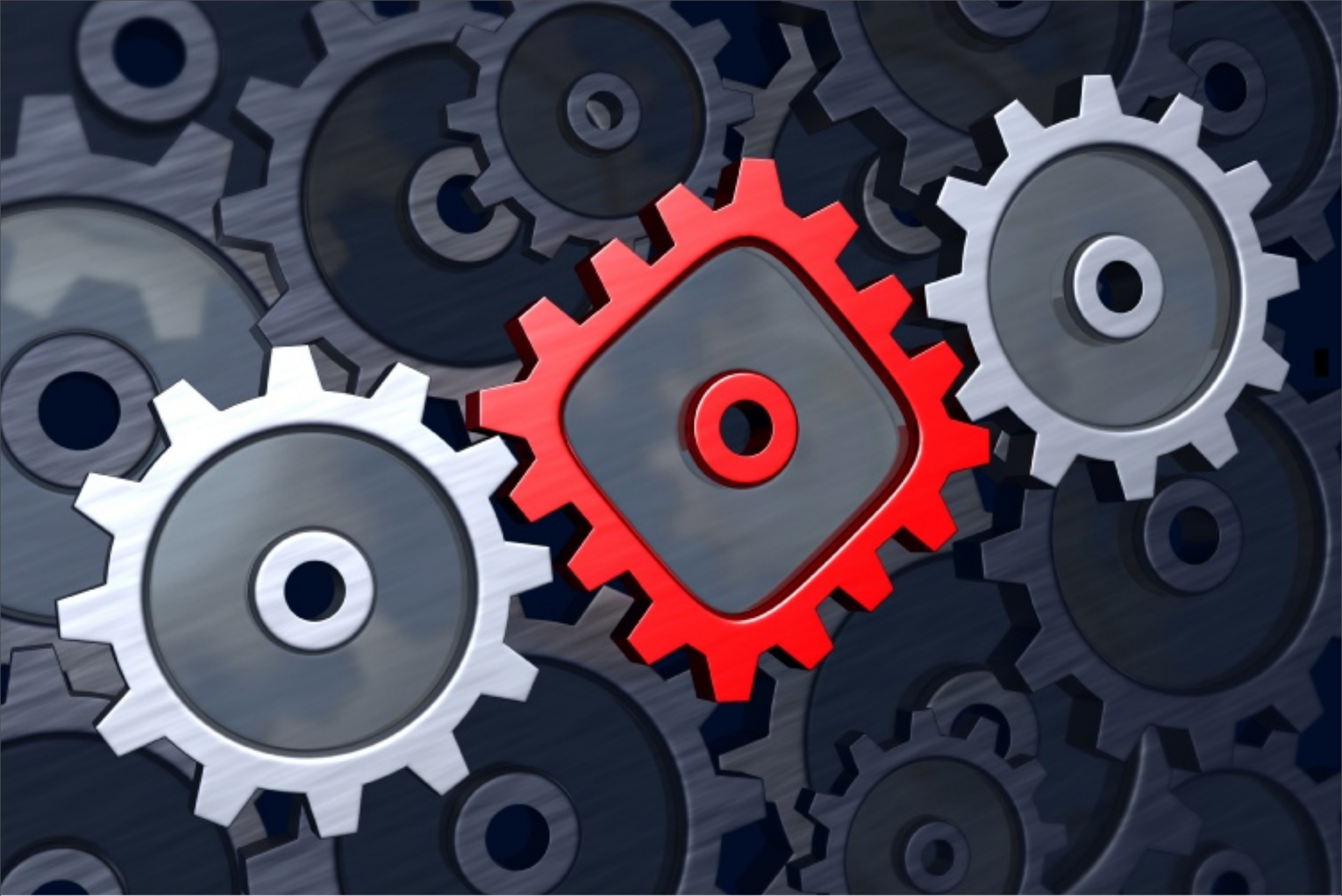


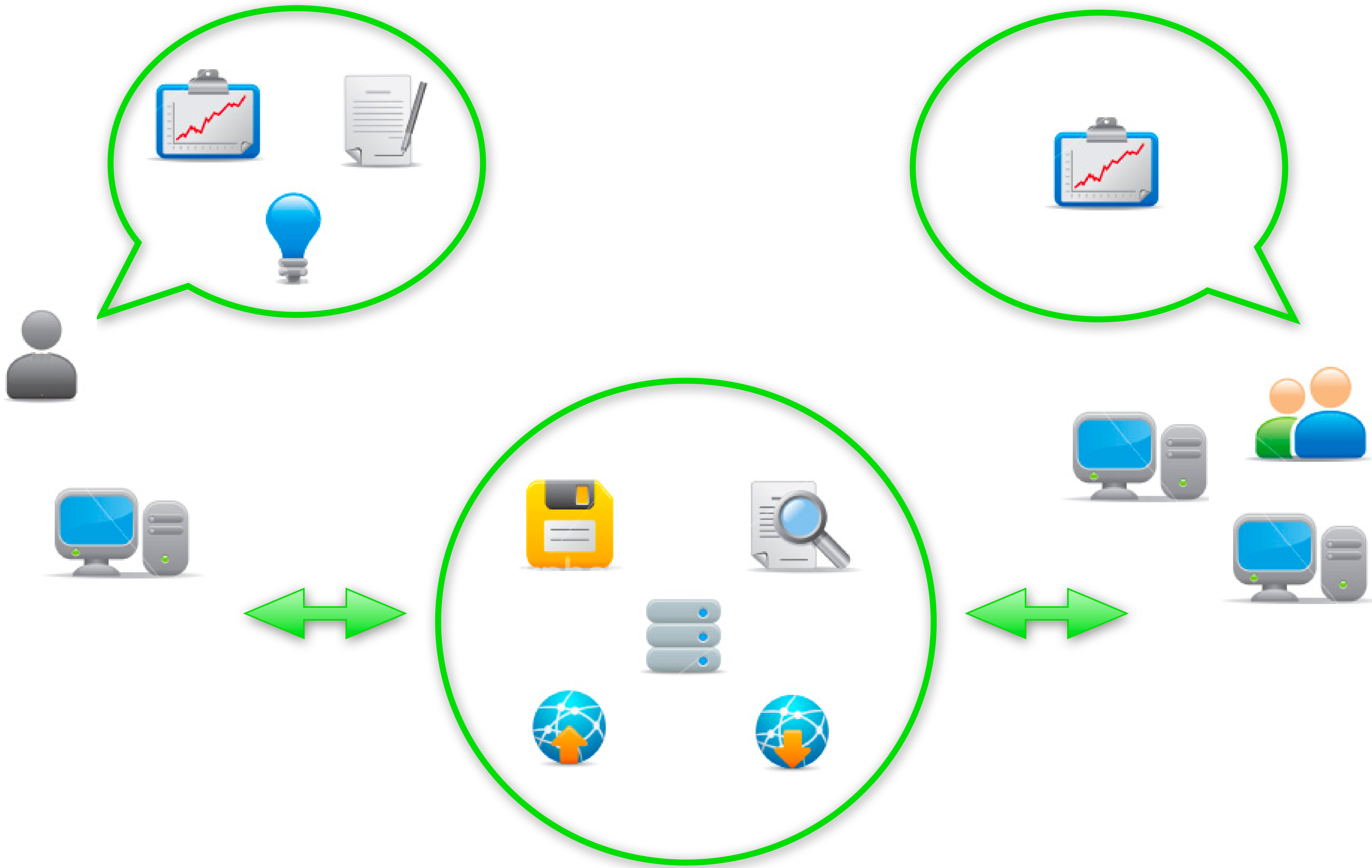
So much is known, and yet, not nearly enough...

Must weave solutions using different methods & tools



Common side-effect: compatibility problems

Models represent knowledge to be exchanged



SBML

SBML = Systems Biology Markup Language

Format for representing quantitative models

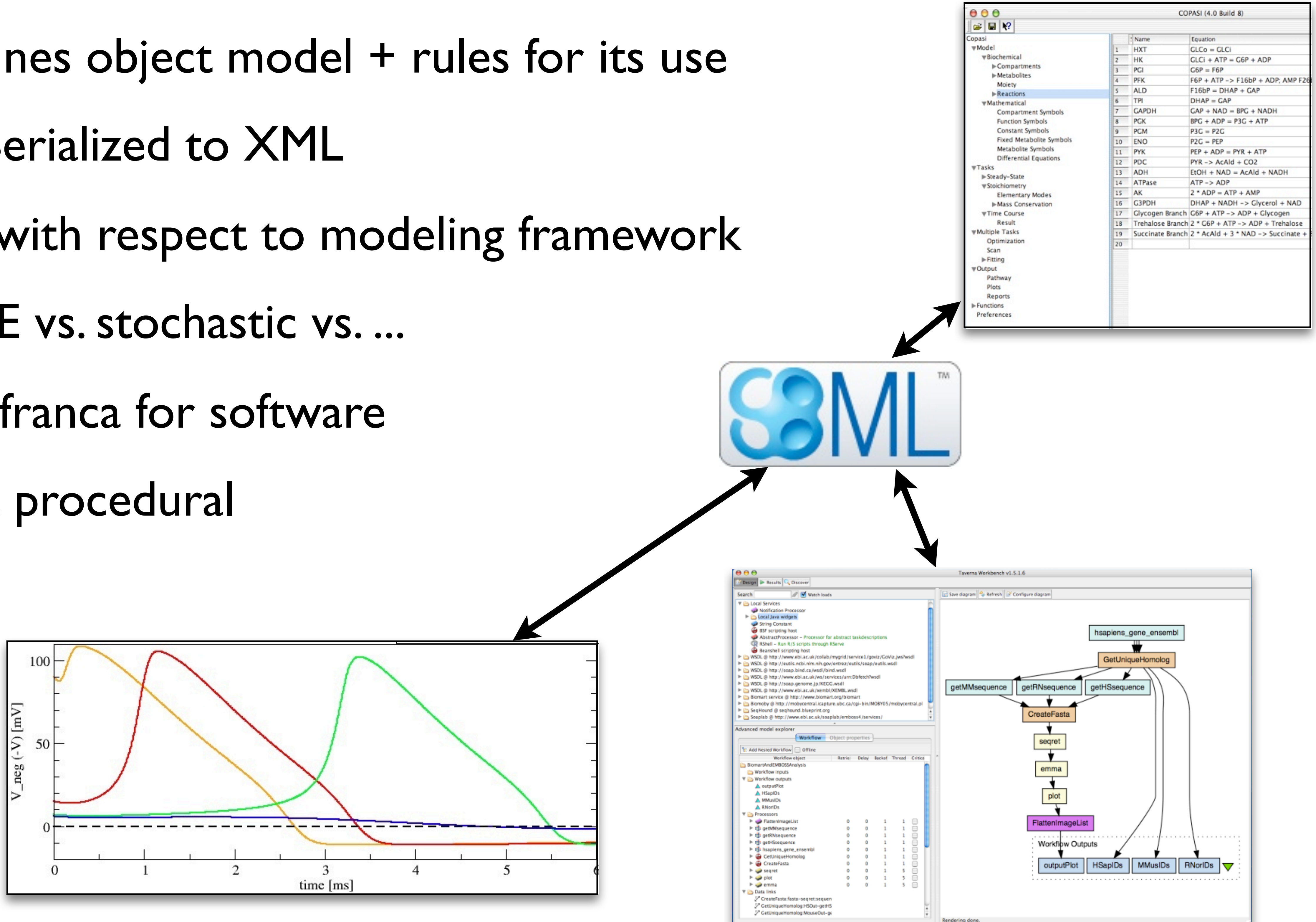
- Defines object model + rules for its use
  - Serialized to XML

Neutral with respect to modeling framework

- ODE vs. stochastic vs. ...

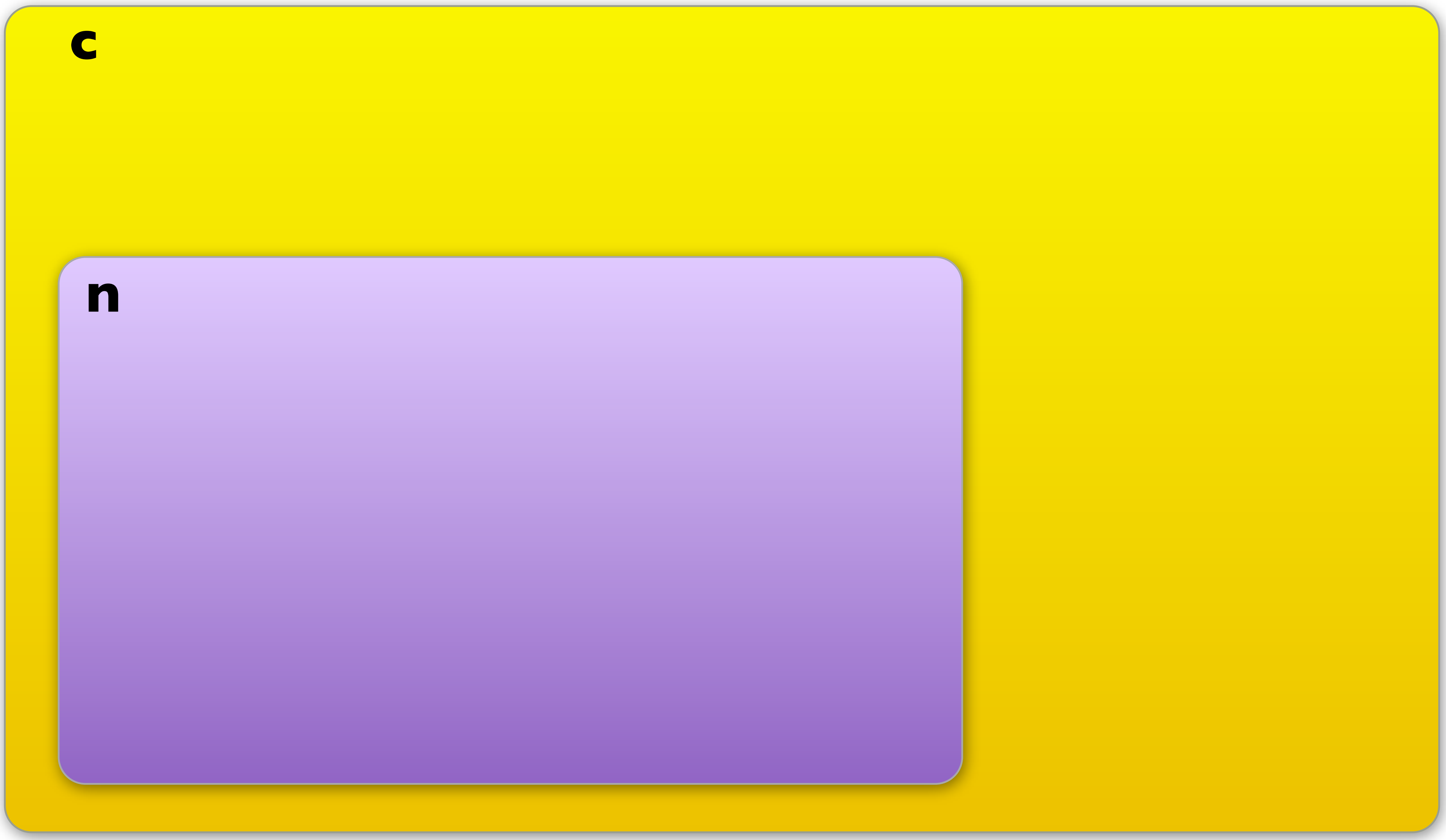
A lingua franca for software

- Not procedural

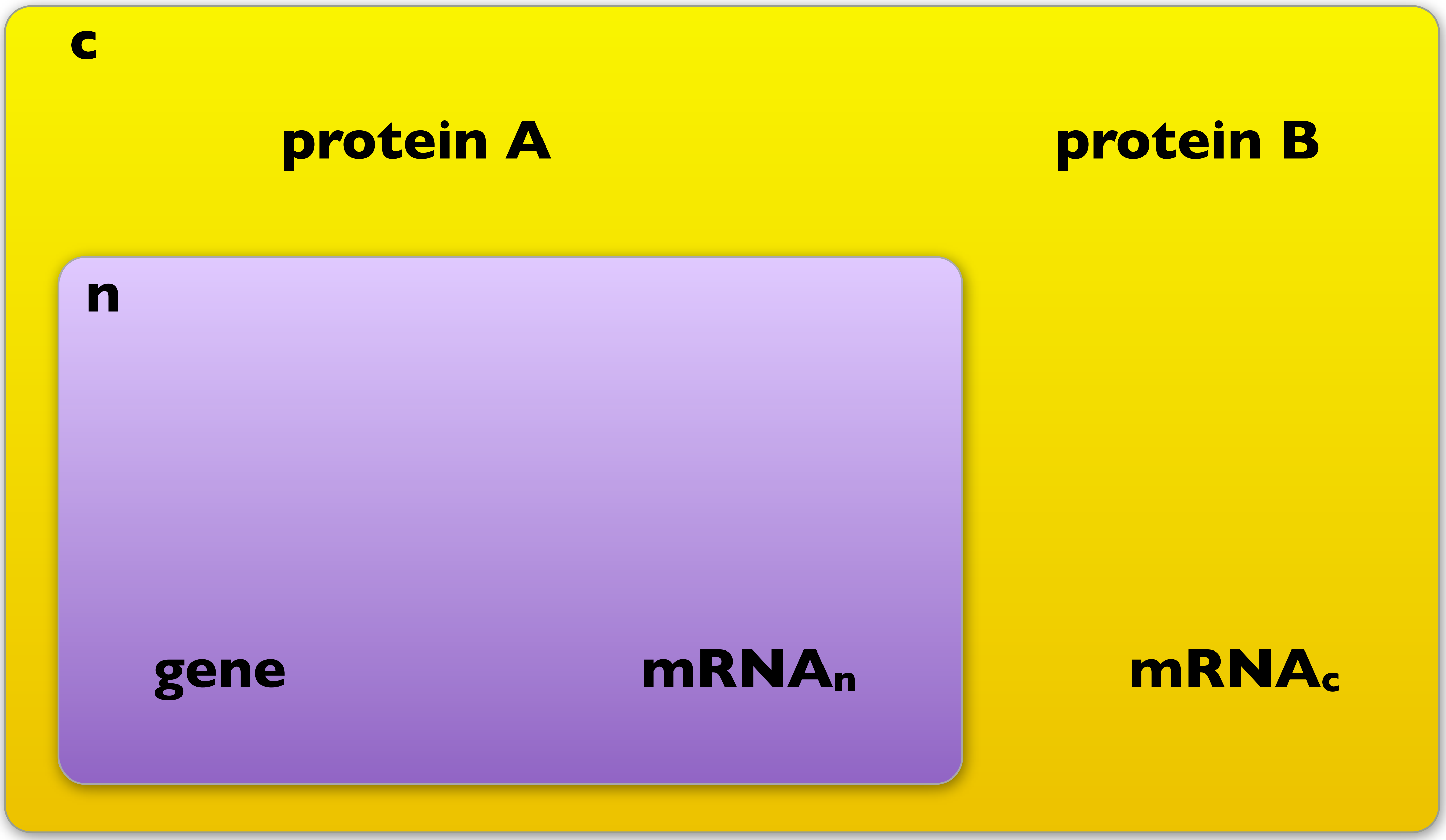


Some basics of SBML model encoding

- Well-stirred compartments

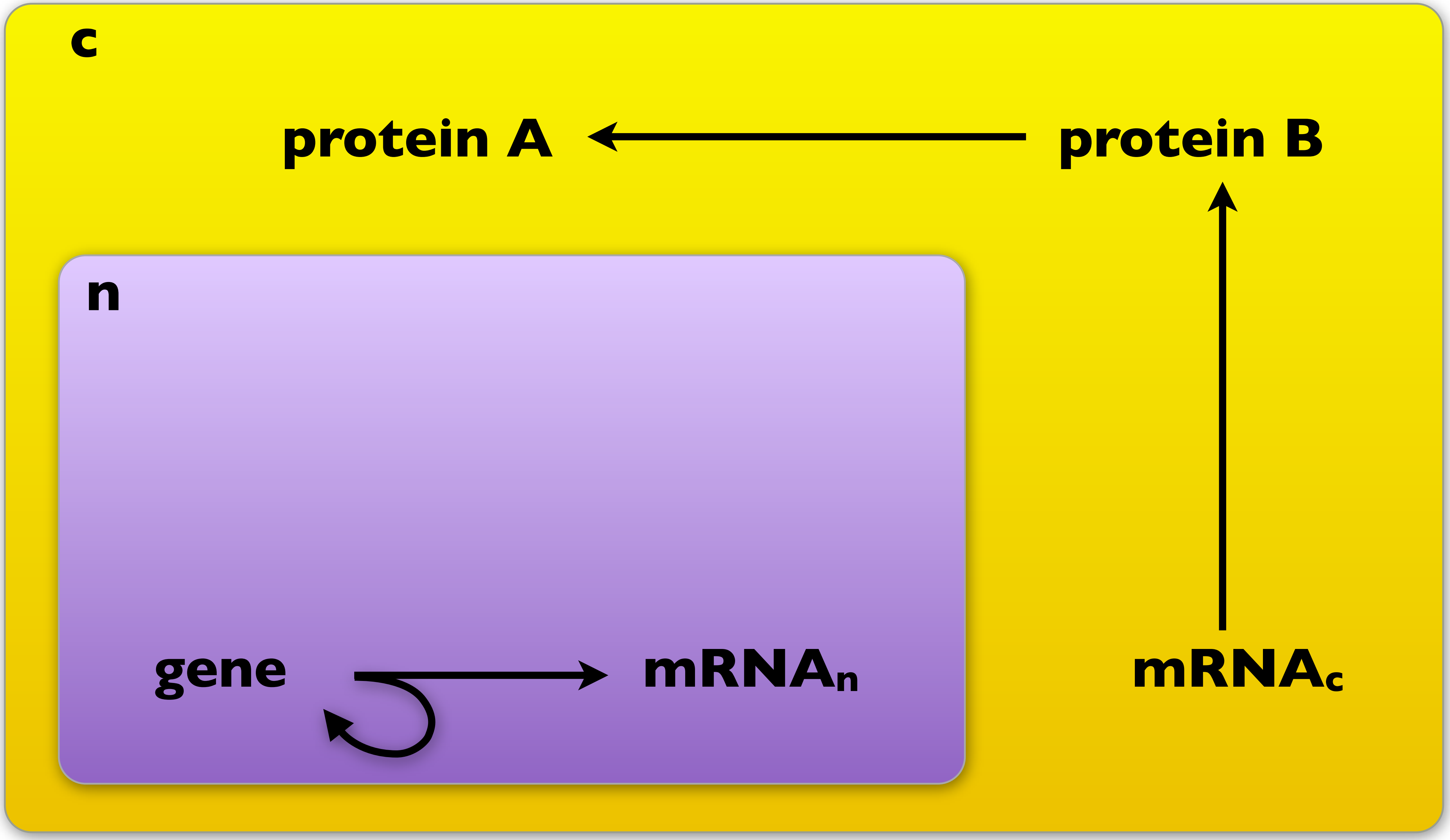


Some basics of SBML model encoding



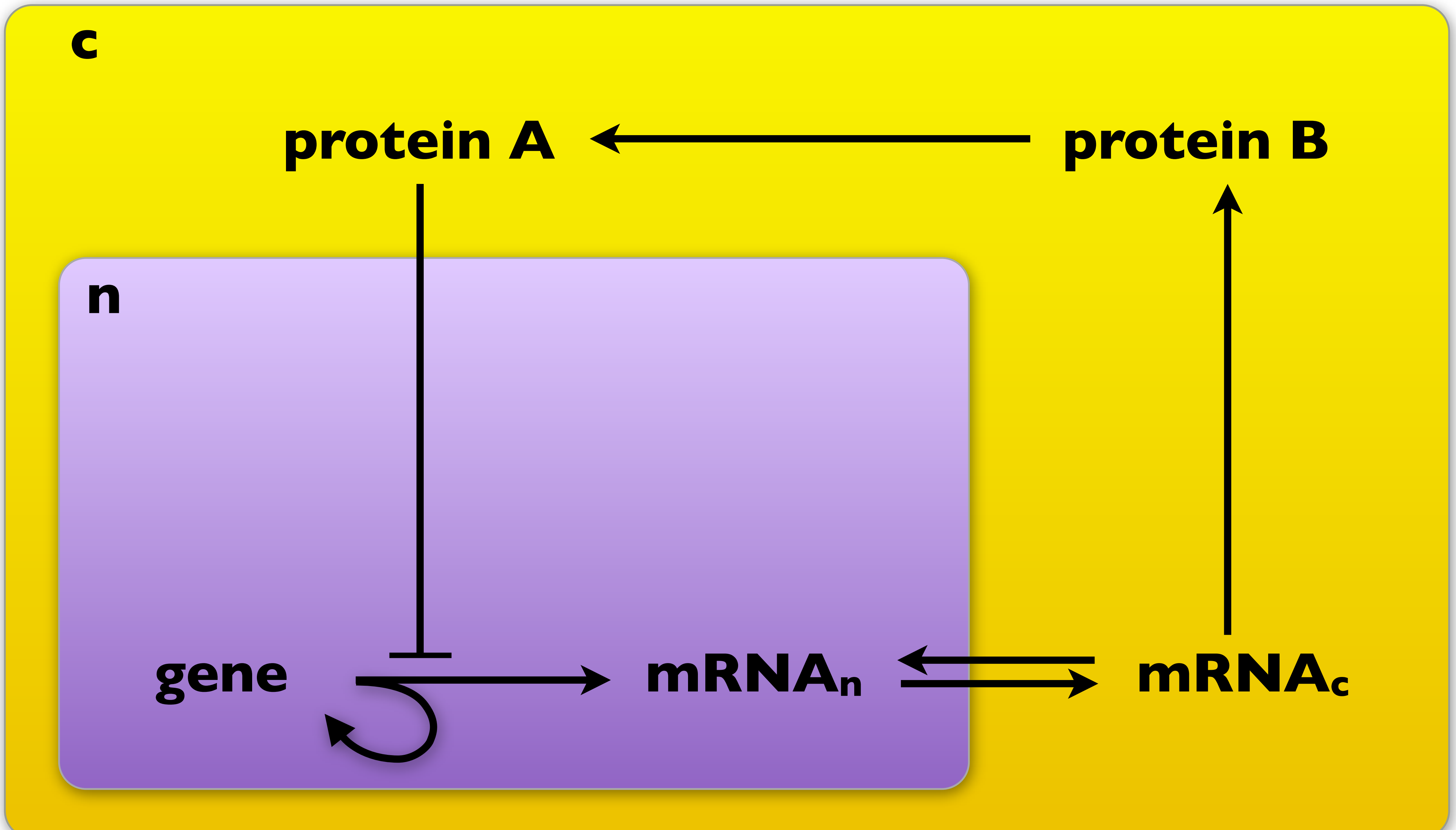
Some basics of SBML model encoding

- Reactions can involve any species anywhere



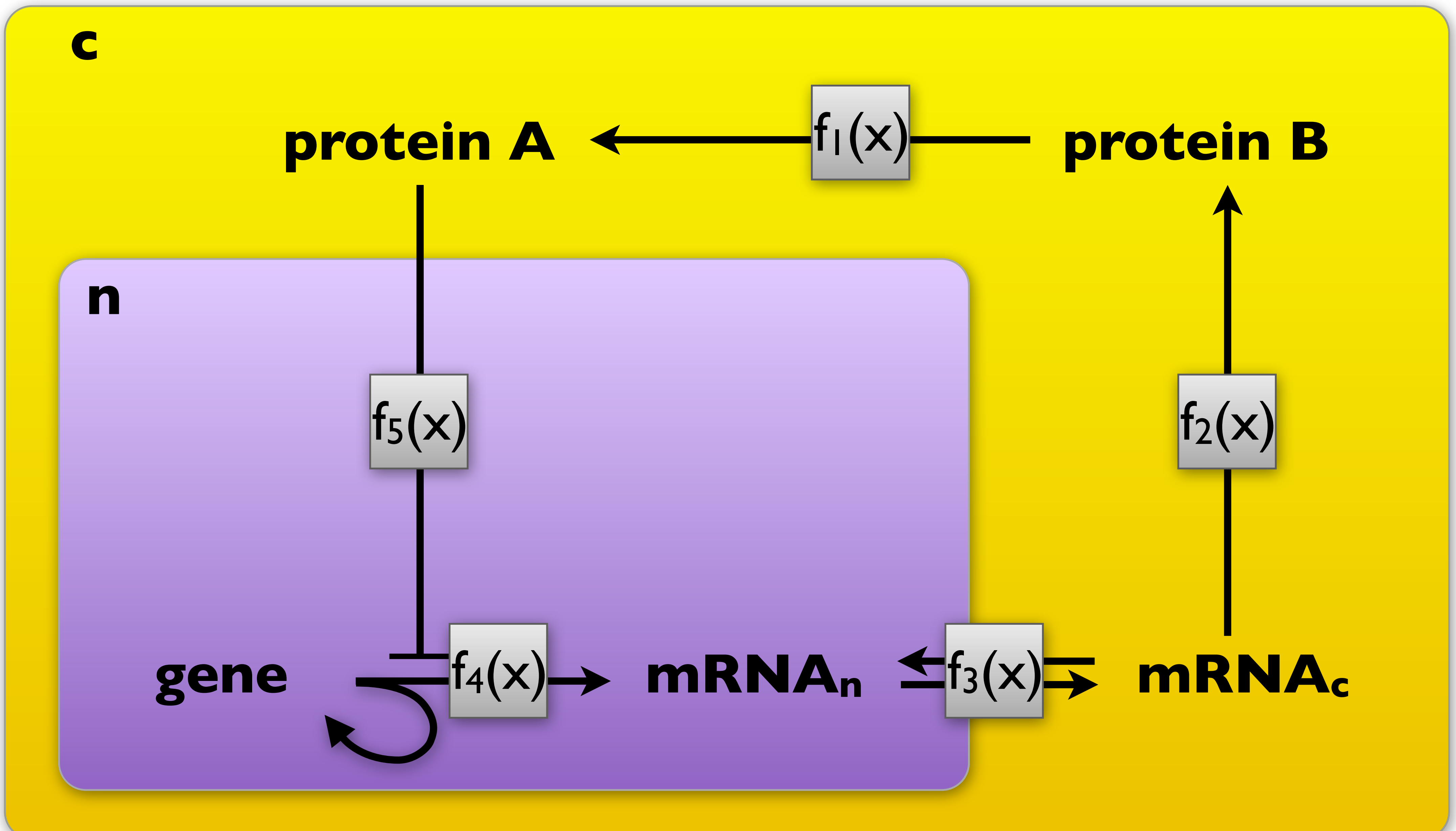
Some basics of SBML model encoding

- Reactions can cross compartment boundaries



Some basics of SBML model encoding

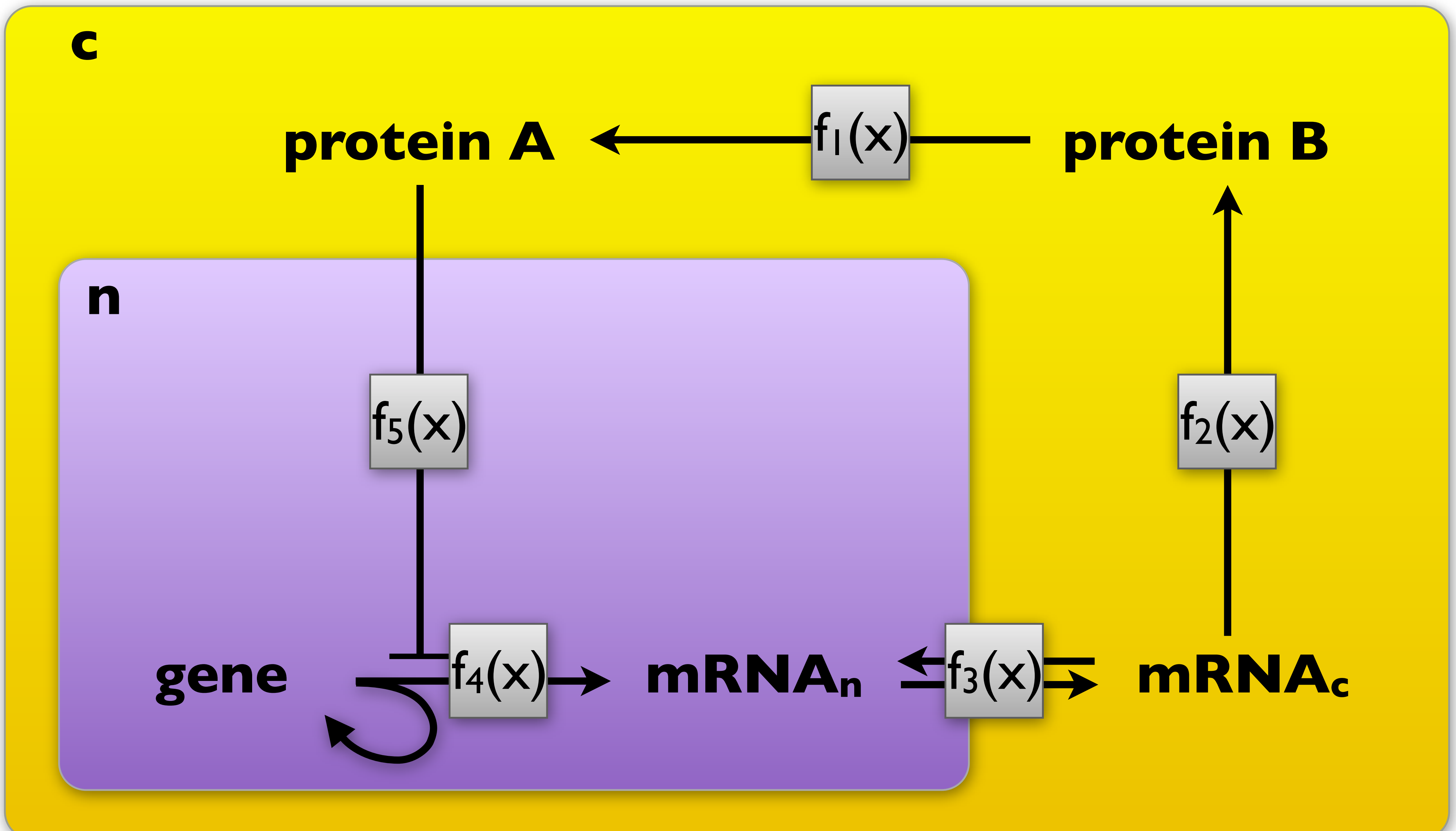
- Reaction/process rates can be (almost) arbitrary formulas



Some basics of SBML model encoding

- "Rules": equations expressing relationships in addition to reaction sys.

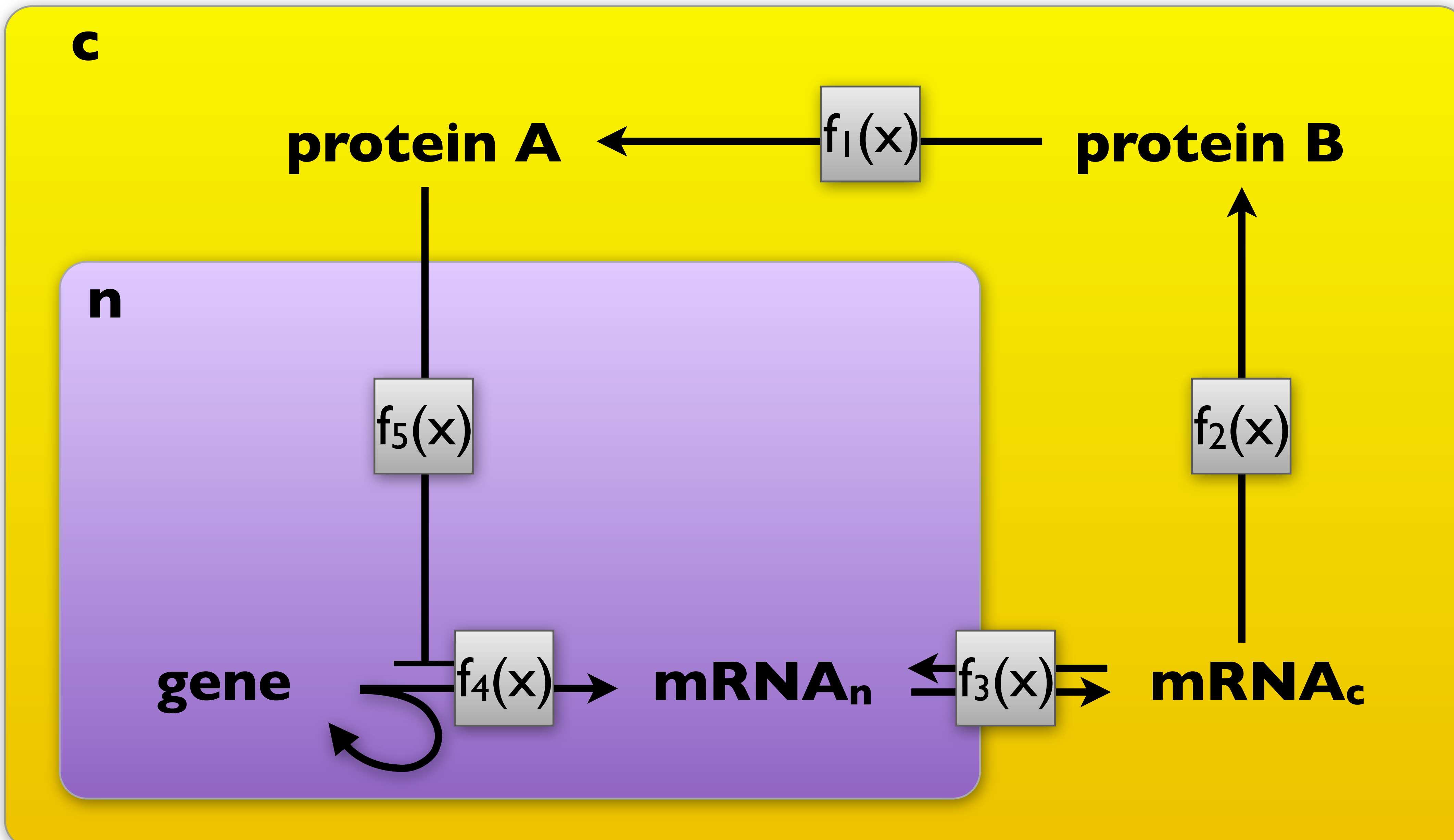
$g_1(x)$
$g_2(x)$
.
.
.



Some basics of SBML model encoding

- "Events": discontinuous actions triggered by system conditions

$g_1(x)$
$g_2(x)$
.
.
.

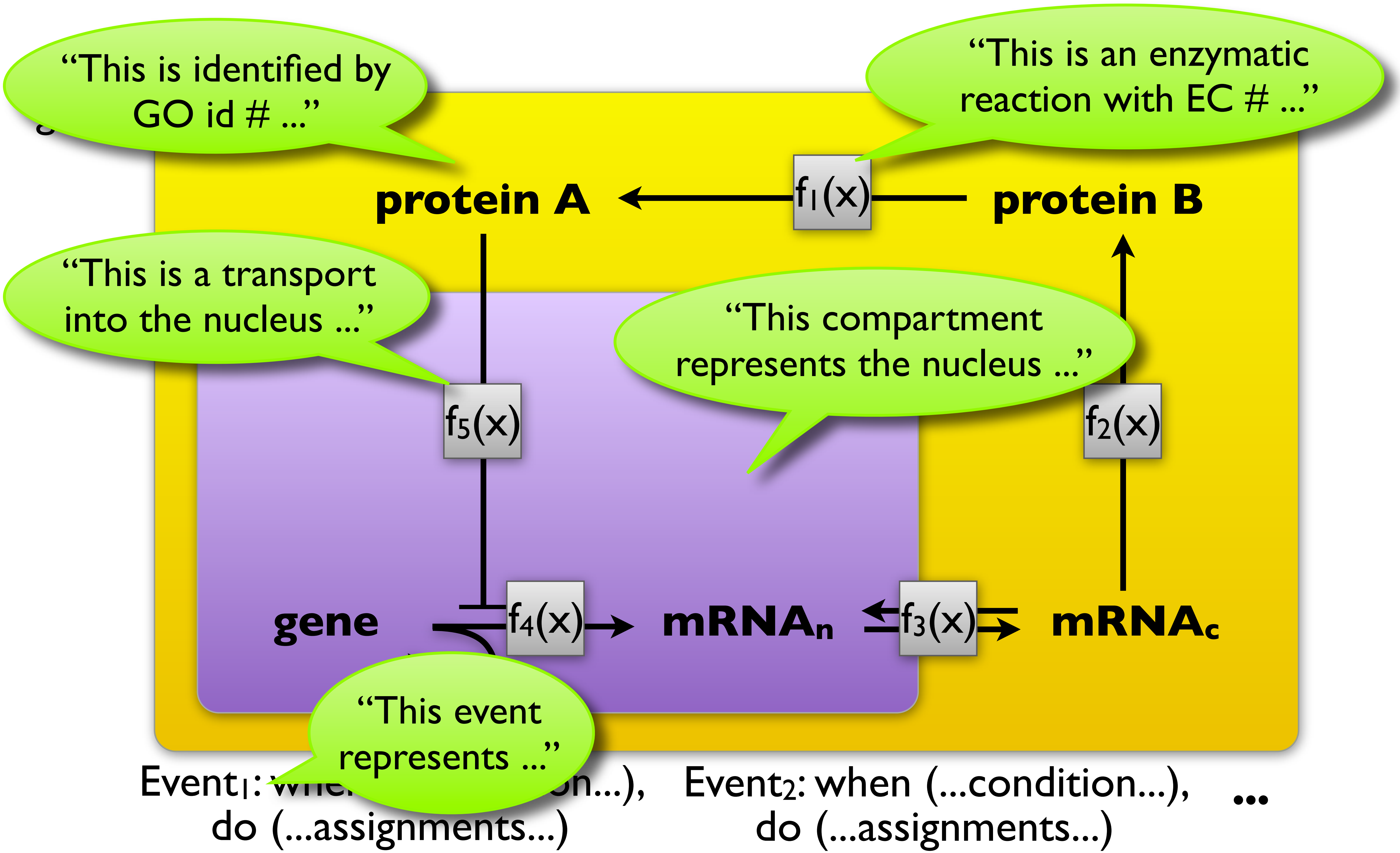


Event$_1$: when (...condition...), do (...assignments...)

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

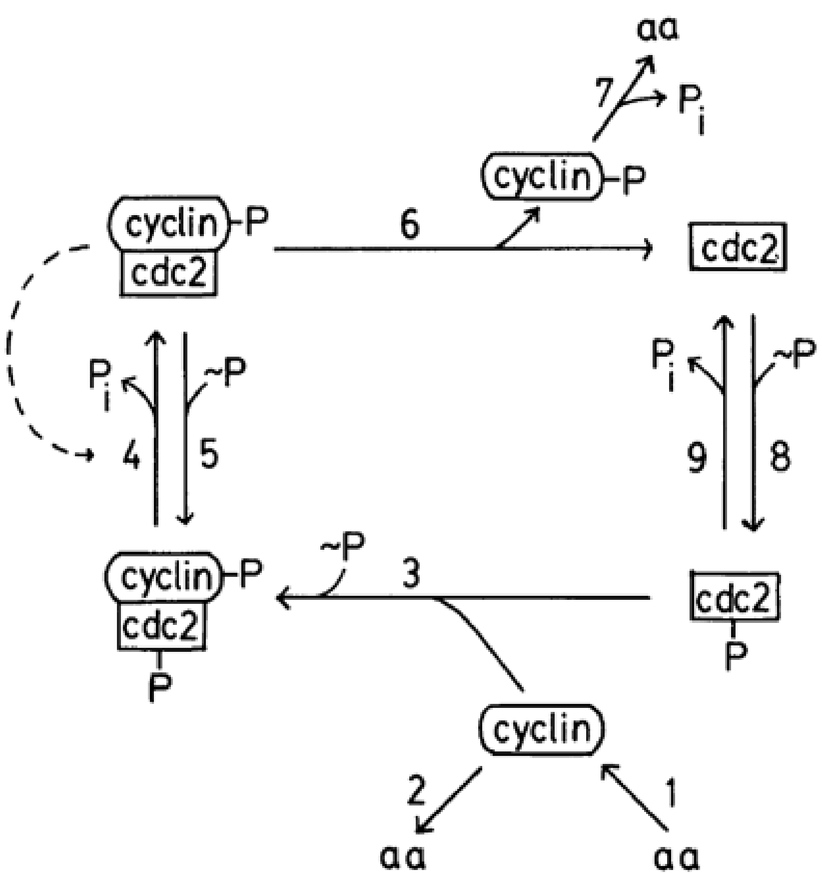
...

Some basics of SBML model encoding

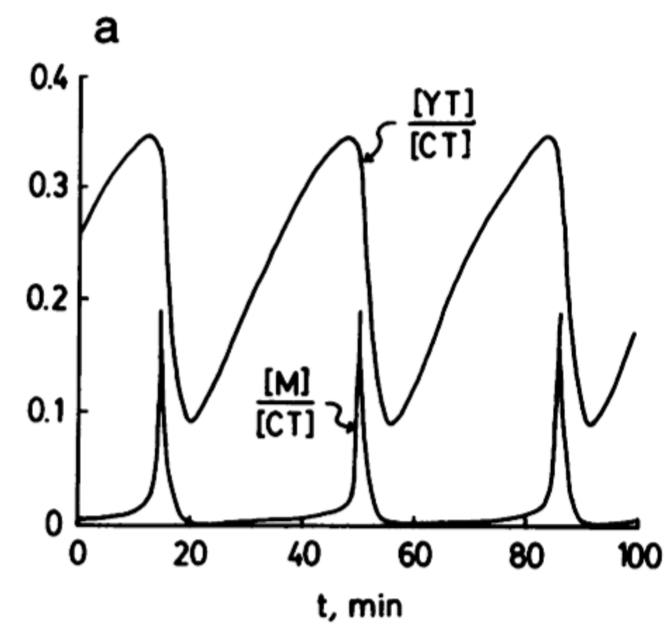


Example of "classical" kind of model encoded in SBML

$$d[C2]/dt = k_6[M] - k_8[\sim P][C2] + k_9[CP]$$
$$d[CP]/dt = -k_3[CP][Y] + k_8[\sim P][C2] - k_9[CP]$$
$$d[pM]/dt = k_3[CP][Y] - [pM]F([M]) + k_5[\sim P][M]$$
$$d[M]/dt = [pM]F([M]) - k_5[\sim P][M] - k_6[M]$$
$$d[Y]/dt = k_1[aa] - k_2[Y] - k_3[CP][Y]$$
$$d[YP]/dt = k_6[M] - k_7[YP]$$



Simulation output



Tyson et al. (1991)
PNAS 88(1):7328–32

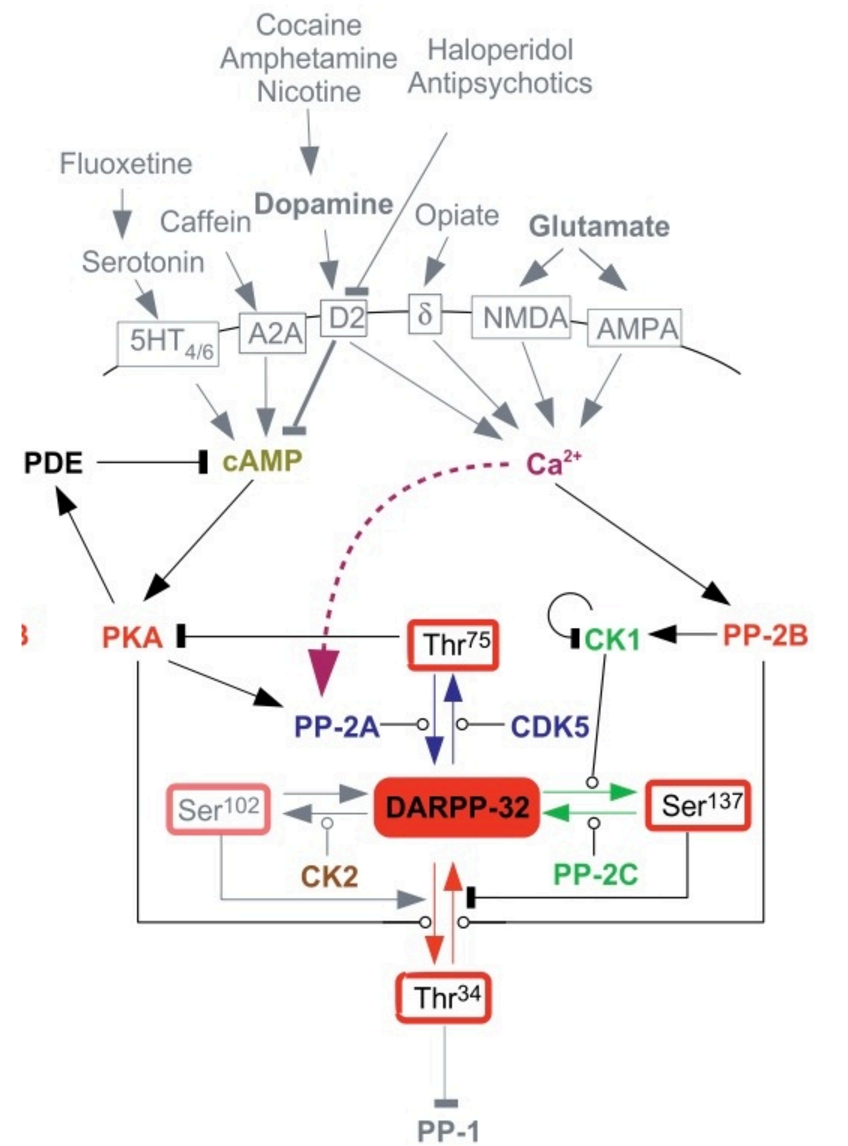
Signaling pathway models

Fernandez et al. (2006)

DARPP-32 Is a Robust Integrator of Dopamine and Glutamate Signals

PLoS Computational Biology

BioModels Database model #BIOMD0000000153



Scope of SBML is not limited to one kind of model

Signaling pathway models

Conductance-based models

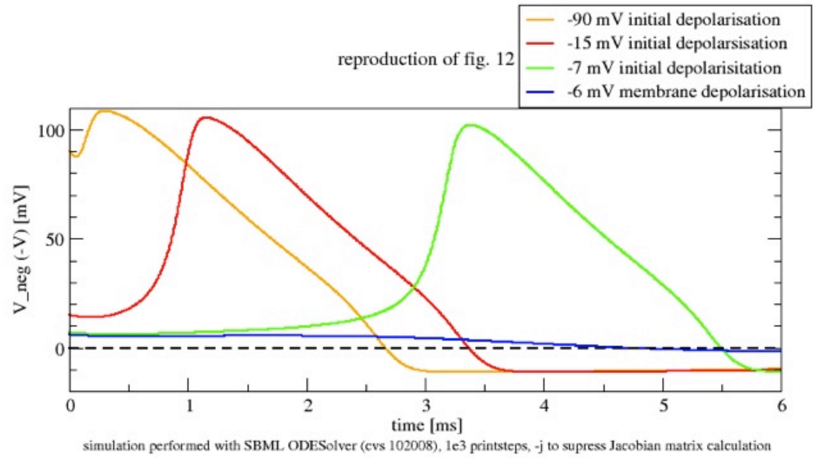
- "Rate rules" for temporal evolution of quantitative parameters

Hodgkin & Huxley (1952)

A quantitative description of membrane current and its application to conduction and excitation in nerve

J. Physiology 117:500–544

BioModels Database model #BIOMD0000000020



Scope of SBML is not limited to one kind of model

Signaling pathway models

Conductance-based models

- "Rate rules" for temporal evolution of quantitative parameters

Neural models

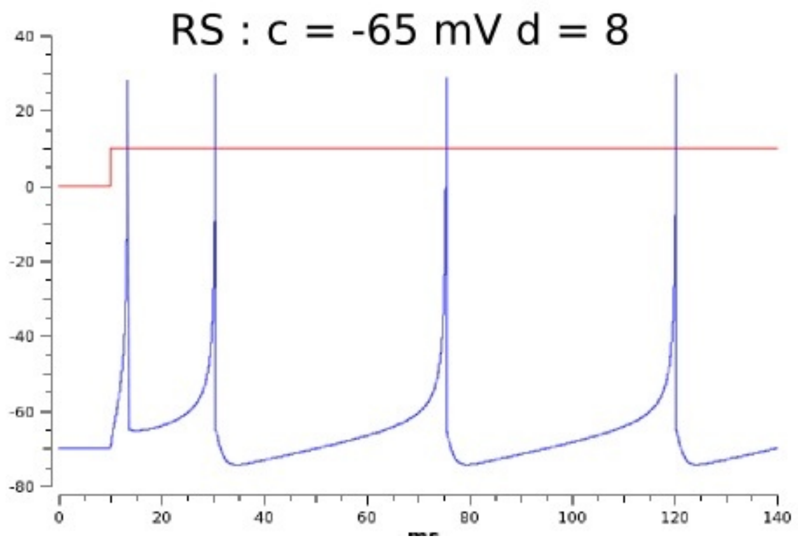
- "Events" for discontinuous changes in quantitative parameters

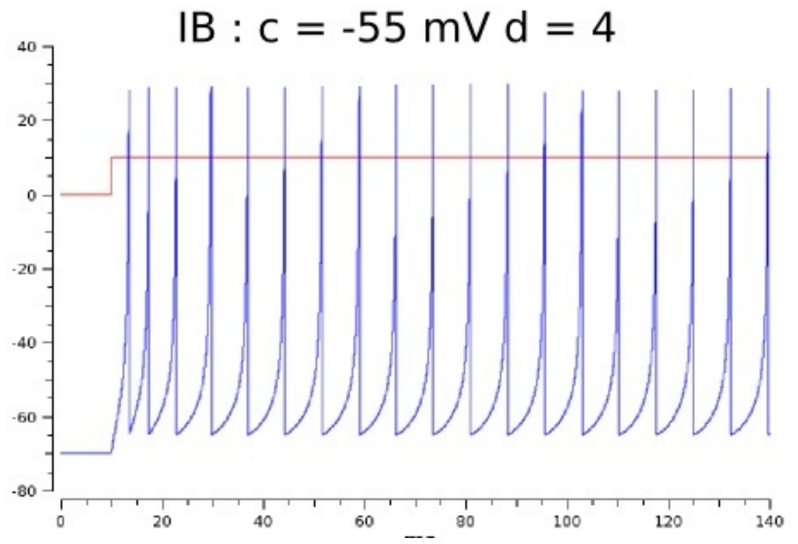
Izhikevich EM. (2003)

Simple model of spiking neurons.

IEEE Trans Neural Net.

BioModels Database model #BIOMD0000000127





Scope of SBML is not limited to one kind of model

Signaling pathway models

Conductance-based models

- "Rate rules" for temporal evolution of quantitative parameters

Neural models

- "Events" for discontinuous changes in quantitative parameters

Pharmacokinetic/dynamics models

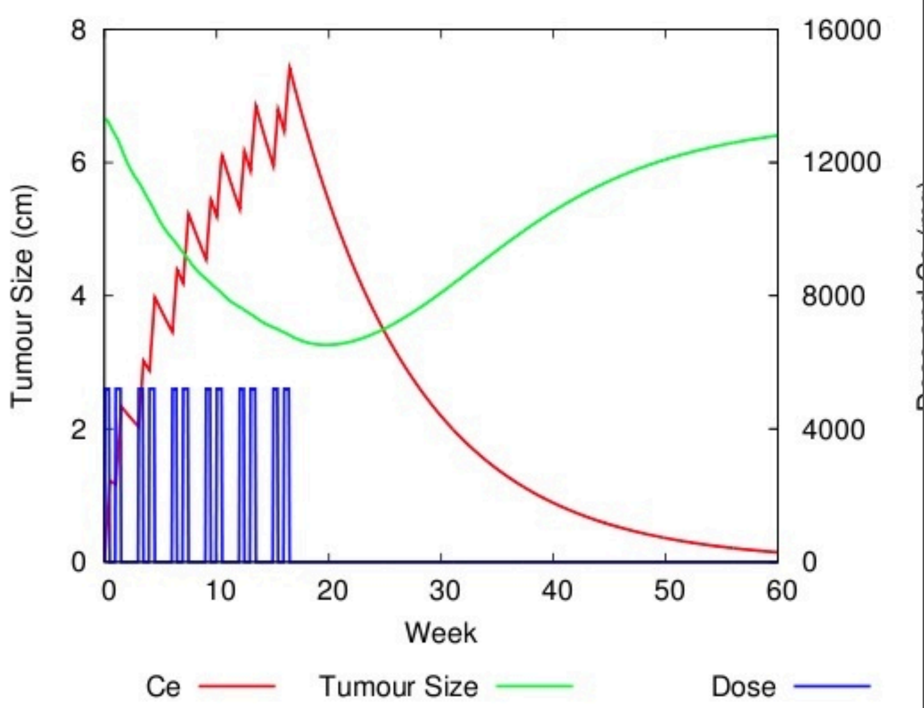
- "Species" is not required to be a biochemical entity

Tham et al. (2008)

A pharmacodynamic model for the time course of tumor shrinkage by gemcitabine + carboplatin in non-small cell lung cancer patients

Clin. Cancer Res. 14

BioModels Database model #BIOMD0000000234



Scope of SBML is not limited to one kind of model

Signaling pathway models

Conductance-based models

- “Rate rules” for temporal evolution of quantitative parameters

Neural models

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Pharmacokinetic/dynamics models

- “Species” is not required to be a biochemical entity

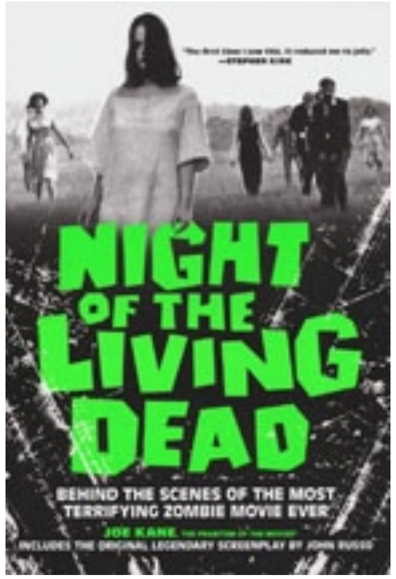
Infectious diseases

Munz et al. (2009)

When zombies attack!: Mathematical modelling of an outbreak of zombie infection

Infectious Disease Modelling Research Progress, eds. Tchuenche et al., p. 133–150

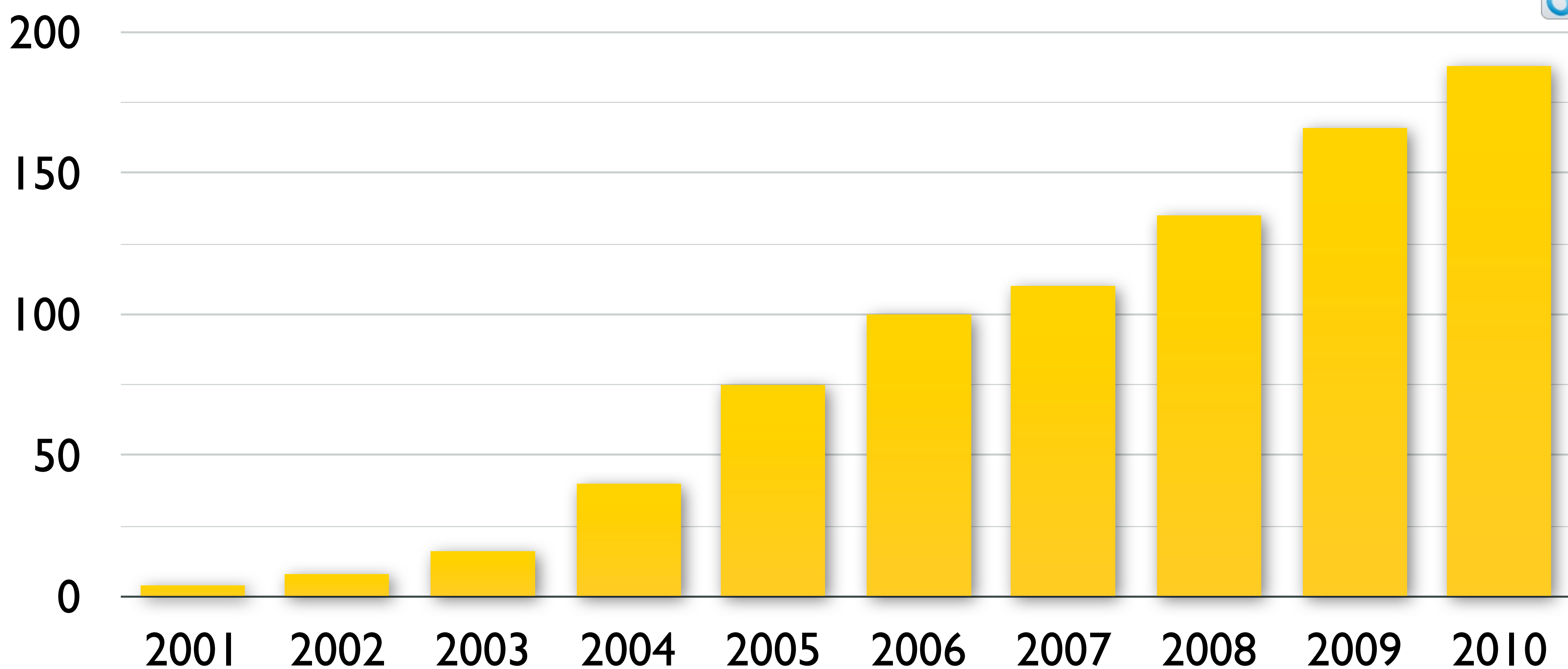
BioModels Database model #MODEL1008060001



Scope of SBML is not limited to one kind of model

Number of software systems supporting SBML

213 as of Apr. 17 ↓

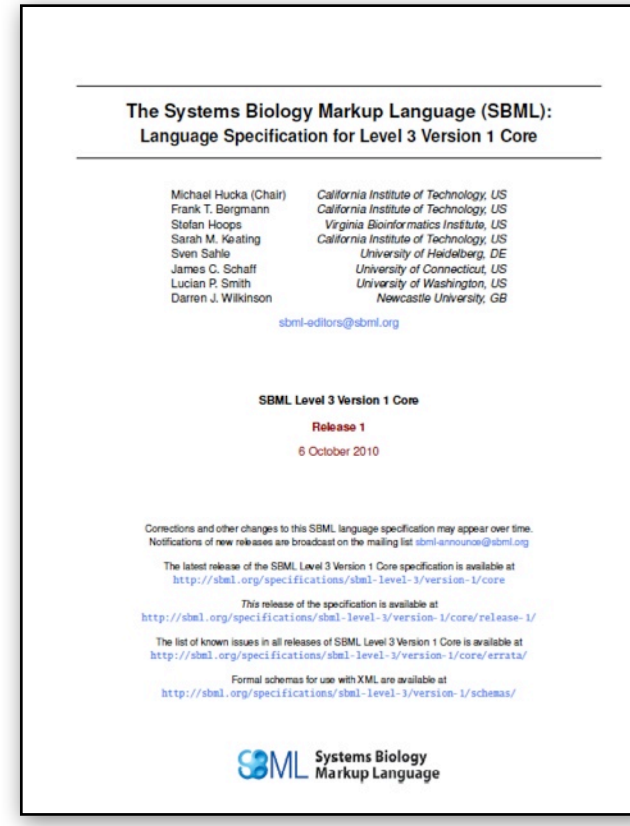


(counted in middle of each year)

What are SBML "Levels"?

Specification document available from

http://sbml.org/Documents



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

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SBML Level 3 Version 1 Core

Release 1

6 October 2010

Corrections and other changes to this SBML language specification may appear over time. Notifications of new releases are broadcast on the mailing list sbml-announce@sbml.org

The latest release of the SBML Level 3 Version 1 Core specification is available at http://sbml.org/specifications/sbml-level-3/version-1/core

This release of the specification is available at http://sbml.org/specifications/sbml-level-3/version-1/core/release-1/

The list of known issues in all releases of SBML Level 3 Version 1 Core is available at http://sbml.org/specifications/sbml-level-3/version-1/core/errata/

Formal schemas for use with XML are available at http://sbml.org/specifications/sbml-level-3/version-1/schemas/

SBML Systems Biology Markup Language

Newest: **Level 3 Version 1 Core**

- Oct. 2010

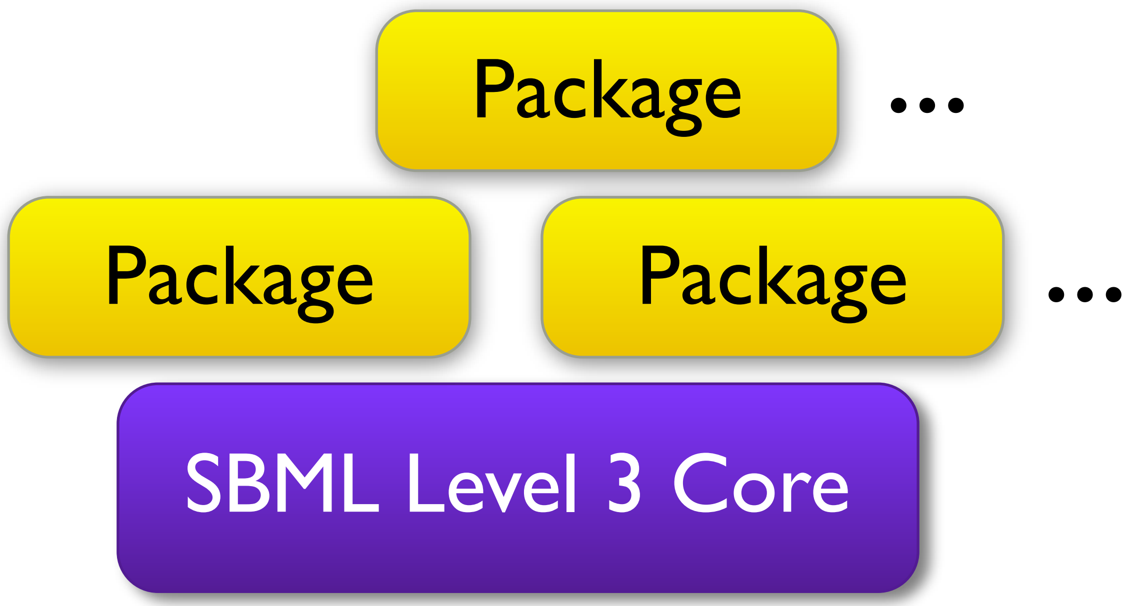
About SBML "Levels":

- Levels help manage significant restructuring of SBML architecture
- Levels coexist
  - E.g., Level 2 models will remain valid and exist for a long time
- A Level is *not* solely a vertical change (i.e., more features)—there is horizontal change too (i.e., changes to existing elements)

SBML Level 3

SBML Level 3 is modular:

- "Core" defines common aspects
- "Packages" add optional features
  - Models declare which packages they use
  - Tools can tell their users which packages they support



Growing community, greater challenges

	Model	**Procedures**	**Results**
Representation format	SBML	SED ML	SBRML
Minimal info requirements	MIRIAM	MIASE	?
Semantics— *Mathematical*	SBO	KiSAO	TEDDY
Other	MIRIAM annotations	MIRIAM annotations	MIRIAM annotations

(Credit: Nicolas Le Novère)

People on SBML Team & BioModels Team

SBML Team	BioModels.net Team
Michael Hucka	**Nicolas Le Novère**
Sarah Keating	**Camille Laibe**
Frank Bergmann	**Nicolas Rodriguez**
Lucian Smith	**Nick Juty**
Nicolas Rodriguez	**Lukas Endler**
Linda Taddeo	**Vijayalakshmi Chelliah**
Akiya Joukarou	Chen Li
Akira Funahashi	Harish Dharuri
Kimberley Begley	Lu Li
Bruce Shapiro	Enuo He
Andrew Finney	Mélanie Courtot
Ben Bornstein	Alexander Broicher
Ben Kovitz	Arnaud Henry
Hamid Bolouri	Marco Donizelli
Herbert Sauro	
Jo Matthews	
Maria Schilstra	

National Institute of General Medical Sciences (USA)

European Molecular Biology Laboratory (EMBL)

ELIXIR (UK)

Beckman Institute, Caltech (USA)

Keio University (Japan)

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

National Science Foundation (USA)

International Joint Research Program of NEDO (Japan)

JST ERATO-SORST Program (Japan)

Japanese Ministry of Agriculture

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

BBSRC (UK)

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

Air Force Office of Scientific Research (USA)

STRI, University of Hertfordshire (UK)

Molecular Sciences Institute (USA)

Agencies to thank

Where to find out more

SBML	http://sbml.org
BioModels Database	http://biomodels.net/biomodels
MIRIAM	http://biomodels.net/miriam
MIASE	http://biomodels.net/miase
SED-ML	http://biomodels.net/sed-ml
SBO	http://biomodels.net/sbo
KiSAO	http://www.ebi.ac.uk/compneur-srv/kisao/
TEDDY	http://www.ebi.ac.uk/compneur-srv/teddy/
SBRML	http://tinyurl.com/sbrml

Thank you for listening!