

Special SBML L3 Workshop Extension for formal modelling



The **Systems Biology Markup Language (SBML)** is a computer-readable format for representing models of biochemical reaction networks in software. It's applicable to models of metabolism, cell-signaling, and many others. SBML has been evolving since mid-2000 thanks to an international community of software developers and users. This website is the portal for the global SBML development effort; here you can find information about all aspects of SBML.



For the curious

What *is* SBML? Read our [basic introduction](#) and then perhaps browse the [mailing lists](#) to get a sense for what's currently going on in the world of SBML.



For modelers

Are you looking for ready-to-run software that supports SBML? Take a look at our [SBML Software Guide](#). Are you instead looking for ready-to-use models? Visit the [BioModels Database](#), where you can find hundreds of tried and tested models.



For software developers

Are you interested in developing SBML support for your software? Read our [basic introduction](#) and then the [SBML specifications](#) to understand how to use SBML. After that, you may want to look at [libSBML](#), an API library supporting many programming languages.

Whether you use SBML as a modeler or a developer, we invite you to sign up for news updates either through our [RSS feed](#) or one of the [mailing lists](#), and get involved with community efforts to help keep SBML improving.

SBML News

SBML.org problems

(29 May '08) A security break-in on the server, followed by a disk failure, caused SBML.org to be off-line for two days while we rebuilt it.

New SBML FAQ

(7 May '08) A greatly revised and rewritten list of FAQs and answers for SBML is **now available**.

New mailing list introduced

(6 May '08) A new mailing list, [libsbml-development](#), now exists for discussions of libSBML improvement and development.

Older news ...

Community News

SBToolbox² version 2.0

(6 Jun. '08) The latest version of [SBToolbox](#) adds GUIs, new optimization methods, and new sensitivity analysis methods.

Cell Illustrator 4.0

(14 May. '08) [BioBase](#) has released version 4.0 of [Cell Illustrator](#). It supports importing SBML.

COPASI user workshop

(23 Apr. '08) The [COPASI](#) team will hold a 3-day workshop July 22-24, 2008, at the VBI in Virginia.

Older news ...

- Website: SBML is a computer-readable format for representing models of biochemical reaction networks [...]. It's applicable to models of metabolism, cell-signaling, and many others.

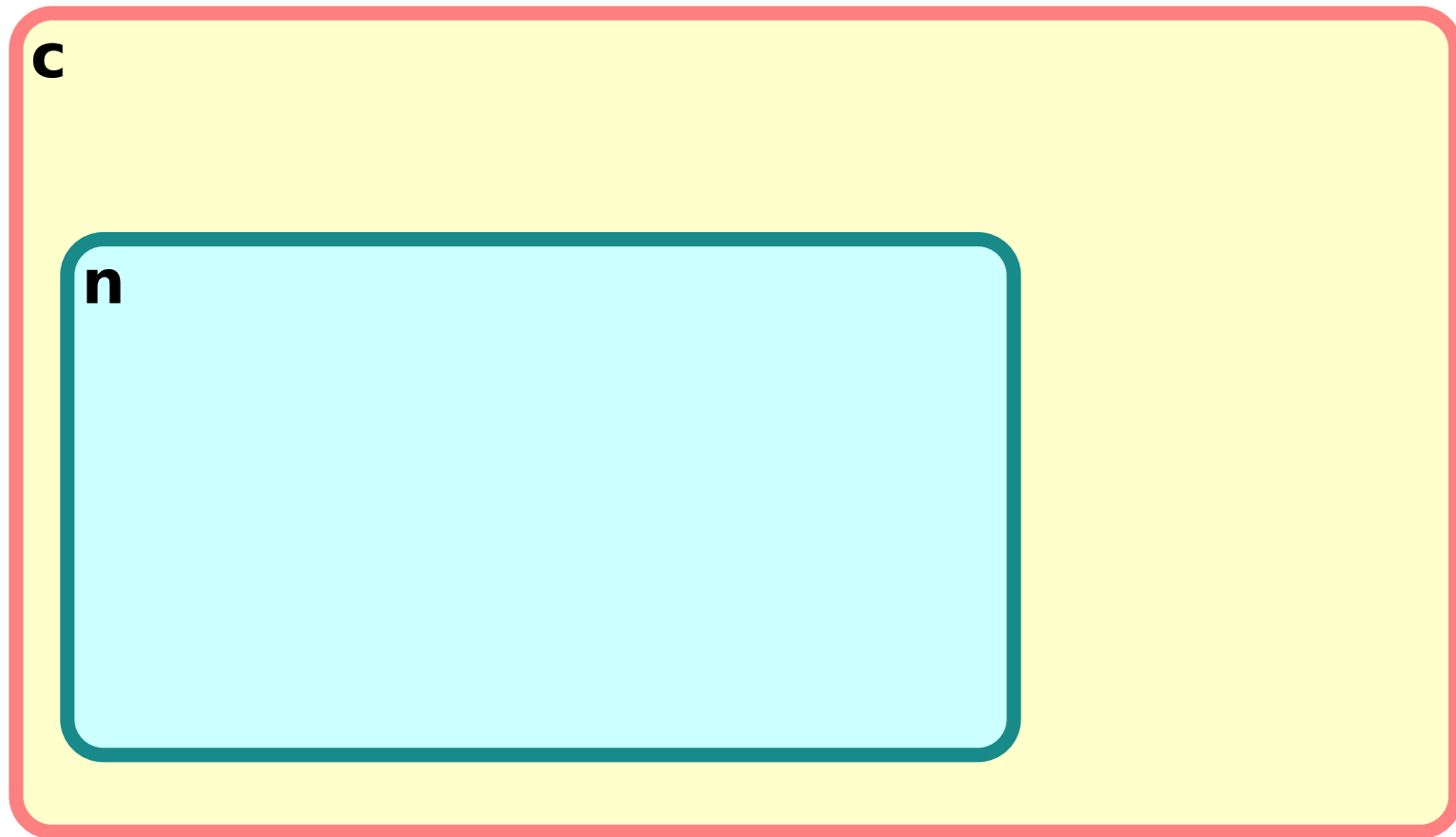


- Website: SBML is a computer-readable format for representing models of biochemical reaction networks [...]. It's applicable to models of metabolism, cell-signaling, and many others.
- SBML allows to encode models of biological processes unambiguously, so that any simulation software interpret them the same way.
- SBML core element is the reaction, not the variable. The final mathematical representation is built by the reading software.
- SBML is neutral when it comes to simulation approaches and algorithms.

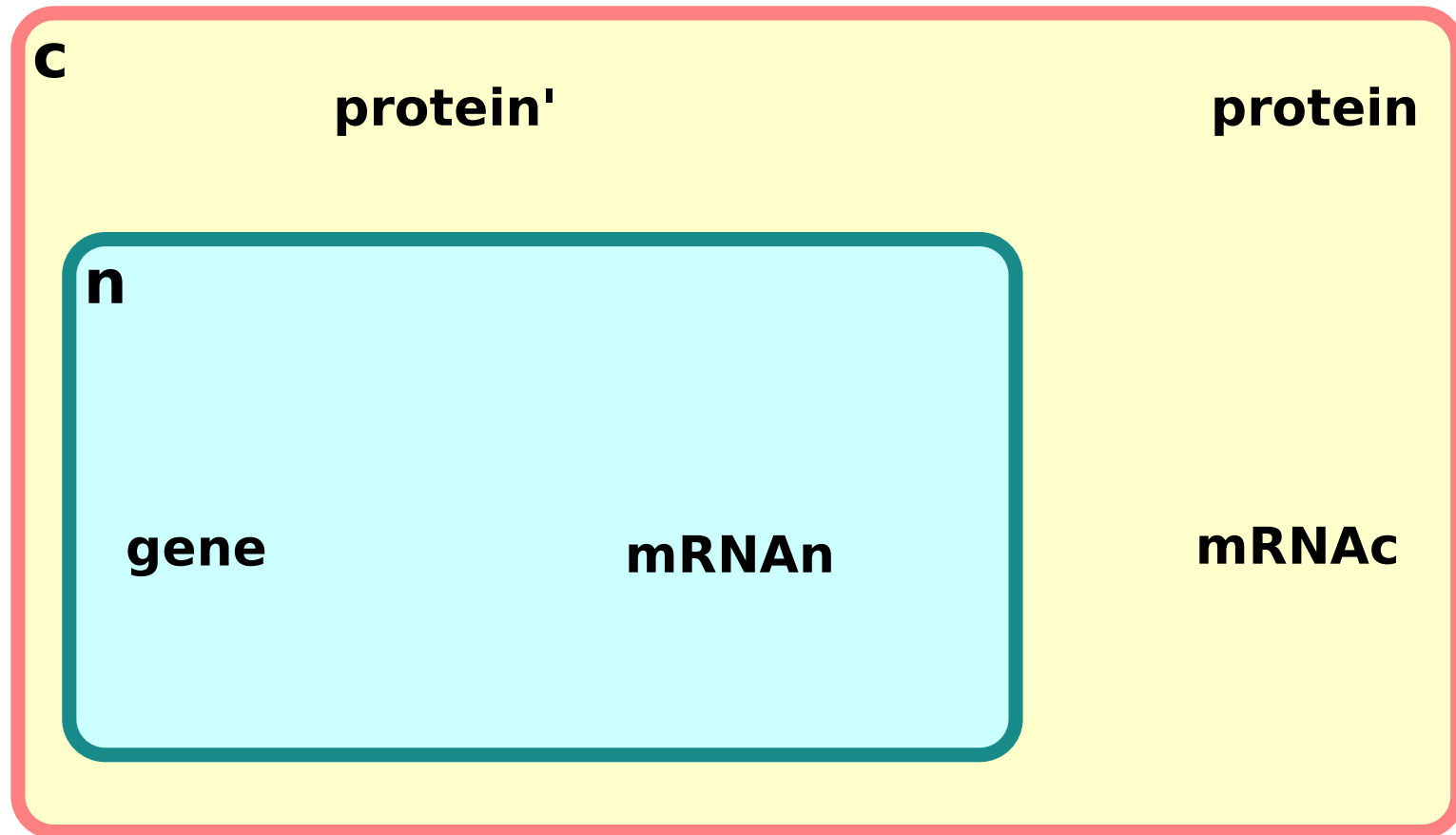


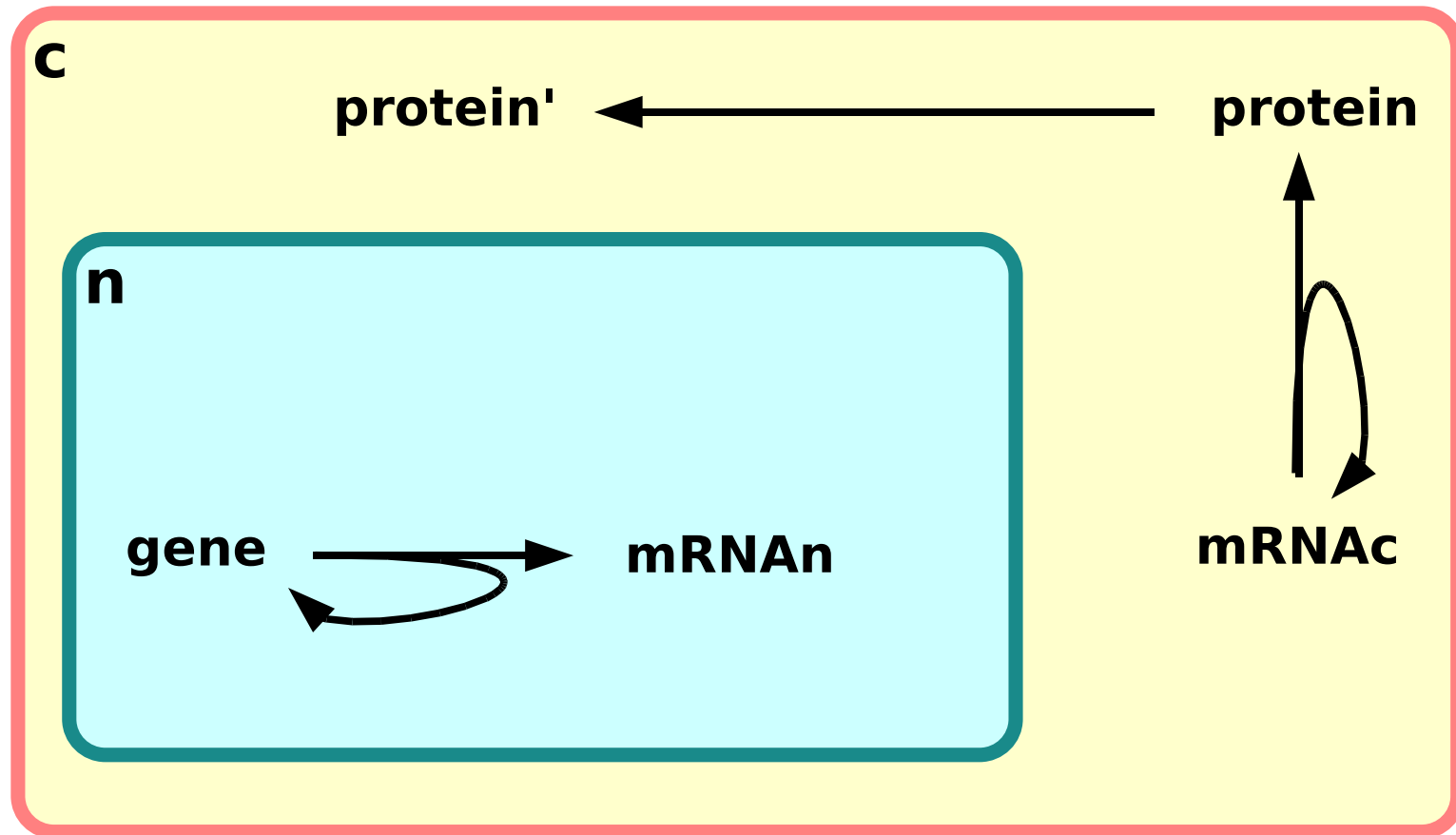


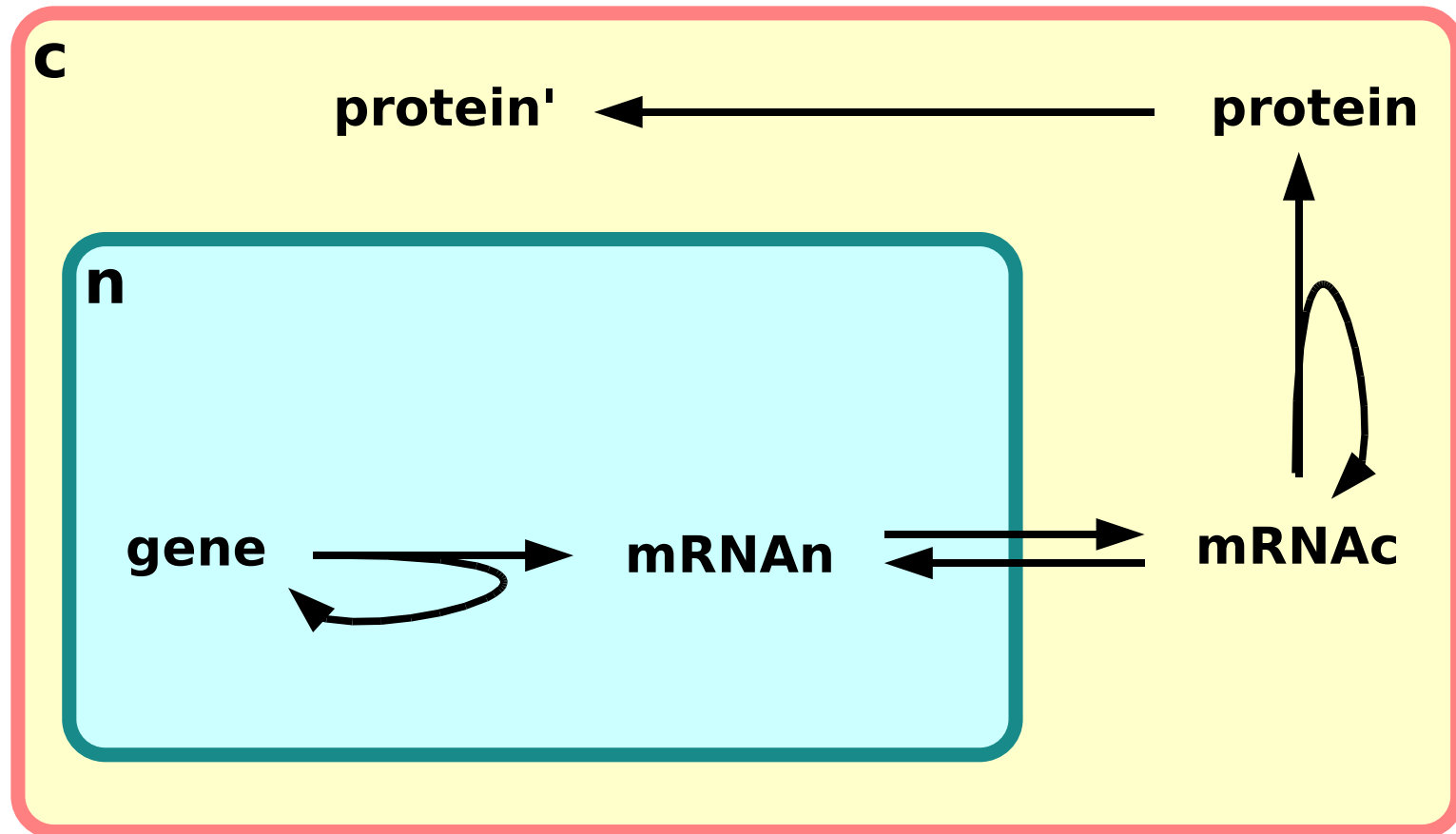
Well-stirred compartments

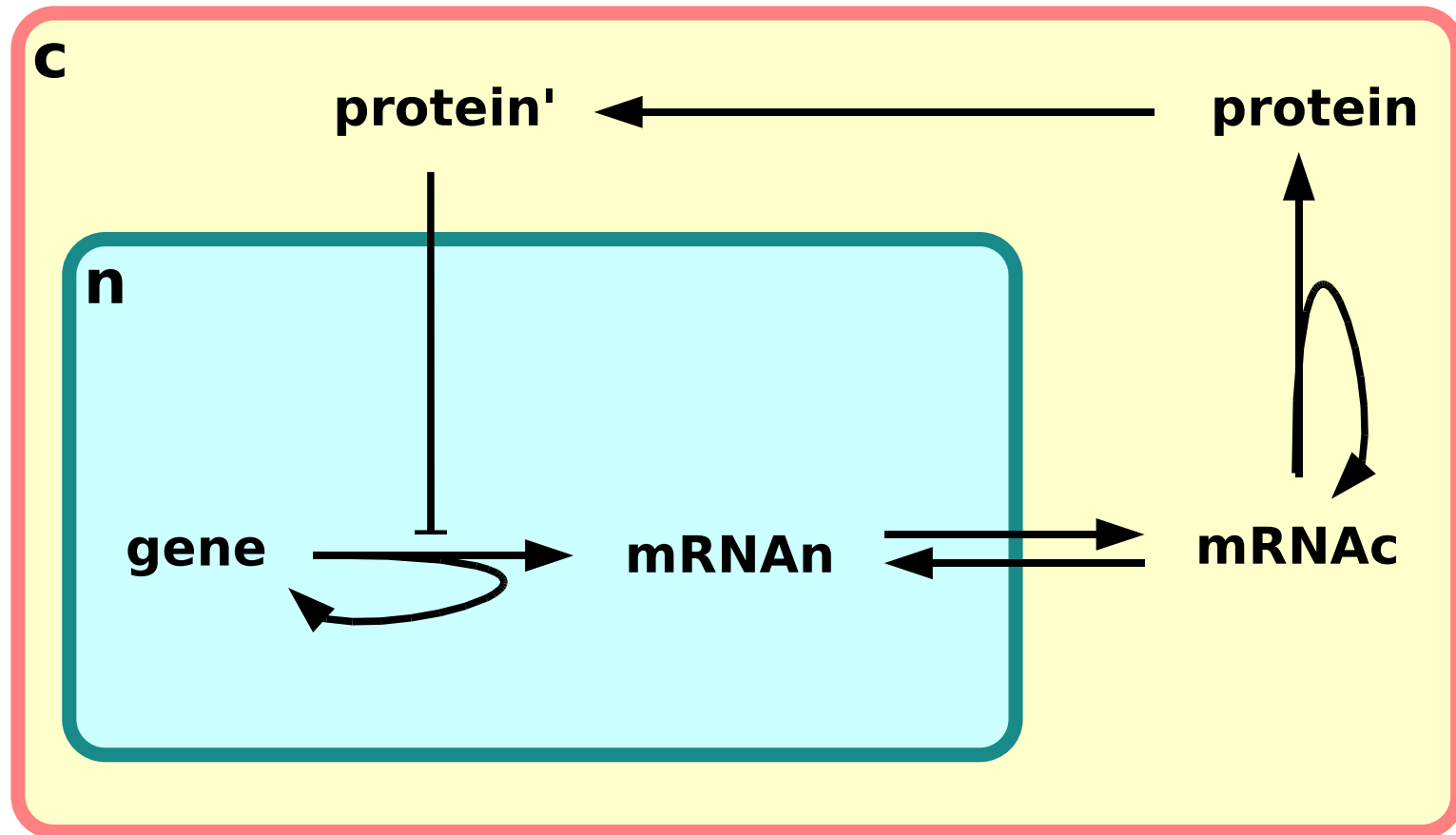


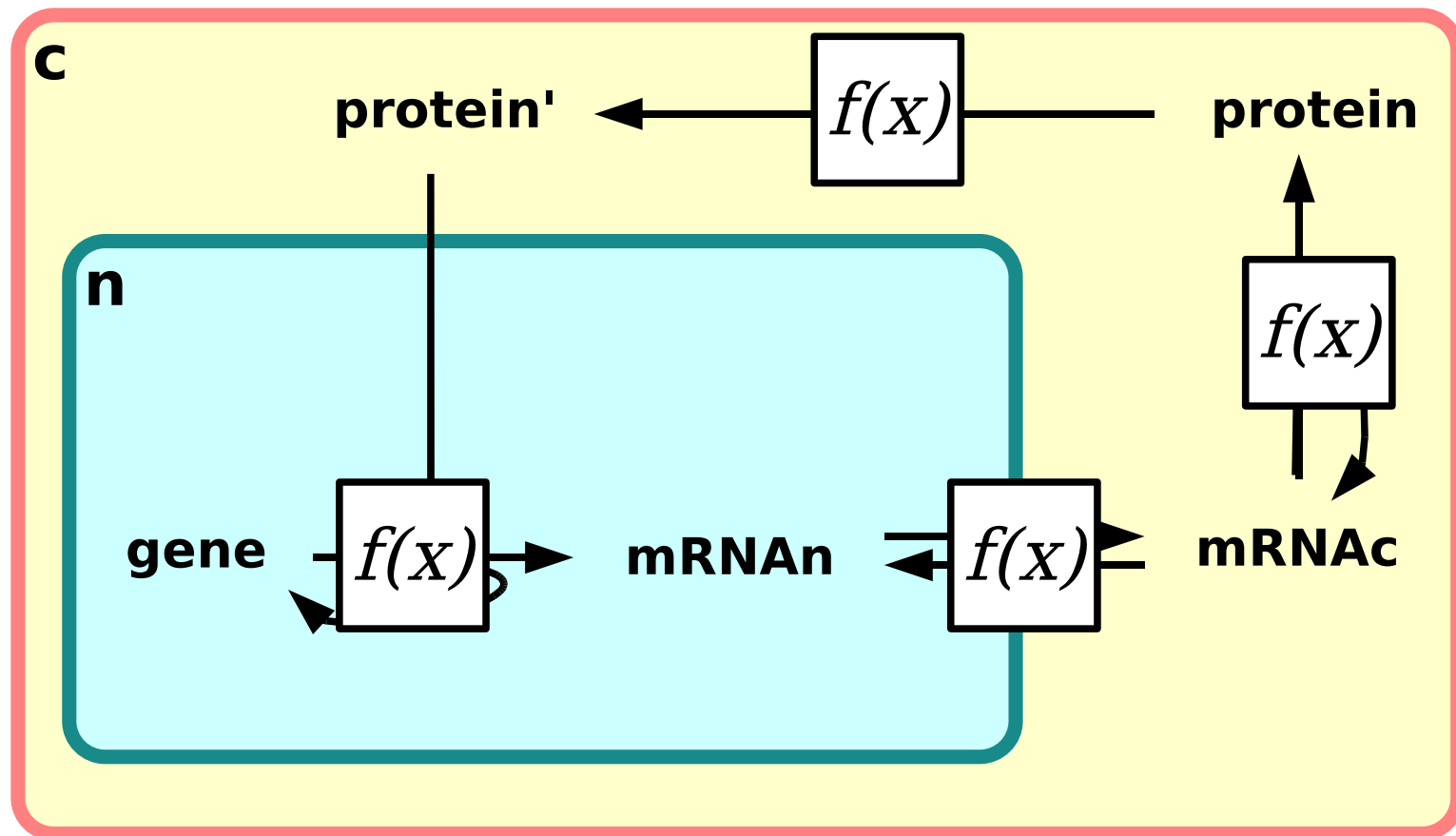
Entity pools

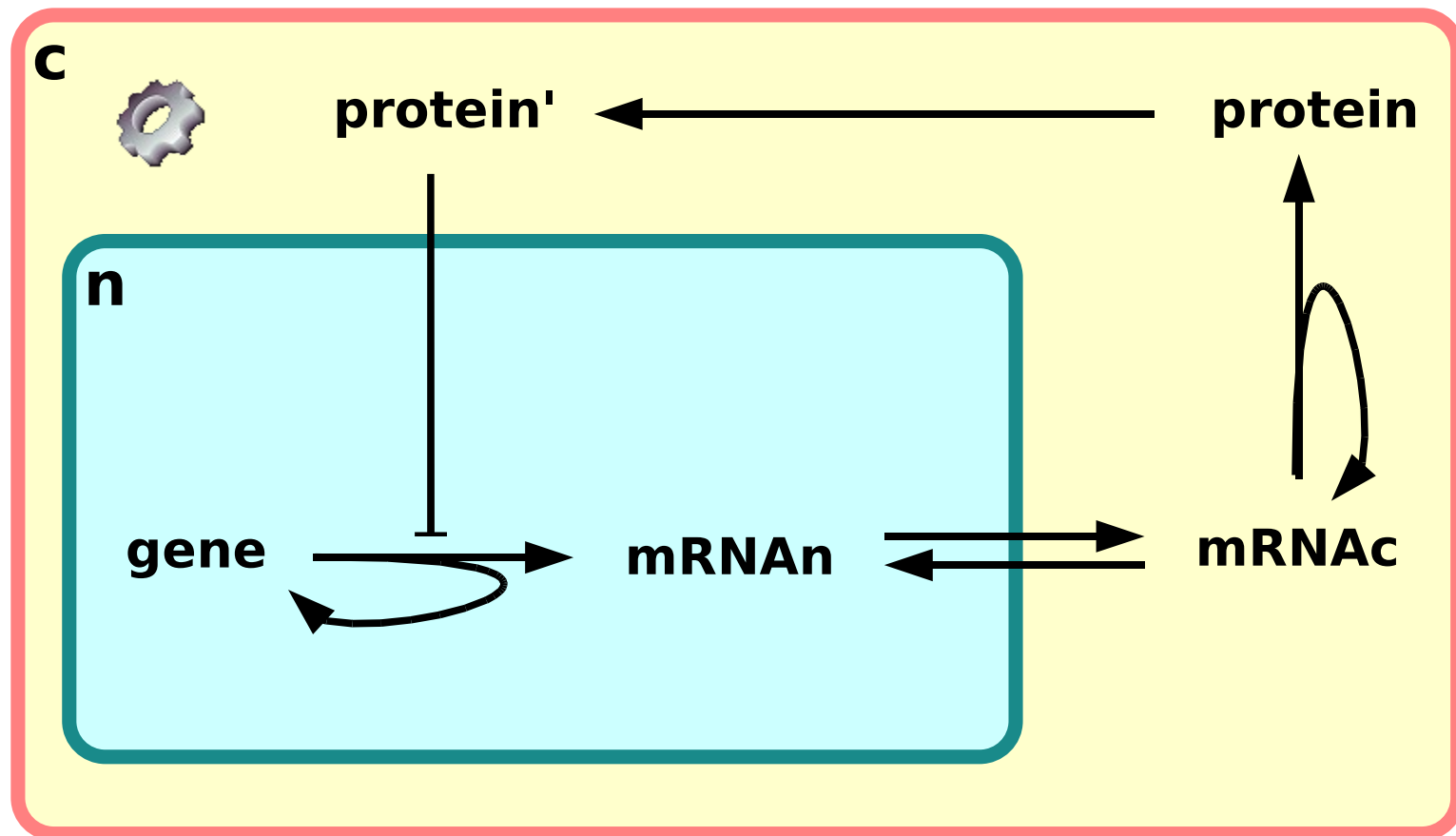


reactions

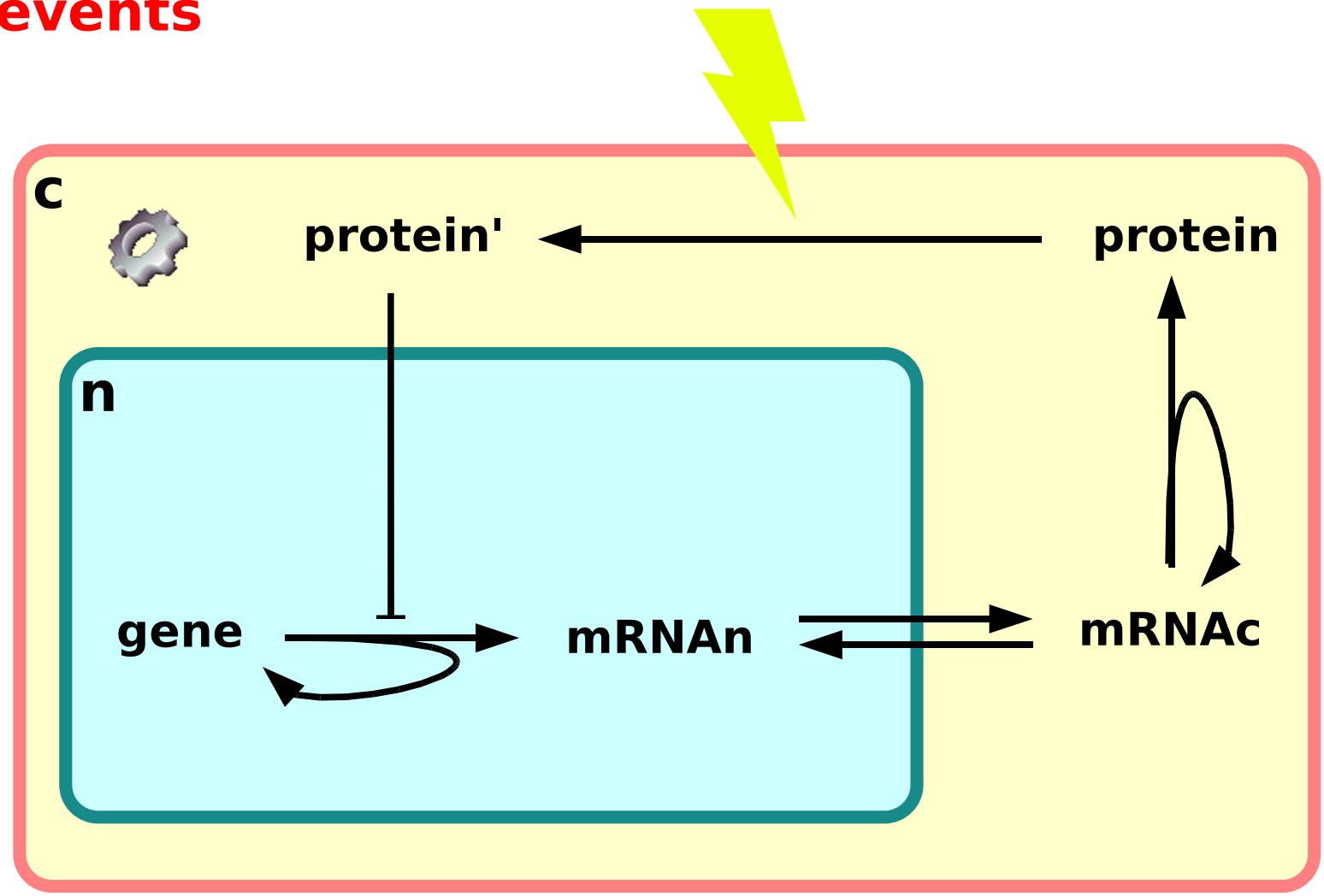
reactions

modulations



rules

events



```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="1" xmlns="http://www.sbml.org/sbml/level2">
  <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>
```



```
<species
  id="A"
  name="α-tubulin"
  compartment="cell"
  initialAmount="1000"
  substanceUnits="item"
  hasOnlySubstanceUnits="true"
  boundaryCondition="true"
  constant="false"
  charge="0"
  metaid="PX"
  sboTerm="SBO:0000252" >
<notes>
  <body xmlns="http://www.w3.org/1999/xhtml">
    <p>One of the components of 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="http://www.uniprot.org/#P68370"/>
          <rdf:li rdf:resource="http://www.geneontology.org/#GO:0045298"/>
        </rdf:Bag>
      </bqbiol:is>
    </rdf:Description>
  </rdf:RDF>
</annotation>
</species>
```





```

sbml
- level: 2
- metaid: _492719
- version: 1
- xmlns: http://www.sbml.org/sbml/level2

```

```

model
- id: Kholodenko2000_MAPK_feedback
- metaid: _000001

```

Creators

Family: Sauro
Given: Herbert
EMAIL: Herbert_Sauro@kgi.edu
Orgname: Keck Graduate Institute

Links

relation
<http://www.ebi.ac.uk/biomodels/#BIOMD0000000010>
<http://www.ncbi.nlm.nih.gov/PubMed/#10712587>

relation
<http://www.geneontology.org/#GO:0000165>
<http://www.ncbi.nlm.nih.gov/Taxonomy/#8355>

```

- listOfUnitDefinitions
- listOfCompartments
- listOfSpecies

```

```

species
- compartment: uVol
- id: MKKK
- initialConcentration: 90
- metaid: _584475
- name: MAPKKK

```

Links

isVersionOf
<http://www.uniprot.org/#P09560>

```

species

```

species

id: MKKK

name: MAPKKK

Compartment: uVol

initial Amount:

initial Concentration: 90

substanceUnits:

spatialSizeUnits:

hasOnlySubstanceUnits:

Boundary Condition:

charge:

Constant:

OK Reset Cancel



Rodriguez et al. (2007)
BMC Bioinformatics, 8:79

- **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;
- 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

→ Systems Biology is scale-free!



■ Level 1 (March 2001)

- Predefined kinetics functions
- One type of reactive substance
- ISO646 encoding

Hucka et al (2003)
Bioinformatics 19: 524-531

■ Level 2 (June 2003)

- Function definitions
- Modifier species
- Events
- All math in MathML
- Unicode encoding

Hucka et al (2004)
IEE Systems Biology 1: 41-53

Hucka et al (2007)
Nature preceedings
hdl:10101/npre.2007.58.1

■ Level 3 (development started)



- Released on September 26th 2007
- Simpler and cleaner (units ...)
- Generic entities (compartmentType, speciesType)
→ path to generalised reactions
- Constraints and initialAssignments
- Controlled (MIRIAM) annotations (+ links to SBO)
- Backward compatible with Level 2 Version 1
- More detailed and bug-free specification ... 166 pages, 10pt, small margin.



- Modular SBML, with common core + optional packages
- Graph Layout (certain; already in use in Level 2 as annotation, shared by several software)
- Generalised reactions [one definition for all compartments] (probable)
- Model composition [models based on submodels] (probable)
- Complex species (multi-components multistates) (probable)
- Formal modeling [logical, petri-net etc.] (probable)
- Arrays or sets of entities (maybe)
- Geometry of physical entities (maybe)
- Spatial anisotropy and movements (maybe)
- Dynamic compartments (maybe)
- ???



- Editorial board
 - 1 chair (head of SBML-team): Michael Hucka
 - 5 elected editors. Single 3 year term: Nicolas Le Novere, Sarah Keating, Stefan Hoops, Darren Wilkinson, Sven Sahle
- One SBML “forum” a year
 - General discussion about the evolution of the language
 - Presentation of SBML-compliant software
- One SBML “hackathon” a year
 - Development of SBML-supporting tools
 - Implementation of SBML-support
 - Writing of specification
- Communication tools
 - SBML-announce mailing list
 - SBML-discuss mailing list
 - SBML-interoperability mailing list
 - Sourceforge trackers to debug the specification



- List of the approaches to support in a first version of the extension: logical models, petri net, pi-calculus? Others ?
- Discussion about the approaches used so far by the different groups: export, import, round-tripping, loss
- Evaluation of the current SBML structures susceptible to be reused as such or modified
- Description of the main structure of the extension
- Sketch of the syntax and grammar
- Formalisation: UML + Schema ...

