

Flux Balance Constraints Version 2

Brett G. Olivier

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2009

2010

2011

2012

2013

2014

2015

We identified the need for an unambiguous format for encoding a GSM in SBML and proposed an SBML Level 2 annotation.

SBML Level 3 is released and the Level 2 proposal is rewritten as a Level 3 package proposal

The package proposal is officially accepted by the SBML community. FBC Package Working Group is established and the proposal is developed into a full specification

The SBML3 FBC Package Version 1 specification is officially approved by the PWG, SBML community and released

Through an intensive, community based, process FBC Version1 is extended and released as the SBML3 FBC Package Version 2



Level 3 core

Species

Reactions

Compartments

Parameters

Annotations

Any SBML element can be strictly annotated with MIRIAM compliant RDF

```
<species metaid="m_atp" id="atp">
  <annotation> <RDF><Description about="#m_atp">
    <bqbiol:is><Bag>
      <li resource="http://identifiers.org/chebi/
        CHEBI:15422"/>
    </Bag></bqbiol:is>
  </Description></RDF>
</annotation>
</species>
```

FluxBounds

An (in)equality representing
either an upper or lower bound

```
<listOfFluxBounds>  
  <fluxBound reaction="R1"  
    operation="greaterEqual" value="0"/>  
  <fluxBound reaction="R1"  
    operation="lessEqual" value="1"/>  
</listOfFluxBounds>
```

FB version 1

Species ext.

Attributes for charge and chemical composition are added to Species

```
<species id="atp" name="ATP" compartment="Cytosol"  
  charge="-4" chemicalFormula="C10H12N5O13P3"  
  boundaryCondition="false"/>
```

Objective functions

Multiple linear objectives may be defined for a single model

```
<listOfObjectives activeObjective="obj1">  
  <objective id="obj1" type="maximize">  
    <listOfFluxObjectives>  
      <fluxObjective reaction="Biomass" coefficient="1"/>  
    </listOfFluxObjectives>  
  </objective>  
</listOfObjectives>
```

Genes

Contain identifiers and annotations
for use in associations

```
<listOfGeneProducts>  
  <geneProduct id="g1" name="dog" label="b1234"/>  
  <geneProduct id="g2" name="cat" label="Rv3452"/>  
  <geneProduct id="g3" name="mouse" label="Y1234"/>  
</listOfGeneProducts>
```

Gene associations

Define logical AND and OR relationships between genes

```
<geneProductAssociation id="allGPR">
  <or>
    <and>
      <geneProductRef geneProduct="g1" />
      <geneProductRef geneProduct="g2" />
    </and>
    <geneProductRef geneProduct="g3" />
  </or>
</geneProductAssociation>
```

FBC version 2

Reaction ext.

Reactions refer to flux bound parameters and contain gene protein associations

```
<reaction id="X1" reversible="false" lowerFluxBound="lb"
  upperFluxBound="ub" >
  <geneProductAssociation> ... </geneProductAssociation>
  <listOfReactants>
    <speciesReference species="A" stoichiometry="1"/>
  </listOfReactants>
  <listOfProducts>
    <speciesReference species="B" stoichiometry="1"/>
  </listOfProducts>
</reaction>
```

```
<listOfParameters>
  <parameter id="lb" value="1" sboTerm="SBO:0000625" />
  <parameter id="ub" value="0" sboTerm="SBO:0000625" />
</listOfParameters>
```


CBMPy
PySCeS Constraint Based Modelling

FBC support: v1 and v2

<http://cbmpy.sourceforge.net>



SBW Flux Balance Analysis tool

FBC support: v1 and v2

<http://fbergmann.github.io/FluxBalance/>



FBC support: v1

<http://f-a-m-e.org>

COBRApy

FBC support: v2

<http://opencobra.github.io/cobrapy>

COBRA

FBC support: v1

<https://opencobra.github.io/cobratoolbox/>



FBC support: v2

<http://www.ebi.ac.uk/biomodels-main>

BiGG 2

FBC support: v2

<http://bigg.ucsd.edu>

libSBML:

is a platform independent library for reading and writing SBML. It has full support for the Flux Balance Constraints package and provides seamless support for translation between the COBRA format and FBC v1 and FBC v2. It also provides language bindings for .net, java, python, perl, ruby, r, octave/Matlab. For more information on libSBML and the full documentation to it, please see:

<http://sbml.org/Software/libSBML>.

JSBML:

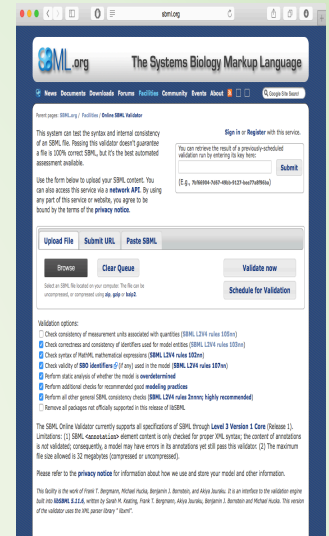
is a community-driven project to create a free, open-source, pure Java library for reading, writing, and manipulating SBML files and data streams. It is an alternative to the mixed Java/native code-based interface provided in [libSBML](#).

Test Suite:

the SBML test suite includes some 2000 test cases, that help implementors to verify their implementation against the specification. We also provide some 11 test cases for the FBC specification so that other implementation can easily adopt the standard. Next to the test case, and a standalone test-runner, there is a online database of test-results available, that allows to compare how other simulators fare in the test cases. For more information, please see: http://sbml.org/Software/SBML_Test_Suite.

Online Validation:

the SBML online validator, available under <http://sbml.org/validator> provides full validation of the FBC v1 and FBC v2 format. It verifies all 79 validation rules defined in the FBC specification. Files can either be uploaded via the website, or via a scriptable web API.



Community:

development of the SBML Level 3 FBC package could not have happened in isolation. We constantly were in contact with the SBML community using the mailing lists: (<https://groups.google.com/d/forum/sbml-discuss>) and sbml-flux (sbml-flux@lists.sourceforge.net.) as well as contributions at HARMONY and COMBINE meetings.

References

Brett G. Olivier and Frank T. Bergmann. *Flux Balance Constraints, Version 2 Release 1*. Available from COMBINE <<http://identifiers.org/combine.specifications/sbml.level-3.version-2.fbc.version-1.release-1>> (2015)

Brett G Olivier and Frank T Bergmann. *The Systems Biology Markup Language (SBML) Level 3 Package: Flux Balance Constraints*. Journal of Integrative Bioinformatics, 12(2):269, 2015. Online Journal: http://journal.imbio.de/index.php?paper_id=269

Michael Hucka, Frank T. Bergmann, Stefan Hoops, Sarah M. Keating, Sven Sahle, James C. Schaff, Lucian P. Smith and Darren J. Wilkinson. *The Systems Biology Markup Language (SBML): Language Specification for Level 3 Version 1 Core*. Journal of Integrative Bioinformatics, 12(2):266, 2015. Online Journal: http://journal.imbio.de/index.php?paper_id=266