SBML Level 3 Package Proposal: Flux Balance

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About this Document

This document describes a very simple package to store information related to flux balance analysis of SBML Level 3 models (the FBA package). In addition, we provide an example of how this package may be implemented and used as an SBML Level 2 annotation.

Elements

In the following sections we describe the individual elements that are defined in the FBA package.

ListOfConstraints

A key feature of a steady-state or constraint based model is that reaction fluxes are bounded by constraints (e.g. thermodynamic, experimentally determined etc). While the reaction is already an attribute of an SBML reaction, an object is required these additional bounds. For this we define a list holding all flux constraints of this model.

Constraint

A constraint extends SBase by:

- An attribute “id” of type Sid, which represents the identity of this constraint.
- An attribute “reaction” of type SIdRef which refers to existing SBML reactions whose flux should be constrained.
- An attribute “operation” which is either “less”, “lessEqual”, “equal”, “greaterEqual” or “greater” which describes the constraint operation.
- Finally, a double valued attribute “value” representing the actual value of the constraint.

Notes:

- In order to use rational constraints one could use an InitialAssignment on the “id” attribute of the constraint.
- Multiple constraints on a single flux are allowed keeping in mind that order is irrelevant and constraint validity checking is left to the modeler/tool/developer.

ListOfObjectives

This list holds the objective functions for the model. Note that we anticipate a need to store more than one objective function. This implies that there should be a way to store the currently active objective function (i.e. the objective function to be used in the next analysis run). Thus the "listOfObjectives" element has one (mandatory) attribute "activeObjective" of type SIdRef which refers to the SId of one element of type "objective".

Objective

An "objective" represents a predefined objective function and consists of the following attributes:

- An attribute "id" of type SId, representing the id of this objective (note that this is mandatory as one should be able to activate it later on, see previous paragraph).
- An attribute "type" specifying whether a maximization or minimization of the linear program is intended. Accordingly the only valid values are "maximize" or "minimize".
- Finally an objective contains a ListOfFluxes.

ListOfFluxes

An objective function is a typically a flux and weight (or a linear combination of fluxes and weights), this is represented as a list of FluxObjective's.

FluxObjective

A flux objective has the following attributes:

- An attribute "reaction" of type SIdRef referring to an existing Reaction Id.
- A double valued attribute "coefficient".

With this the listOfFluxes describes a linear combination of weighted fluxes that make up the objective function.

Extensions of existing Elements

For annotation purposes, the SBML Species element can optionally be extended by two attributes. The first attribute is `fba:charge`, which takes a integer representing the charge of the molecule. The `fba:charge` attribute can be used to verify that reactions in an FBA model are correctly balanced.

The second attribute is `fba:chemicalEquation` is a string attribute holding an experimental chemical equation describing the elemental composition. While we recognize that this information is not intrinsically necessary for use with FBA it is important for model validation and, potentially, other (non FBA) modeling applications.

Implementations

There are currently three software tools available that read the Flux Balance Extension. (In order to fast-track testing, existing model translation and exchange software support has been implemented as an SBML Level 2 annotation (see the example below).

FBA Module

The SBW Flux Balance is a small application designed to perform Flux Balance analysis on small-ish SBML models, it will represent the SBML model graphically to facilitate the formulation of flux balance constraints and objectives. These can then be solved and displayed.

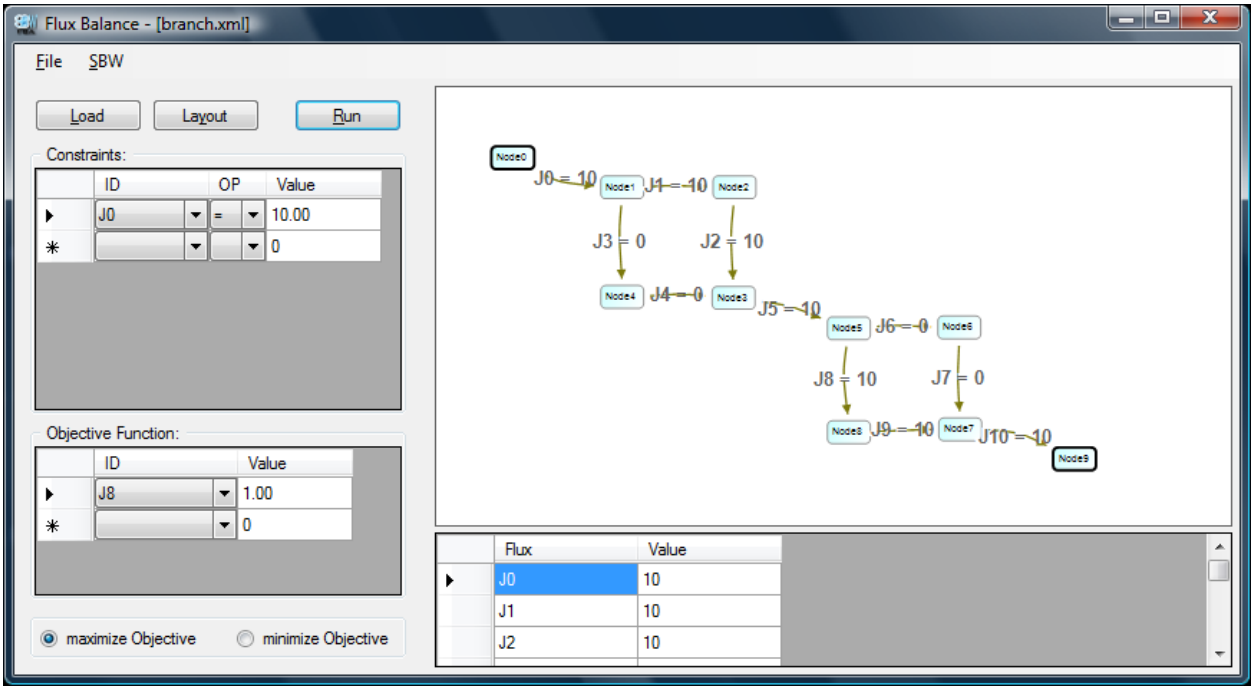

Figure 1: A screenshot of the FBA Module, analyzing the example of the next chapter.

PySCeS FBA

The PySCeS FBA module is being developed to investigate microbial ecosystems using a constraint based approach (FBA). Currently, this involves the reading and translation of existing genome scale models into a form that can be used for multi-state FBA analysis. Multistate experiments are typically output as linear programs in CPLEX and polynomial H-formats. In future more standard FBA analysis will be made available.

Command line Converter

Finally, there is a command line tool that converts models in the COBRA SBML dialect into SBML with the Flux Balance Annotation. As a proof of concept, we are in the process of converting the existing BiGG database (http://bigg.ucsd.edu/), which uses the COBRA dialect, into the proposed Level 2 annotation implementation of the FBA package.

Examples

Even though this extension is meant to be used in SBML Level 3, for the time being we have implemented support for it as SBML Level 2 annotation, which is demonstrated below.

```
<?xml version="1.0" encoding="utf-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2" level="2" version="1" >
        <model id="BranchMultipleCycle" name="BranchMultipleCycle">
                <annotation>
                        <fba:fluxBalance xmlns:fba="http://www.sbml.org/sbml/level3/version1/fba/version1">
                                <fba:listOfConstraints>
                                        <fba:constraint fba:reaction="J0" fba:operation="equal"
                                        fba:value="10" />
                                </fba:listOfConstraints>
                                <fba:listOfObjectives fba:activeObjective="obj1">
                                        <fba:objective id="obj1" fba:type="maximize">
                                                <fba:listOfFluxes>
                                                        <fba:fluxObjective fba:reaction="J8"
                                                        fba:coefficient="1" />
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                                        </fba:objective>
                                </fba:listOfObjectives>
                        </fba:fluxBalance>
                </annotation>
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                                <listOfProducts>
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                        </reaction>
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```

```
                                        <speciesReference species="Node1" stoichiometry="1" />
                                </listOfReactants>
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                                        <speciesReference species="Node4" stoichiometry="1" />
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```