

# Standards at Genome Scale the SBML3 FBC package

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**and lots of other people ...**

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Netherlands Organisation for Scientific Research





# Metabolism to model

1. A genome scale reconstruction



2. Mathematically represent metabolic reactions and constraints



3. At steady state this defines a system of linear equations

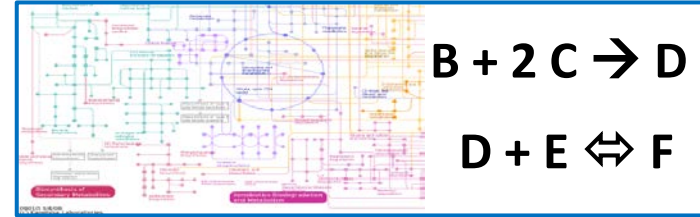


4. Define an objective function

Maximize Biomass (Z)



5. Calculate fluxes that maximize (4)



	Reactions				Biomass	Glucose	Oxygen	
	1	2	...	n				
A	-1							$\begin{matrix} v_1 \\ v_2 \\ \vdots \\ v_n \\ v_{\text{biomass}} \\ v_{\text{glucose}} \\ v_{\text{oxygen}} \end{matrix} = 0$
B	1	-1						
C	1	-2						
D		1						
...								
m					-1	-1		

Stoichiometric matrix, **S**

Fluxes, **v**

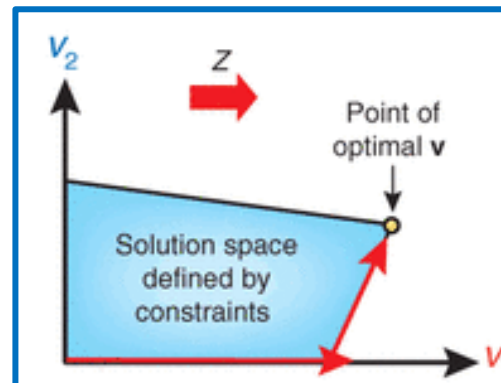
$$\begin{aligned} -v_1 + \dots &= 0 \\ v_1 - v_2 + \dots &= 0 \\ v_1 - 2v_2 + \dots &= 0 \\ v_2 + \dots &= 0 \\ \text{etc.} \end{aligned}$$

Flux Balance  
Analysis (FBA)

Maximize  
Biomass

Such that  
 $NJ = 0$

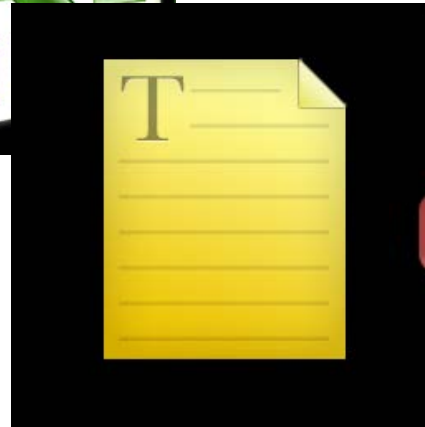
Where

$$\begin{aligned} 0 &\leq J_{\text{irrev}} \leq \text{inf} \\ -\text{inf} &\leq J_{\text{rev}} \leq \text{inf} \\ \text{l.b} &\leq J_{\text{bio}} \leq \text{u.b} \\ C &\leq J_{\text{input}} \end{aligned}$$


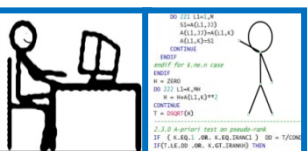
# FBA/GSR models ca. 2009

**“every work of software starts by  
scratching a developer’s itch”**

Eric Raymond (The cathedral and the bazaar)



**COBRA SBML Level 2: a tool specific dialect!**



```

<?xml version="1.0"
  <model xmlns="http://www.sbml.org/sbml/2.0"
    <name>A simple model</name>
    <species>
      <species name="S1" initialAmount="100"
        <compartment>C1</compartment>
      </species>
    </species>
    <reaction>
      <reaction name="R1" reversible="true"
        <math>S1 \rightarrow S2</math>
      </reaction>
    </reaction>
  </model>
  
```

# SBML Level 3 FBC

- Proposed in 2009, Version 1 specification accepted March 2013
- Community driven development process, both SBML and FBA
- Included in official libSBML 5.8.0+ release ([sbml.org/downloads](http://sbml.org/downloads))

SBML Level 3 Package Specification

**SBML Level 3 Package: Flux Balance Constraints  
(‘fbc’)**

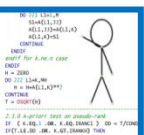
Brett G. Olivier <a href="mailto:b.g.olivier@vu.nl">b.g.olivier@vu.nl</a> Systems Bioinformatics VU University Amsterdam Amsterdam, NH, The Netherlands	Frank T. Bergmann <a href="mailto:fbergmann@caltech.edu">fbergmann@caltech.edu</a> Computing and Mathematical Sciences California Institute of Technology Pasadena, CA, US
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Version 1, Release 1

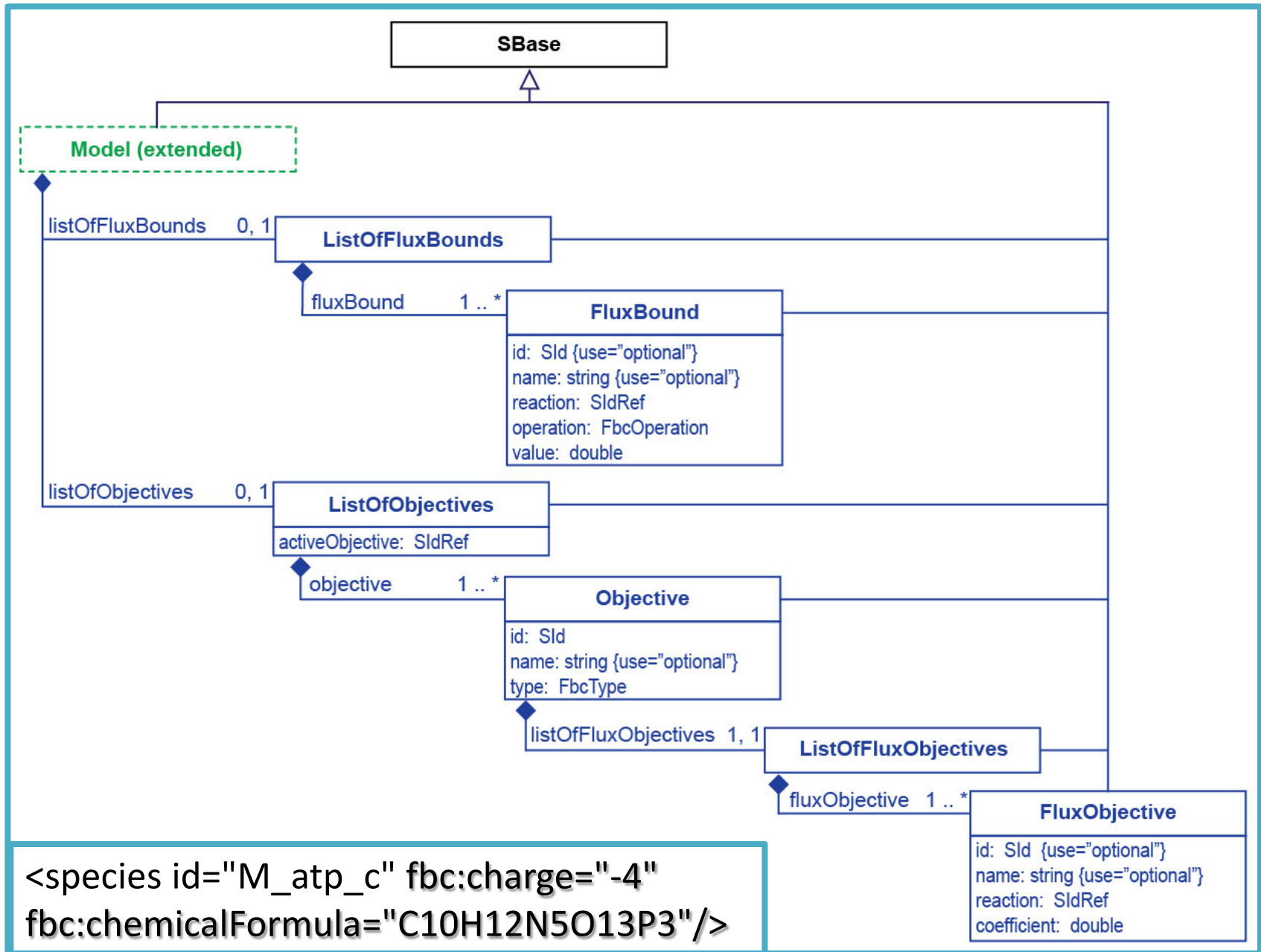
February 11, 2013

Available from CO.MBINE.org

<http://identifiers.org/combine.specifications/sbml.level-3.version-1.fbc.version-1.release-1>



# FBC in a nutshell



# Flux Bounds

The upper and lower values a flux can obtain is expressed as one or more FluxBounds:

$$10 \leq R\_ATPX \leq 20.3$$

```
<fluxBound id="ub1" reaction="R_ATPX"  
  operation="greaterEqual" value="10"/>
```

```
<fluxBound id="lb1" reaction="R_ATPX"  
  operation="lessEqual" value="20.3"/>
```

# Objective Function

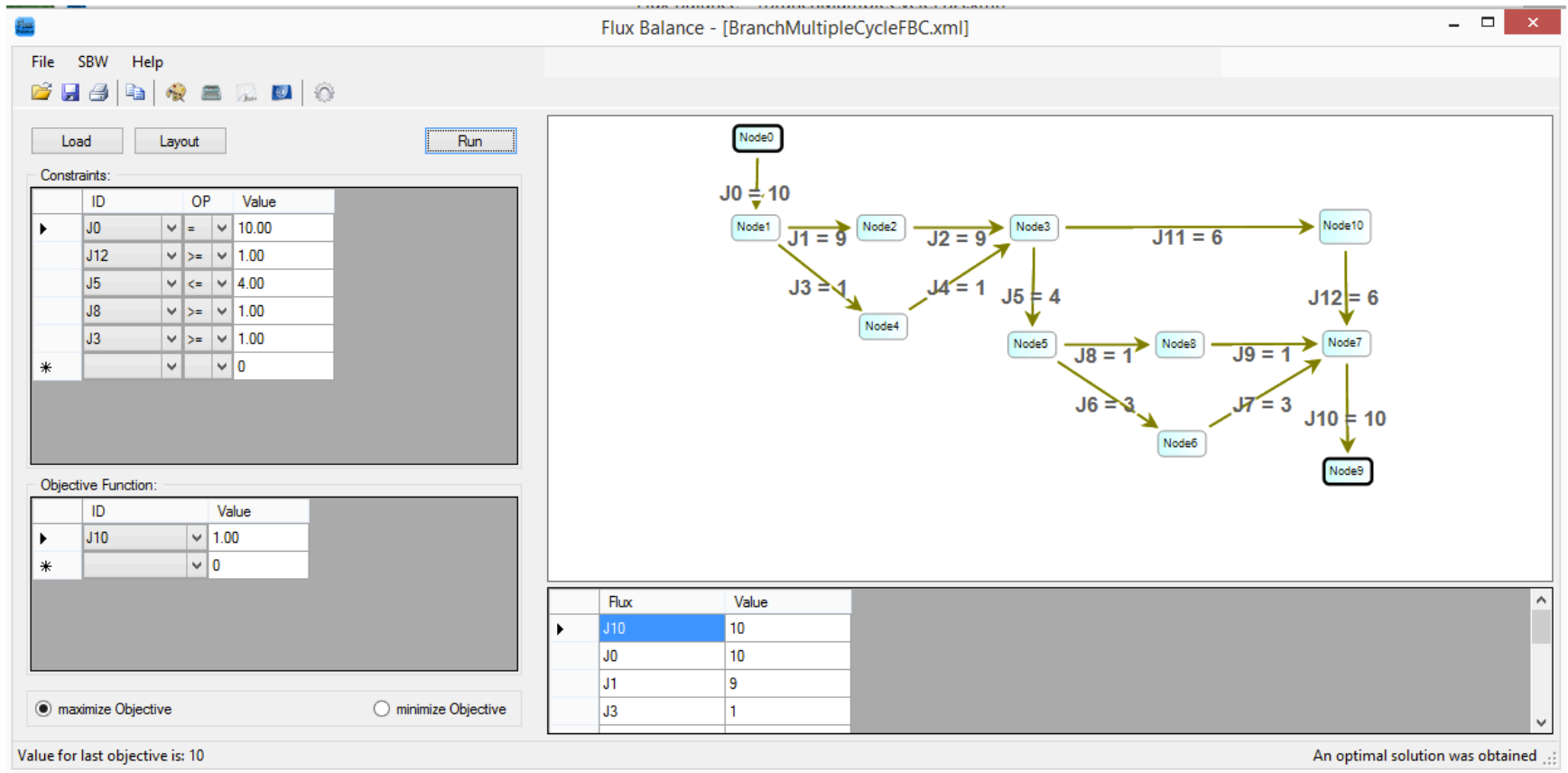
Multiple objective functions may be defined, each containing multiple fluxes:

Maximize: 2 RGLy

```
<listOfObjectives activeObjective="obj1">  
<objective id="obj1" type="maximize">  
<listOfFluxObjectives>  
<fluxObjective reaction="RGLy" coefficient="2"/>  
</listOfFluxObjectives>  
</objective>  
<objective id="obj2" type="minimize">  
...  
</objective>  
</listOfObjectives>
```

# Flux Balance Tool

Teaching Tool: explore fluxes along a network, define flux bounds, run fba.



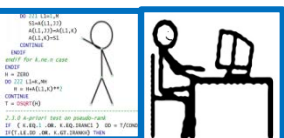


# CBMPy

## Constraint Based Modelling in Python

- Flexible: FBA, FVA, cFBA, dFBA, MEMESA, media design, ...
- **Object-oriented** data structures, reactions, metabolites, genes
- Implements **community standards** e.g. SBML/MIRIAM
- **Multiple user interfaces**: CLI, GUI's, web services
- **Extendible**: high level functionality with low level access
- **Open source** and free to use

<http://cbmpy.sourceforge.net>





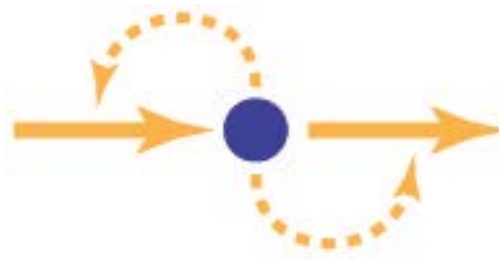
# FAME

The Flux Analysis and Modeling Environment

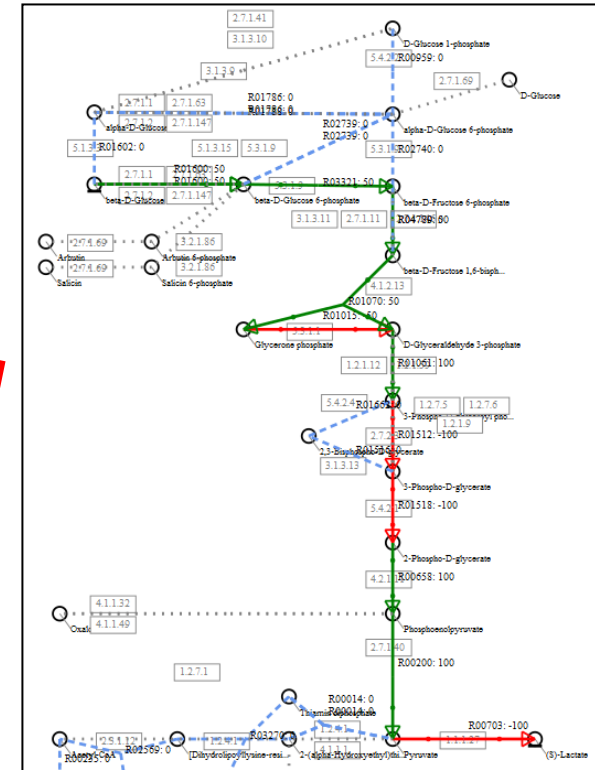
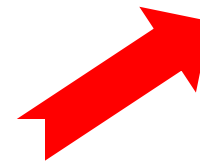
<http://f-a-m-e.org/>



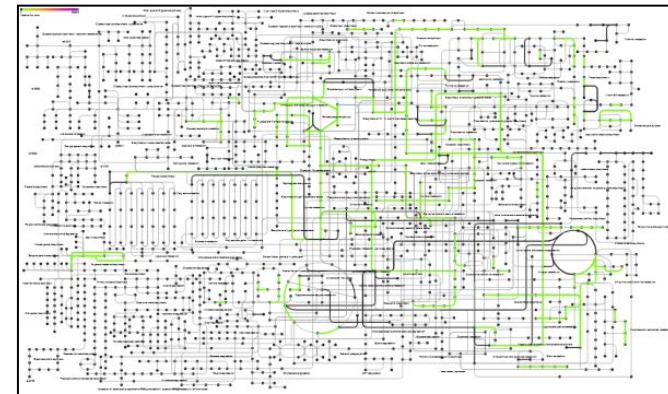
FAME forwards model  
to CBMPy for solving



CBMPy solves  
model; returns  
results to FAME



Visualization on KEGG  
maps or user-supplied SVG



## Software

**FAME, the Flux Analysis and Modeling Environment**

Joost Boele<sup>1,2</sup>, Brett G Olivier<sup>1,2,3</sup> and Bas Teusink<sup>1,2\*</sup>

BMC Systems Biology 2012, 6:8 doi:10.1186/1752-0509-6-8

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Highly accessed

Open Access



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- Everyone involved in discussions ...