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# Flux annotations in SBML

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# Introduction

- Constraint-based methods are quite popular for analysis of biochemical systems
- Flux Balance Analysis (FBA) models need to be stored in SBML
- Currently not much direct support... workarounds are in use
- BIOMODELS.NET has flux models, but they **have not been curated**

# Critical points

- FBA is an *operation* performed on a model, essentially specified by the objective function, unlike a kinetic model *definition*
  - Flux bounds may be biochemical constraints on the model (or based on the simulation)
- ***Fundamental question:*** should SBML also allow
  - exchange of simulation results (flux values), esp. for FBA?
  - Specification of a model *instance*, in terms of a particular objective function

# Current annotations – Models

[http://sbml.org/wiki/Known\\_SBML\\_annotations](http://sbml.org/wiki/Known_SBML_annotations)

```
<annotation xmlns:flux="http://arep.med.harvard.edu/fluxns">
  <flux:listOfAnalysisTypes>
    <flux:analysisType id="fba" name="Flux Balance Analysis"/>
    <flux:analysisType id="moma" name="Minimization of Metabolic
Adjustment"/>
    <flux:analysisType id="room" name="Regulatory On/Off mechanism"/>
  </flux:listOfAnalysisTypes>
  <flux:listOfAnalyses>
    <flux:analysis id="wild_type" name="Wild-Type FBA" analysisType="fba"/>
    <flux:analysis id="mutant_fba" name="Mutant FBA" analysisType="fba"/>
    <flux:analysis id="mutant_moma" name="Mutant MOMA"
analysisType="moma"/>
  </flux:listOfAnalyses>
</annotation>
```

- This annotation includes information about what kinds of analysis will be performed with the model which is **strictly outside** the scope of SBML

# Current annotations – Reactions

[http://sbml.org/wiki/Known\\_SBML\\_annotations](http://sbml.org/wiki/Known_SBML_annotations)

```
<annotation xmlns:flux="http://arep.med.harvard.edu/fluxns">
  <flux:limit analysis="wild_type" upper="INF" lower="-INF" objective="0"
prediction="10"/>
  <flux:limit analysis="mutant_fba" upper="INF" lower="-INF" objective="0"
prediction="0"/>
  <flux:limit analysis="mutant_moma" upper="INF" lower="-INF" objective="10"
prediction="6.7"/>
</annotation>
```

- This information includes objective and prediction, which are simulation parameters and simulation results, which are, strictly speaking, **outside the scope of SBML**

# Workarounds – Palsson's models

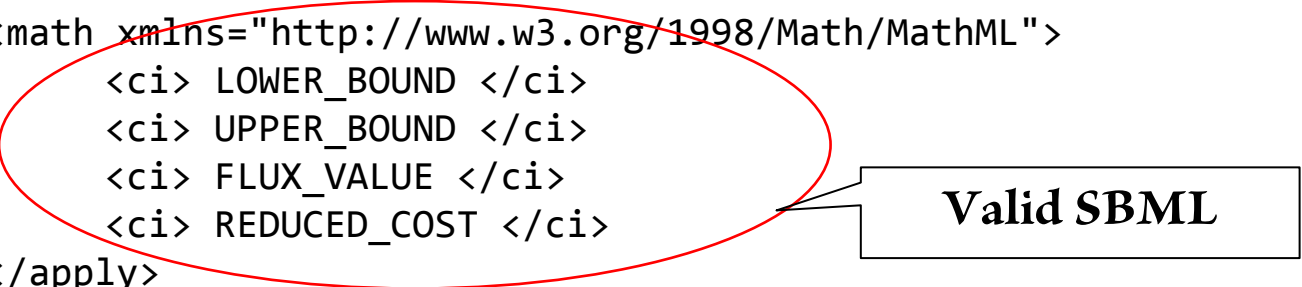
```
<kineticLaw>
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <ci> LOWER_BOUND </ci>
      <ci> UPPER_BOUND </ci>
      <ci> FLUX_VALUE </ci>
      <ci> REDUCED_COST </ci>
    </apply>
  </math>
  <listOfParameters>
    <parameter id="LOWER_BOUND" value="-999999.000000"
units="mmol_per_gDW_per_hr"/>
    <parameter id="UPPER_BOUND" value="999999.000000"
units="mmol_per_gDW_per_hr"/>
    <parameter id="FLUX_VALUE" value="0.000000"
units="mmol_per_gDW_per_hr"/>
    <parameter id="REDUCED_COST" value="0.000000"/>
  </listOfParameters>
</kineticLaw>
```

**Invalid SBML; also,  
FLUX\_VALUE is a  
simulation result**

- FLUX\_VALUE can also be viewed as a property of the steady state model, but it is dependent on the objective function...

# Workarounds

```
<kineticLaw>
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <ci> LOWER_BOUND </ci>
    <ci> UPPER_BOUND </ci>
    <ci> FLUX_VALUE </ci>
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  <parameter id="LOWER_BOUND" value="-999999.000000"
units="mmol_per_gDW_per_hr"/>
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units="mmol_per_gDW_per_hr"/>
  <parameter id="FLUX_VALUE" value="0.000000"
units="mmol_per_gDW_per_hr"/>
  <parameter id="REDUCED_COST" value="0.000000"/>
</listOfParameters>
</kineticLaw>
```



Valid SBML

- But should these really be a part of the **kineticLaw**?!

# Pointers for Discussion

- Standard for representation of flux models in SBML (l3?)?
  - Alternative Reactions (l3)?
  - Test suite for FBA/MoMA analyses?
  - Software for FBA/MoMA
    - FluxAnalyzer/CellAnalyzer
    - Fluxor?
    - PathwayAnalyser?
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