



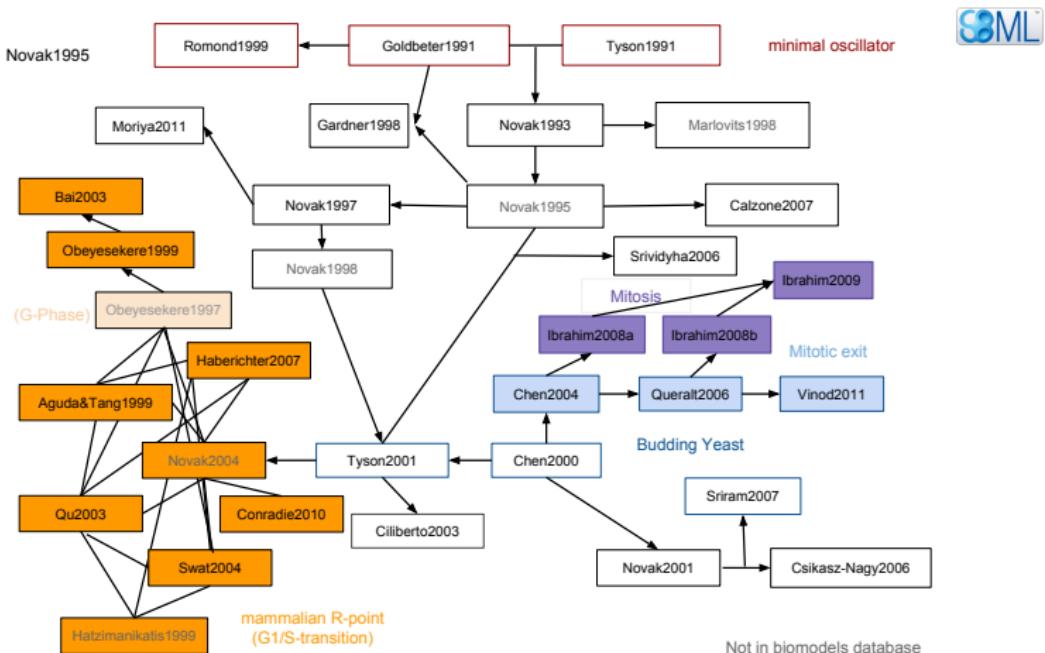
Characterising differences between model versions

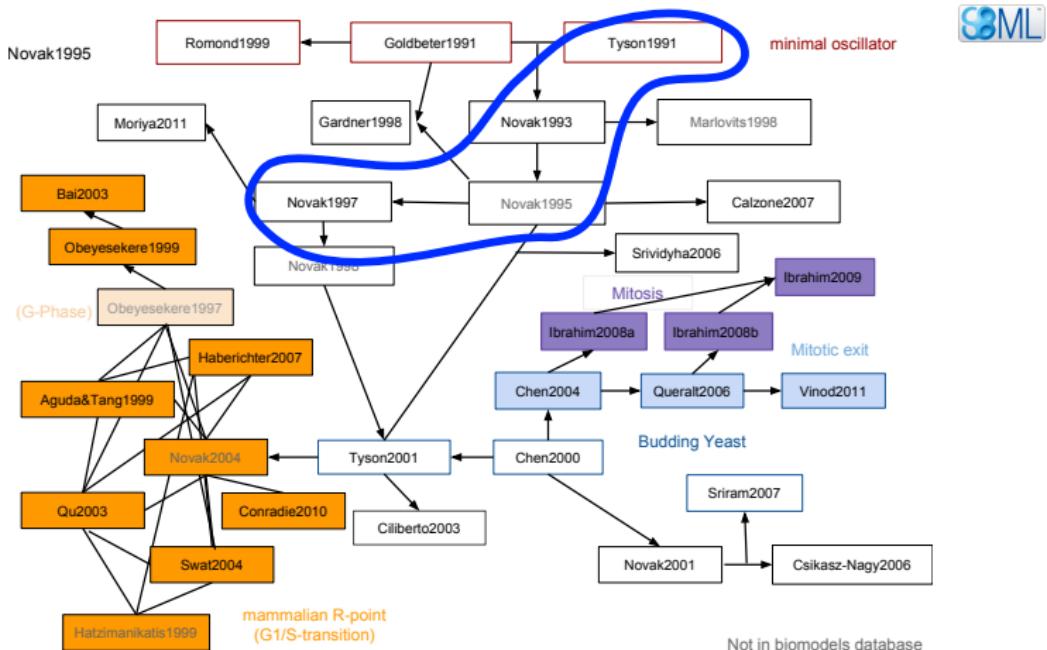
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<http://sems.uni-rostock.de>



e:Bio Status Seminar 2015
University of Duisburg-Essen

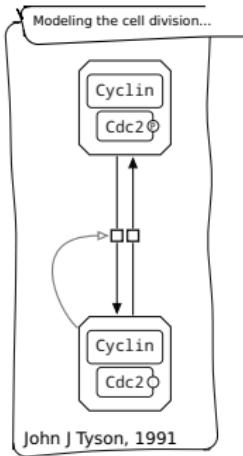


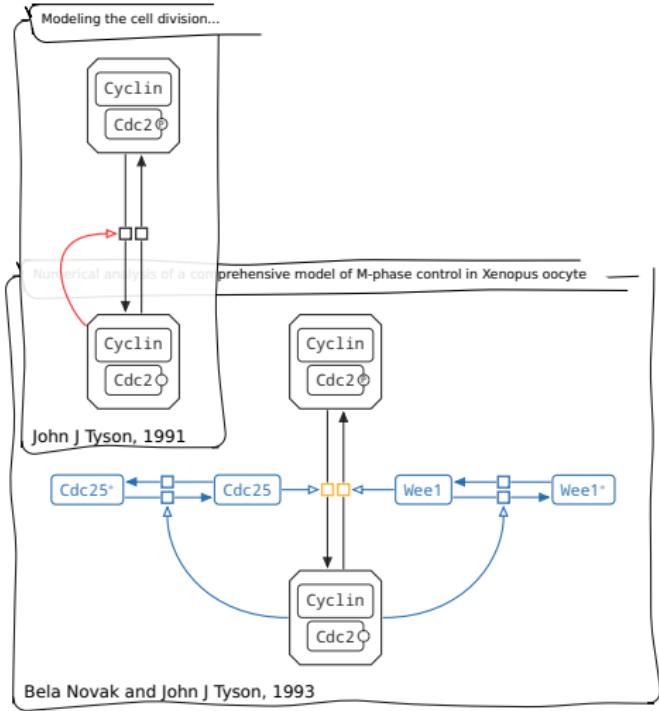


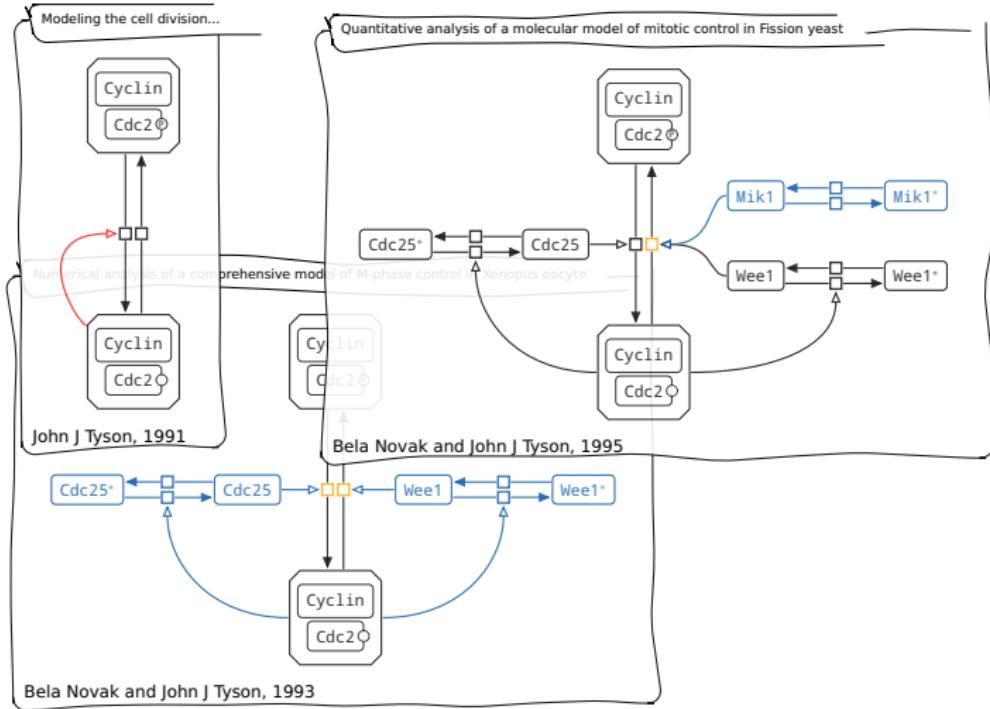


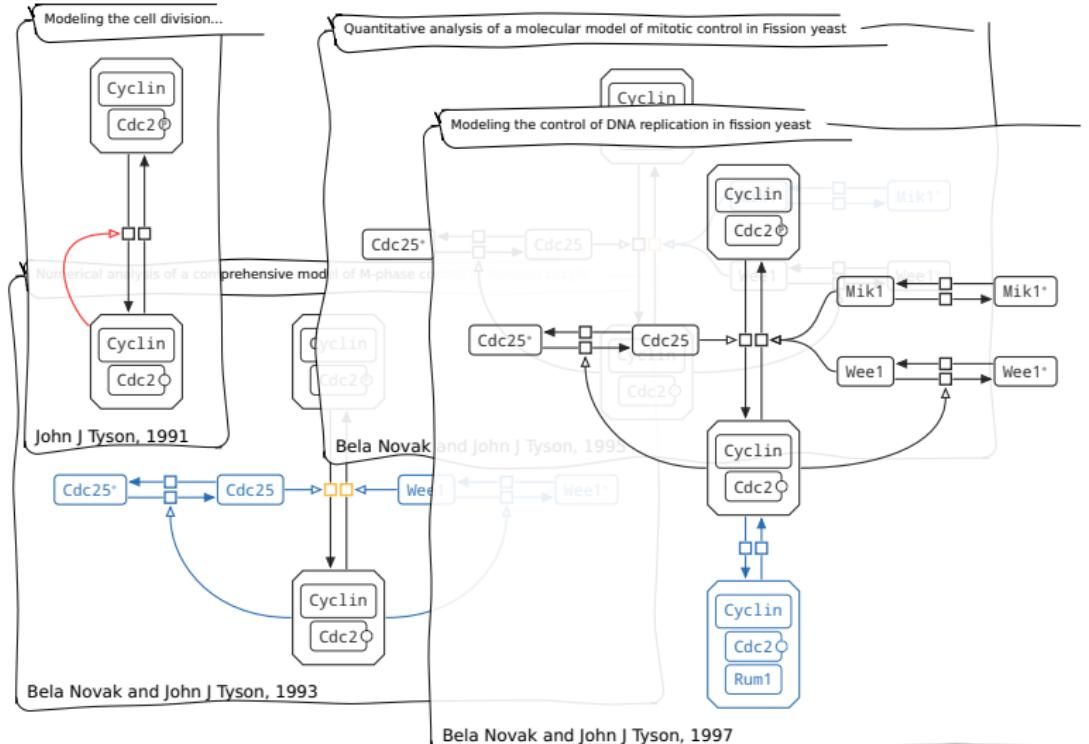
Model Evolution

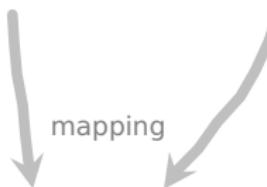
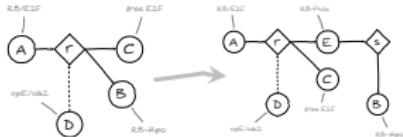
Example: Cell Cycle





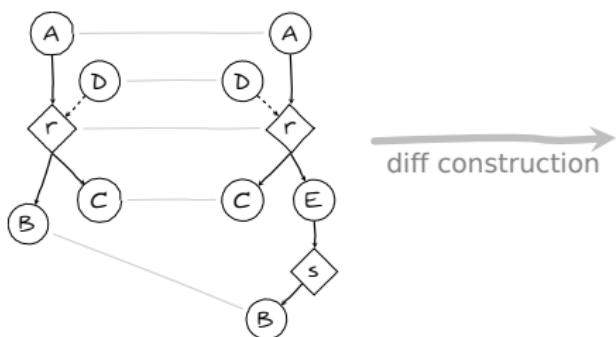




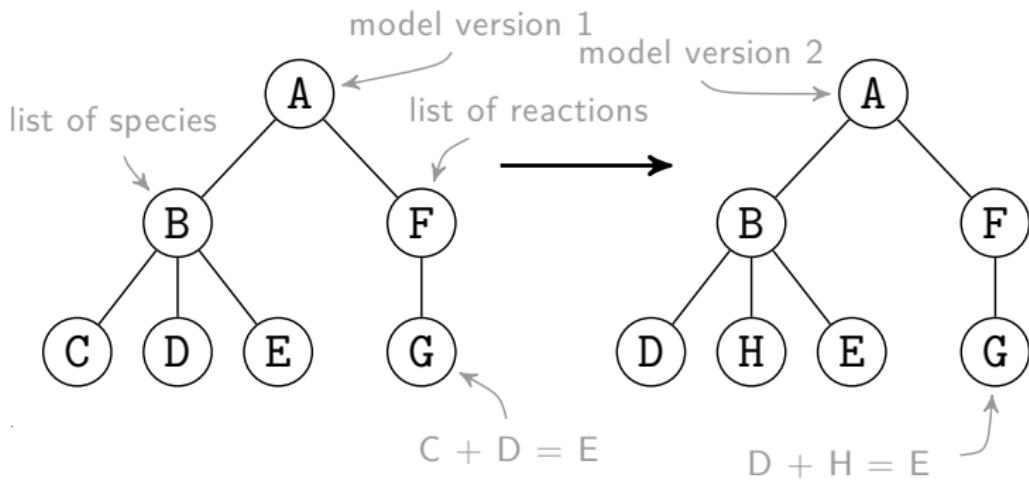


Biochemical Model Version Control System

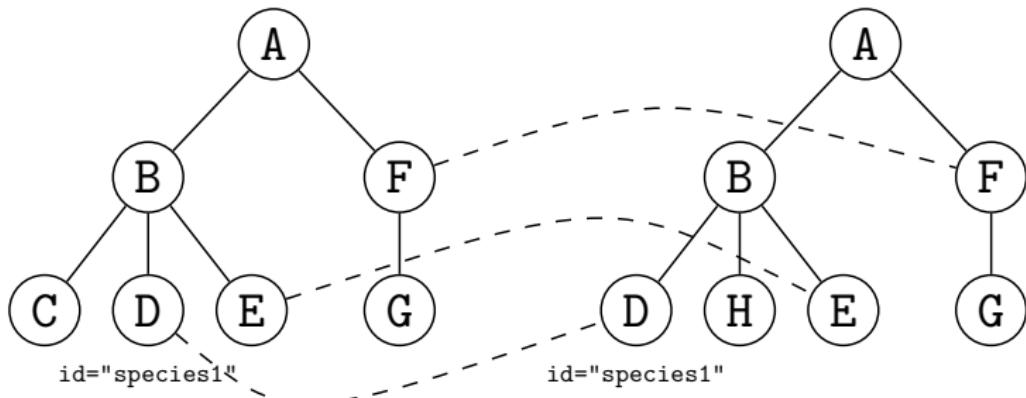
- compares models encoded in standardised formats (currently: SBML and CellML)
- maps hierarchically structured content
- evaluates and communicates the differences



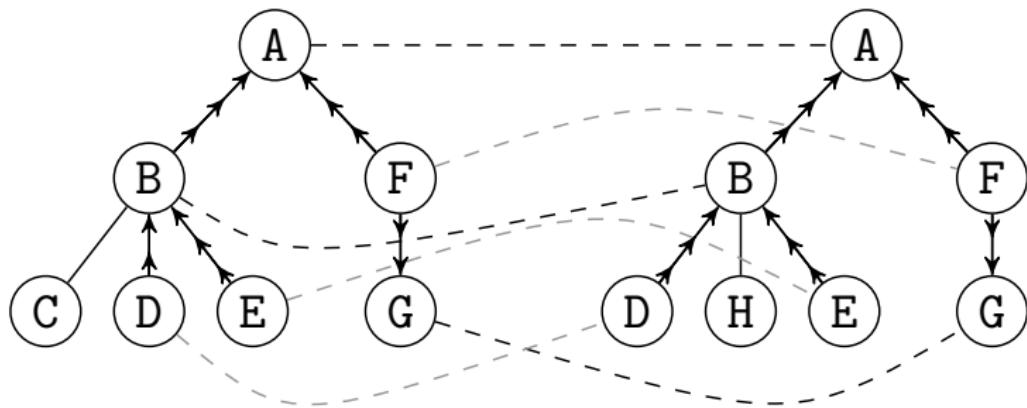
```
<XML>
  Diff
    moves
      product of r: C
    deletes
      product of r: B
    inserts
      species: E
      product of r: E
    reaction s
</XML>
```



take two versions of a computational model



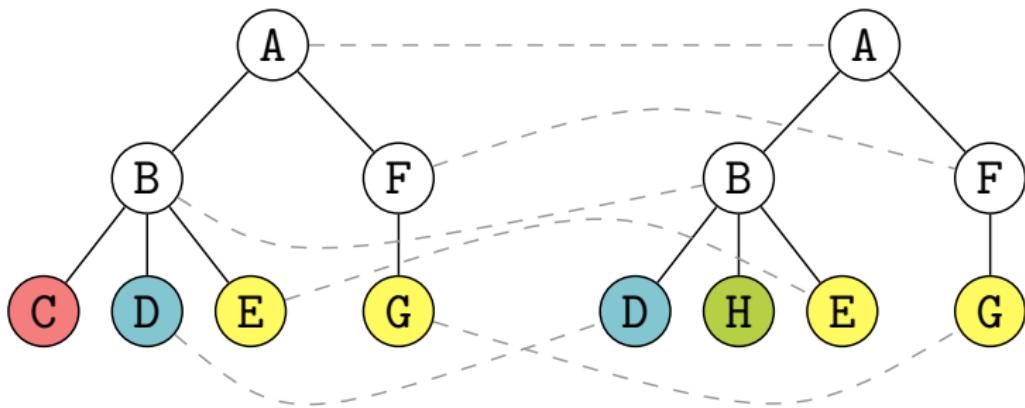
connect entities which are *for sure* the same



propagate this initial mapping into the rest of the tree



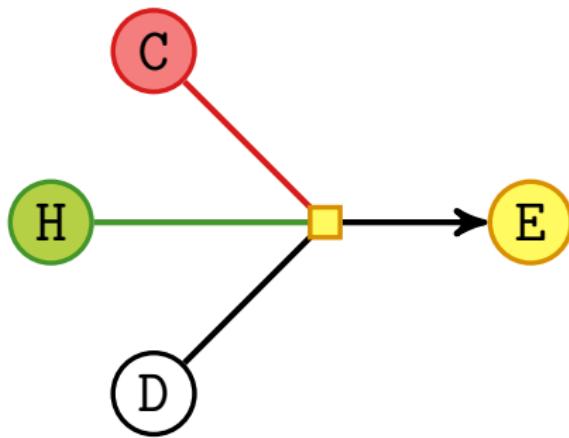
BiVeS identifies differences
in versions of computational models



evaluate the mapping and identify *inserts*, *deletes*, *updates*, and *moves*



BiVeS identifies differences
in versions of computational models



communicate the differences to the user

BiVeS identifies differences in versions of computational models

Reactions

R19 (wee1 deactivation)

- $\text{wee1} \rightarrow \text{wee1_p}$
- Modifiers: dimer_p[unknown];

R17 (cdc25 activation)

- $\text{cdc25} \rightarrow \text{cdc25_p}$
- Modifiers: dimer_p[unknown];

R18 (cdc25 deactivation)

- $\text{cdc25_p} \rightarrow \text{cdc25}$

R13 (Tyr15 dephosphorylation)

- $\text{p_dimer_p} \rightarrow \text{dimer_p}$
- Modifiers: cdc25[unknown]

R12 (Tyr15 phosphorylation)

- $\text{dimer_p} \rightarrow \text{p_dimer_p}$
- Modifiers: wee1[unknown]

R24 (ubiquitin conjugating enzyme deactivation)

- $\text{UbE_star} \rightarrow \text{UbE}$

R23 (ubiquitin conjugating enzyme activation)

- $\text{UbE} \rightarrow \text{UbE_star}$
- Modifiers: IE_p[unknown];

R22 (intermediary enzyme deactivation)

- $\text{IE_p} \rightarrow \text{IE}$

R21 (intermediary enzyme activation)

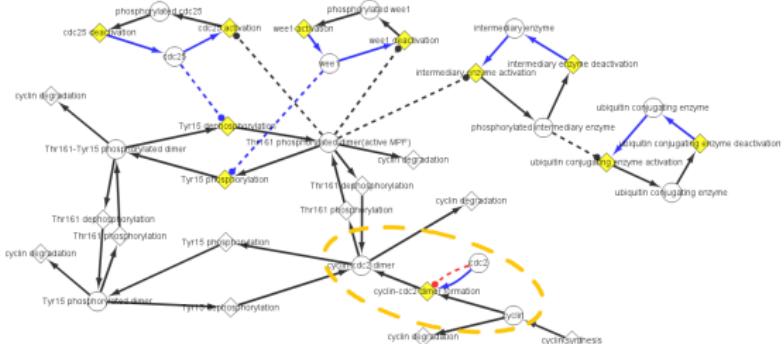
- $\text{IE} \rightarrow \text{IE_p}$
- Modifiers: dimer_p[unknown];

R20 (wee1 activation)

- $\text{wee1_p} \rightarrow \text{wee1}$

R3 (cyclin-cdc2 dimer formation)

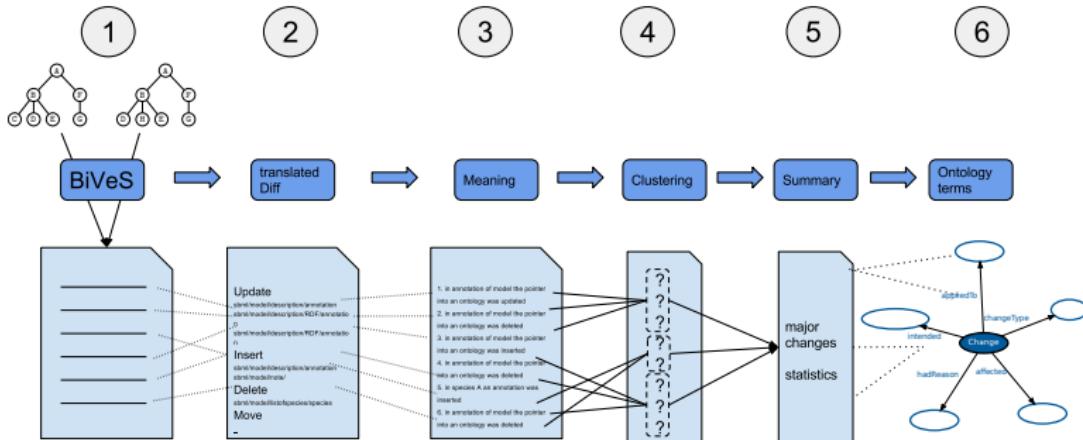
- $\text{cyclin} + \text{cdc2} \rightarrow \text{dimer}$
- Modifiers: cdc2[unknown]



```

<?xml version="1.0" encoding="UTF-8" standalone="no"?>
<bives type="fullDiff">
  <update>
    <delete>
      [...]
      <node id="6" oldChildNo="1">
        oldParent"..../listOfModifiers[1]"
        oldPath.."../listOfModifiers[1]/modifierSpeciesReference[1]"
        oldTag="modifierSpeciesReference" triggeredBy="5"/>
        <attribute id="7" name="species">
          oldPath.."../modifierSpeciesReference[1]"
          oldValue="cdc2" triggeredBy="6"/>
      </delete>
      <insert>
        [...]
        <node id="12" newChildNo="2">
          newParent"..../listOfReactants[1]"
          newPath.."../listOfReactants[1]/speciesReference[2]"
          newTag="speciesReference"/>
          <attribute id="13" name="species">
            newPath.."../speciesReference[2]"
            newValue="cdc2" triggeredBy="12"/>
          <attribute id="14" name="metid" newValue=".B18337" triggeredBy="12"/>
        </insert>
        [...]
    
```

What do these changes look like?



analysis of more than 150 diffs

study of
modifications

derivation of
a vocabulary



What do these changes look like?

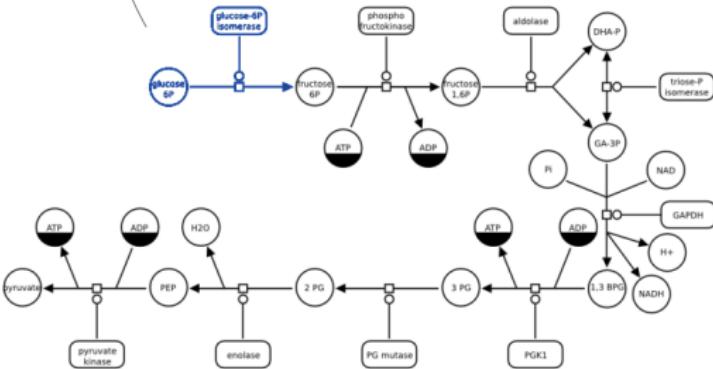
insertion

```
<species name="Glucose-6-Phosphate" initialConcentration="0.6" />
```

Type: new node

Intention: probably an extension of the model

Affects: the reaction network





insertion

```
<species name="Gulcose-6-Phosphate" initialConcentration="0.6" />
```

update

```
<parameter name="ka" value="0.3" />  
<parameter name="ka" value="0.1" />
```

Type: updated attribute

Affects: the mathematical model

$$\frac{dcdc25}{dt} = \frac{ka \times dimer_p \times (total_cdc25 - cdcs5_p)}{K_a + total_cdc25 - cdcs5_p}$$

Intention: correction

Reason: mismatch with publication



What do these changes look like?

insertion

```
<species name="Gulcose-6-Phosphate" initialConcentration="0.6" />
```

update

```
<parameter name="ka" value="0.3" />  
<parameter name="ka" value="0.1" />
```

```
<species name="Gulcose-6-Phosphate" initialConcentration="0.6" />  
<species name="Glucose-6-Phosphate" initialConcentration="0.6" />
```

Type: updated attribute



Reason: typo



What do these changes look like?

insertion

```
<species name="Gulcose-6-Phosphate" initialConcentration="0.6" />
```

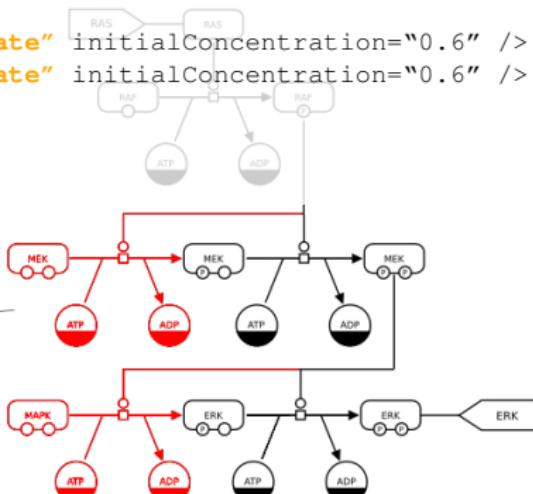
update

```
<parameter name="ka" value="0.3" />
<parameter name="ka" value="0.1" />
```

```
<species name="Gulcose-6-Phosphate" initialConcentration="0.6" />
<species name="Glucose-6-Phosphate" initialConcentration="0.6" />
```

deletion

```
<reaction id="r23">
  ...
</reaction>
```



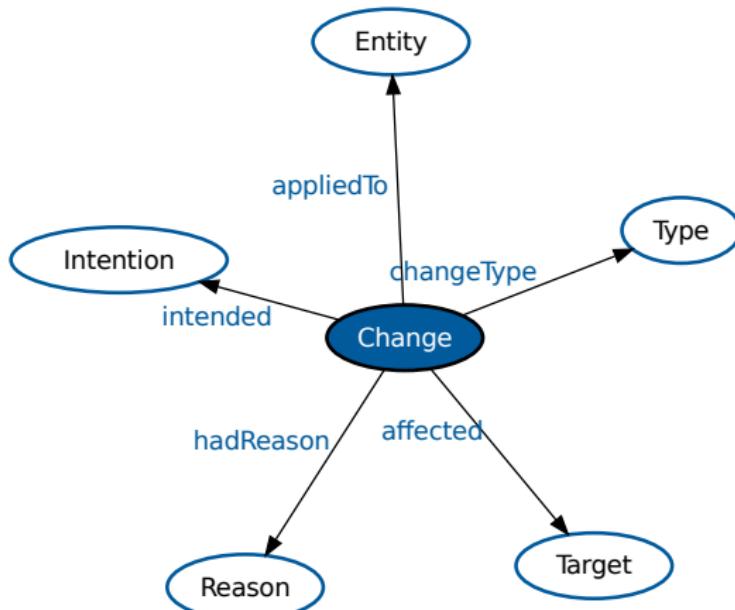
Type: deletion of node and attributes

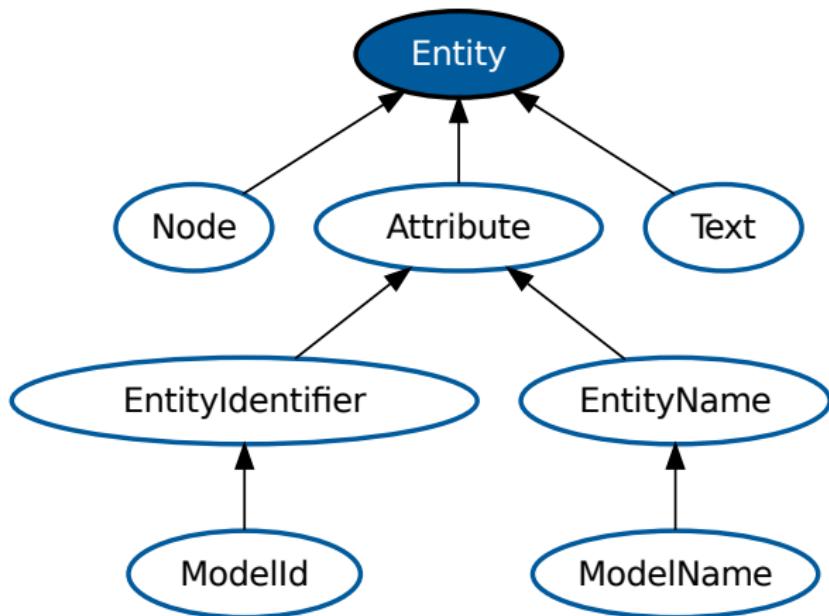
Affects: reaction network and mathematical model

Intention: simplification



We're building an ontology, because **CO**mputational **MO**dels **DI**ffer.

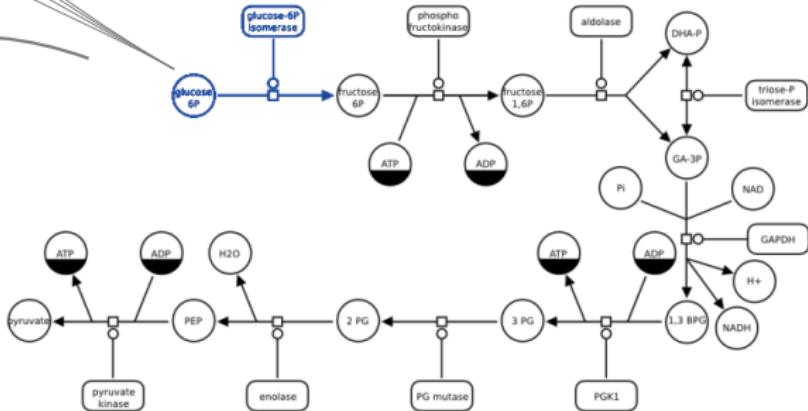
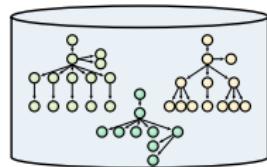






What do these changes look like?

is_a comodi:Change
 comodi:changeType comodi:Insertion
 comodi:affected comodi:ReactionNetwork
 comodi:intended comodi:Extension



Masymos



- How did my collaborator change our model?
- Did someone update the model that I retrieved from the database?
- Weird behaviour since the last update..!? Show me all versions that changed the kinetics of reaction $r23$.
- Who changed reaction $r23$? When and why did they do that!?



Thank you for your attention!

SEMS group

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Fabienne Lambusch
Olaf Wolkenhauer



@SemsProject

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