

# Towards model version control

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# Versions of models

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JOURNAL ARTICLES

**Numerical analysis of a comprehensive model of M-phase control in *Xenopus* oocyte extracts and intact embryos**

B. Novak and J.J. Tyson

Author Affiliations

**Summary**

To contribute to a deeper understanding of M-phase control in eukaryotic cells, we have constructed a model based on the biochemical properties of M-phase promoting factor (MPF) in *Xenopus* oocyte extracts, where there is evidence for two positive feedback loops (MPF

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December 1, 1993 J Cell Sci 106, 1153-1168

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## Modeling the control of DNA replication in fission yeast

Bela Novak\* and John J. Tyson†

Author Affiliations

Edited by Paul Nurse, Imperial Cancer Research Fund, London, United Kingdom, and approved May 21, 1997 (received for review December 31, 1996)

A central event in the eukaryotic cell cycle is the decision to commence DNA replication (S phase). Strict controls normally operate to prevent repeated rounds of DNA replication without intervening mitoses ("endoreplication") or initiation of mitosis before DNA is fully replicated ("mitotic catastrophe"). Some of the genetic interactions involved in these controls have recently been identified in yeast. From this evidence we propose a molecular mechanism of "Start" control in *Schizosaccharomyces pombe*. Using established principles of biochemical kinetics, we compare the properties of this model in detail with the observed behavior of various mutant strains of fission yeast: *wee1<sup>-</sup>* (size control at Start), *cdc13Δ* and *rum1<sup>OP</sup>* (endoreplication), and *wee1<sup>-</sup> rum1Δ* (rapid division cycles of diminishing cell size). We discuss essential features of the mechanism that are responsible for characteristic properties of Start control in fission yeast, to expose our proposal to crucial experimental tests.

Proceedings of the National Academy of Sciences of the United States of America

PNAS

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PNAS August 19, 1997 vol. 94 no. 17 9147-9152

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1993

1997

Novak, Tyson, 1993

Numerical analysis of a comprehensive model of M-phase control in *Xenopus* oocyte extracts and intact embryos: parameter values have been taken from the original published paper to reproduce figure 4A.

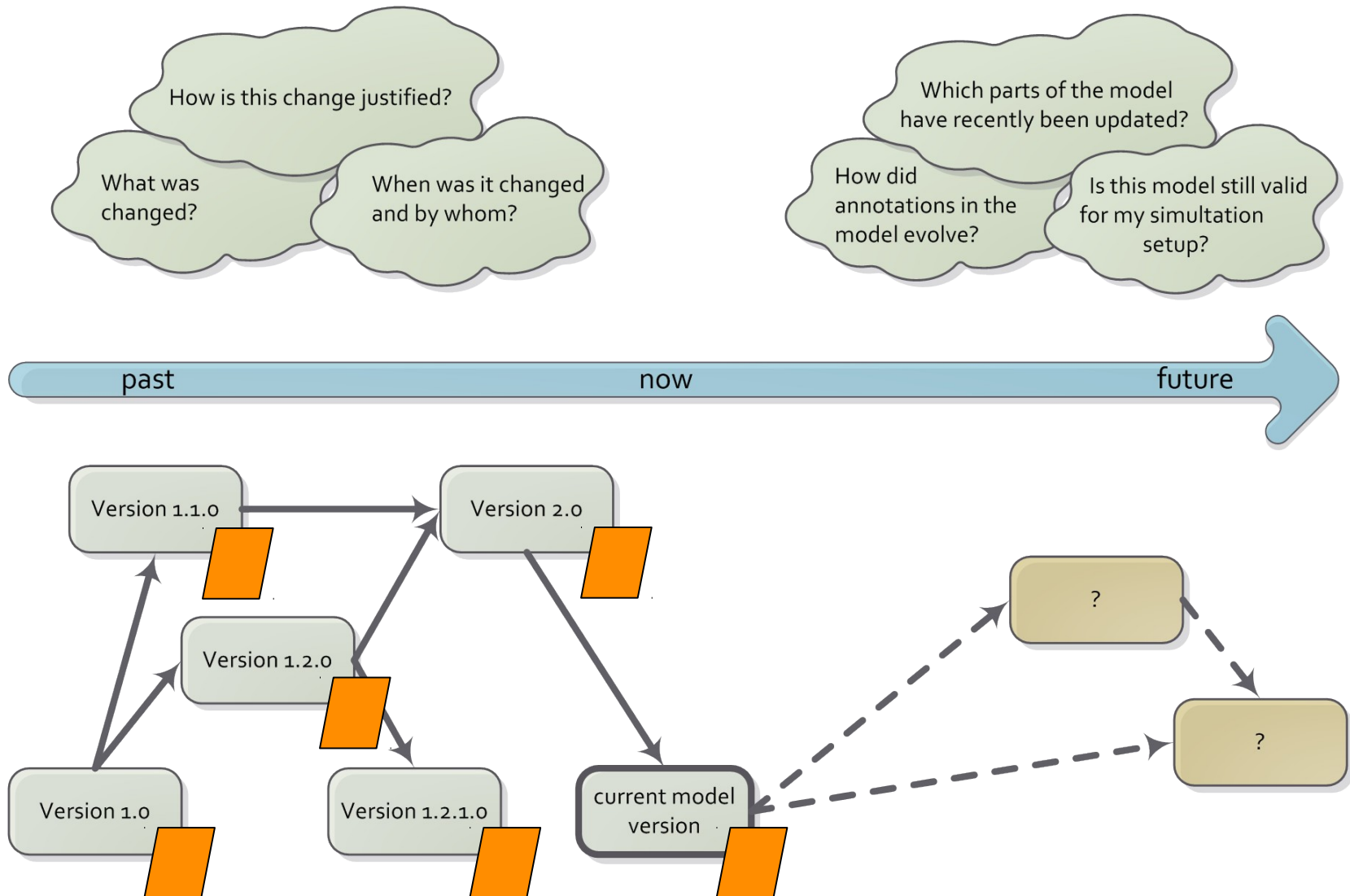
Novak, Tyson, 1993

Numerical analysis of a comprehensive model of M-phase control in *Xenopus* oocyte extracts and intact embryos: parameter values have been taken from the SBML model in the BioModels Database and the model simulates the synthesis and degradation of cyclin.

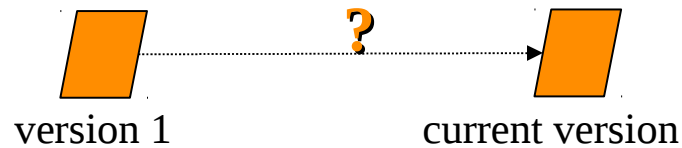
PMR2

BMDB

# Evolution of a model over time



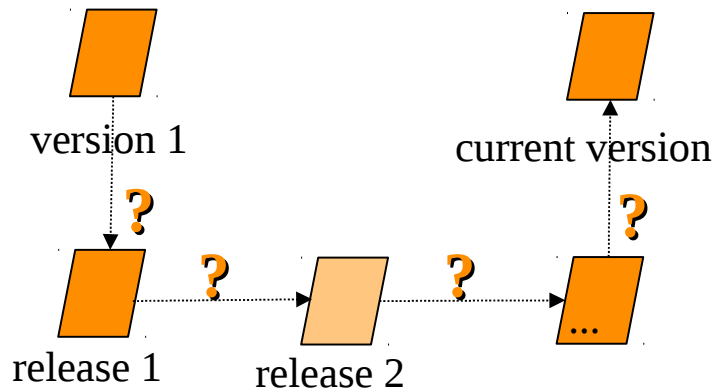
Waltemath et al., 2012 (submitted)



|  |          |  |                   |         |  |
|--|----------|--|-------------------|---------|--|
| Download SBML  |          | Other formats (auto-generated)   |                   | Actions |  |
| Model  | Overview | Math   | Physical entities | Para    |  |
| <p>Novak B, Tyson JJ<br/>                     Numerical analysis of a comprehensive model of M-phase control in Xenopus<br/>                     J Cell Sci 1993 Dec;106 ( Pt 4): 1153-68<br/>                     Department of Biology, Virginia Polytechnic Institute and State University, E</p> |          |  |                   |         |  |
| Publication ID: <a href="#">312697</a>   |          |  |                   |         |  |
| Original Model: <a href="#">BIC4G0000000107.xml.org</a>  |          | bioModel homologTo: <a href="#">Reactions: PEACT_152</a>                                     |                   |         |  |
| Submitter: <a href="#">Harish Chatur</a>   |          | set #: <a href="#">bioModel versionOf: <a href="#">Gene Ontology: mitotic cell cycle</a></a> |                   |         |  |
| Submission ID: MODEL5876465734   |          | bioModel occursIn: <a href="#">Taxonomy: Archaea</a>   |                   |         |  |
| Submission Date: 09 Apr 2007 19:29:15 UTC  |          |  |                   |         |  |
| Last Modification Date: 05 Jul 2012 14:43:50 UTC   |          |  |                   |         |  |
| Creation Date: 05 Apr 2007 08:42:03 UTC  |          |  |                   |         |  |
| Encoders: <a href="#">Nicolas Le Novre</a><br><a href="#">Harish Chatur</a>  |          |  |                   |         |  |

Directly accessible from the repository:

- Original model file (any format)
- Current model file
- Date of creation and last modification



Implicitly accessible:

- Model file(s) at each BioModels Database release

|  |                        |
|--|------------------------|
| Index of <a href="http://ftp.ebi.ac.uk/pub/databases/bi">http://ftp.ebi.ac.uk/pub/databases/bi</a> |                        |
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| 2006-06-05   | 02/08/2012 05:27:00 PM |
| 2006-10-03   | 07/20/2012 03:17:00 PM |
| 2007-01-05   | 08/02/2012 09:58:00 AM |
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## Numerical analysis of a comprehensive model of M-phase control in Xenopus oocyte extracts and intact embryos: parameter values have been taken from the original published paper to reproduce figure 4A.





### Model Status

This CellML version of the model has been checked in COR and OpenCell. This variant of the model runs to replicate the original published results as depicted in figure 4A of the paper. Please note that actual concentrations are displayed by this model, instead of the percentage concentrations used in the paper. The units have been checked and they are consistent.

### Model Structure

ABSTRACT: To contribute to a deeper understanding of M-phase control in eukaryotic cells, we have constructed a model

### Model Curation

Curation Status:   
 OpenCell:   
 JSim:   
 COR: 

### Source

Derived from workspace [Novak, Tyson, 1993](#) at changeset [a39b4d26855a](#).

You are here: [Home](#) > [Workspaces](#) > [Novak, Tyson, 1993](#)

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## Changelog Entries

- [\(0\)](#)
- [tip](#)

| Date                   | Author | Log   |
|------------------------|--------|---|
| 2010-07-05 22:14 +1200 |        | Updated documentation and added meaningful names to the two model variants. |
| 2010-07-05 14:24 +1200 |        | Tidied session file   |
| 2009-11-25 14:00 +1300 |        | Added images in ai svg and png format                                       |
| 2009-11-10 10:39 +1300 |        | Removed non pub med reference   |
| 2009-11-10 09:32 +1300 |        | Added keyword   |
| 2009-06-17 15:26 +1200 |        | committing version02 of novak_tyson_1993                                    |
| 2009-01-14 04:19 +1300 |        | committing version01 of novak_tyson_1993                                    |

- CellML metadata specification
  - <http://www.cellml.org/specifications/metadata/>
  - Elements from rdf, dc, dcterms, vcard
  - Trivial vs substantial changes
- SBML History concept
  - dc:creator *model creators*
  - dcterms:created *creation date*
  - dcterms:modified *modification date*

# What is the problem?

Version information is not propagated to the users.

Currently used algorithms are not suitable for difference detection in XML models (SBML, CellML, NeuroML).

- Find the difference between two model versions,
- understand what a change is about,
- and understand why a model update had been necessary.

1. XML-aware algorithm for difference detection
2. Transparent changes
3. Justification for changes



# 1. XML difference detection: DiffList

```
1 @@ -661,13 +661,11 @@
2 [...]
3 -     <rdf:Description rdf:about="#_905882">
4 -         <bqbiol:isVersionOf>
5 -             <rdf:Bag>
6 -                 <rdf:li rdf:resource="urn:miriam:obo.go:GO%3A0043037" />
7 -             </rdf:Bag>
8 -         </bqbiol:isVersionOf>
9 -     </rdf:Description>
10 +<rdf:Description rdf:about="#_905882">
11 +<bqbiol:isVersionOf><rdf:Bag>
12 +<rdf:li rdf:resource="urn:miriam:obo.go:GO%3A0043037" />
13 +</rdf:Bag></bqbiol:isVersionOf>
14 +</rdf:Description>
15 [...]
```

# 1. XML difference detection: DiffList

- Detects all diffs
  - insert, delete, update, move
  - for two model files,
  - typically two versions of the same model
- Adaptation of *XyDiff*,
  - entity-based
  - ignores XML formatting
  - <http://leo.saclay.inria.fr/software/XyDiff/>

Diff:

```
<updates>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='Cdc25_Reaction']" elementName="reaction"/>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='Cdc2Phos']" elementName="reaction"/>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='G1R_Binding']" elementName="reaction"/>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='G2R_Creation']" elementName="reaction"/>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='IE_Reaction']" elementName="reaction"/>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='PG2R_Creation']" elementName="reaction"/>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='UbE2_Reaction']" elementName="reaction"/>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='UbE_Reaction']" elementName="reaction"/>
  <attribute attributeName="reversible" value="true" oldValue="false"
    path="[@id='Wee1_Reaction']" elementName="reaction"/>
</updates>
```

Waltemath et al., 2012 (submitted)

## 2. Transparent changes: model history

Table 1: Version information about model BIOM007

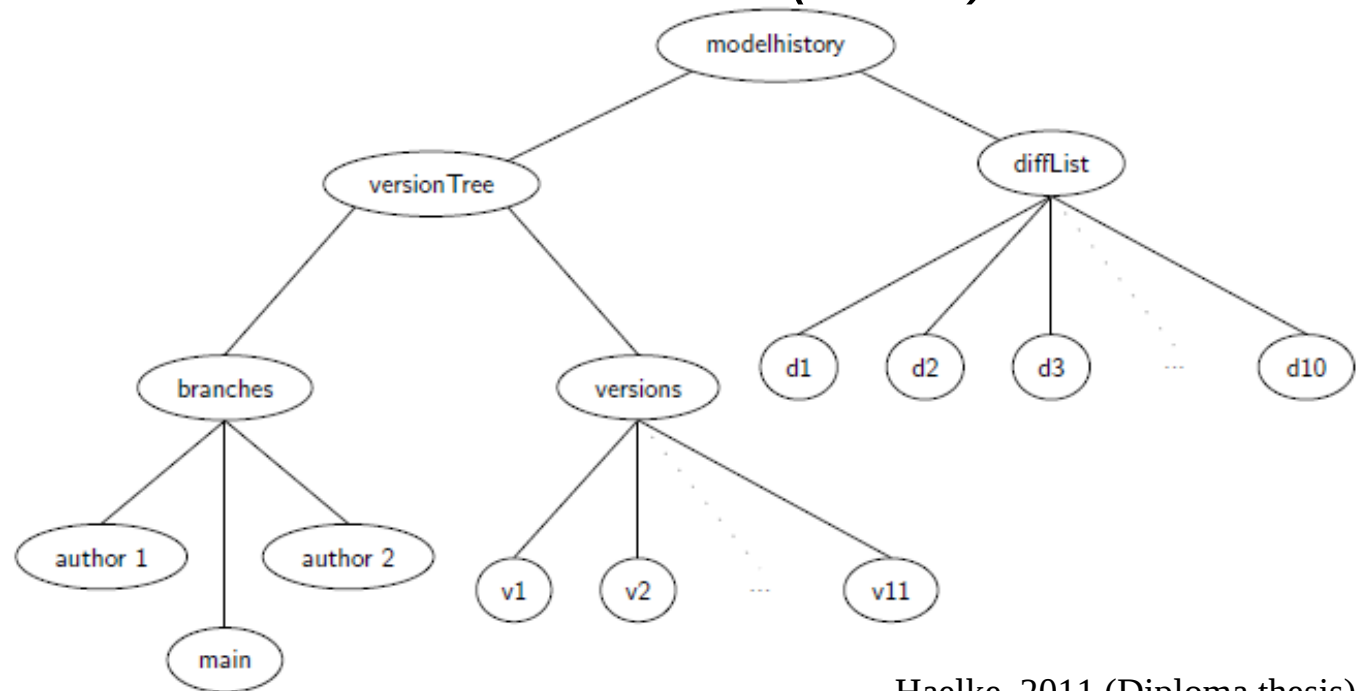
| Revision    | Date       | SVN Comment   |
|-------------|------------|---|
| R2* initial | 06/16/2009 | original models.  |
| R3*         | 06/16/2009 | the latest version when implementing revision control   |
| R37         | 07/29/2009 | four assignment rules (k2, k6, kwee and k25) were changed to function definitions.  |
| R51         | 08/10/2009 | converted to SBML Level2 Version 4 and curated. Attributes 'spatialSizeUnits' in element, and 'timeUnits' and 'substanceUnits' in element, which are not part of SBML Level 2 Version 4 element are eliminated. |
| R57         | 08/13/2009 | The model should remain in SBML L2V1. The model was integrated and simulated using Mathematica 6.0 - MathSBML 2.7.1, which does not support SBML L2V4.  |
| R194        | 10/15/2009 | corrected one error in a kinetic law (Ube1 activation) and changed the file a bit to get it to l2v3 [line break] recurated it, but still problems with the initial conditions                                   |

Waltemath et al., 2012 (submitted)

## 2. Transparent changes: model history

### Model history (version tree)

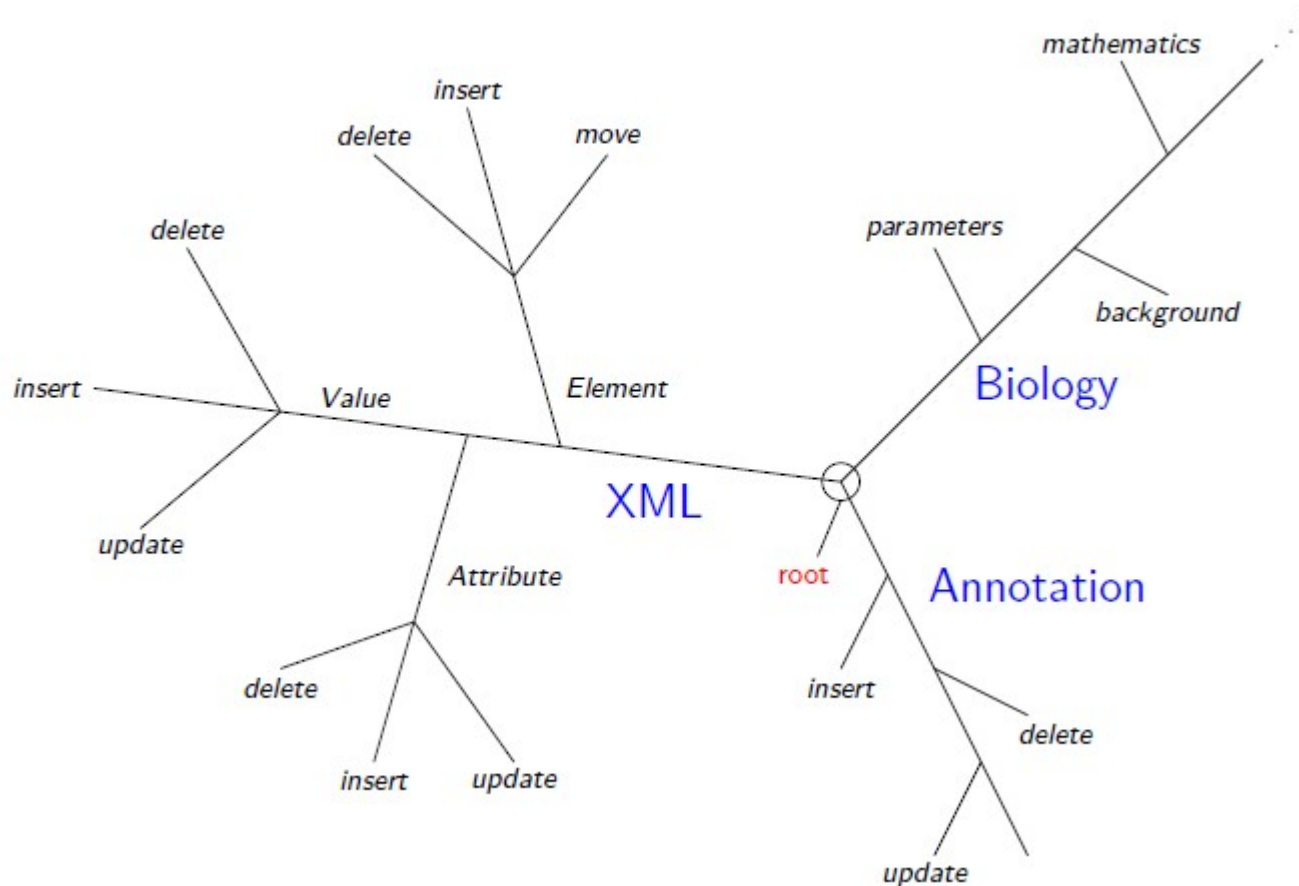
- Diff list
- *adapted from Rosado et al., 2009 (EDBT)*



Haelke, 2011 (Diploma thesis)

### 3. Justification of changes: Ontology

Controlled vocabulary for annotation of the diff file



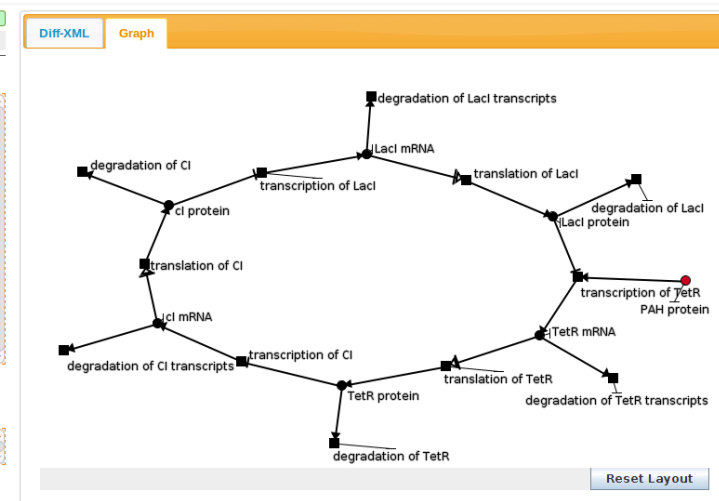
Haelke, 2011 (Diploma thesis)

## Biochemical Model Versioning System (BiVeS)

(Waltemath et al., submitted)

- Java library for **diffList** and **model history**
- Can be used on top of SVN/Mercurial systems to store differences between two model versions, and maintain a history of versions
- Tested on: SBML@BioModels Database
- <http://sourceforge.net/projects/bives/>

- Tree-based view of model versions (history)
- Difference between two models
  - XML representation (diff format)
  - Graphical representation (GraphViz)



- Targeting single versions of a model, e.g. to build the model history
- Change annotation
- Detecting merges in models
- Support of CellML, NeuroML, SED-ML etc in the diff tool



