

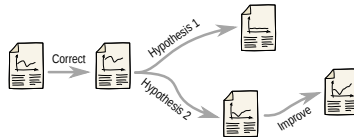
Improving Reproducibility and Reuse of Modelling Results in the Life Sciences

MARTIN SCHARM

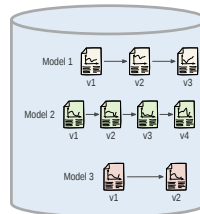
Department of Systems Biology & Bioinformatics, University of Rostock

<https://sbi.uni-rostock.de/scharm>

Rostock, 30 August 2018

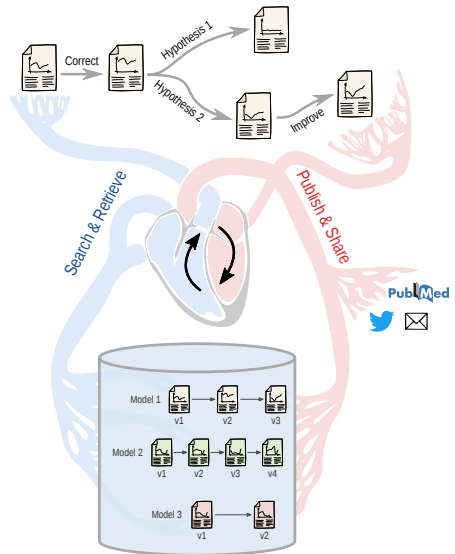


A method to characterise differences in
computational models (Chapters 2 and 3)



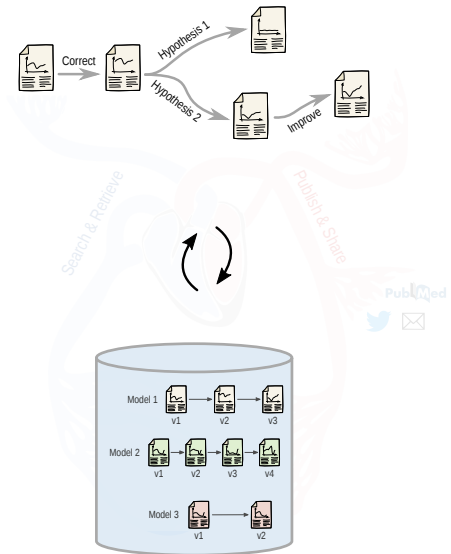
A method to characterise differences in computational models (Chapters 2 and 3)

Support for shareable and reproducible simulation studies (Chapter 4)

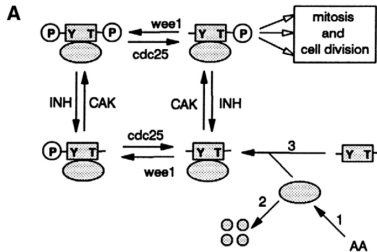


A method to characterise differences in computational models (Chapters 2 and 3)

Support for shareable and reproducible simulation studies (Chapter 4)

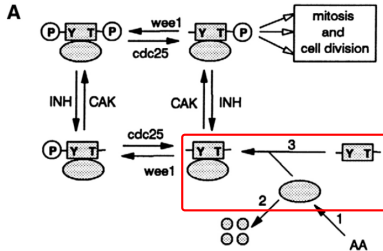


Models evolve: I not just witnessed changes, but induced model evolution myself.



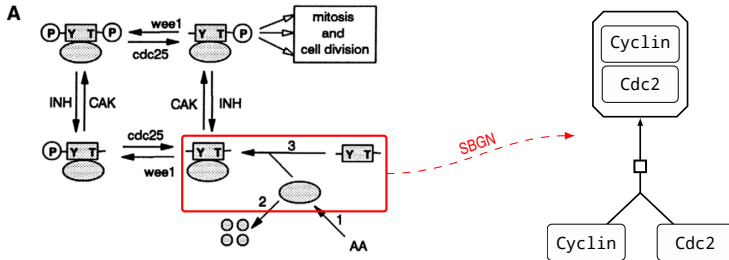
Novak and Tyson: *Numerical analysis of a comprehensive model of M-phase control in *Xenopus* oocyte extracts and intact embryos.*
In *Journal of Cell Science* 1993 106:1153-1168

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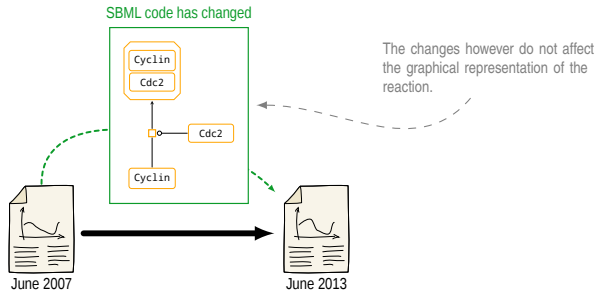


June 2007

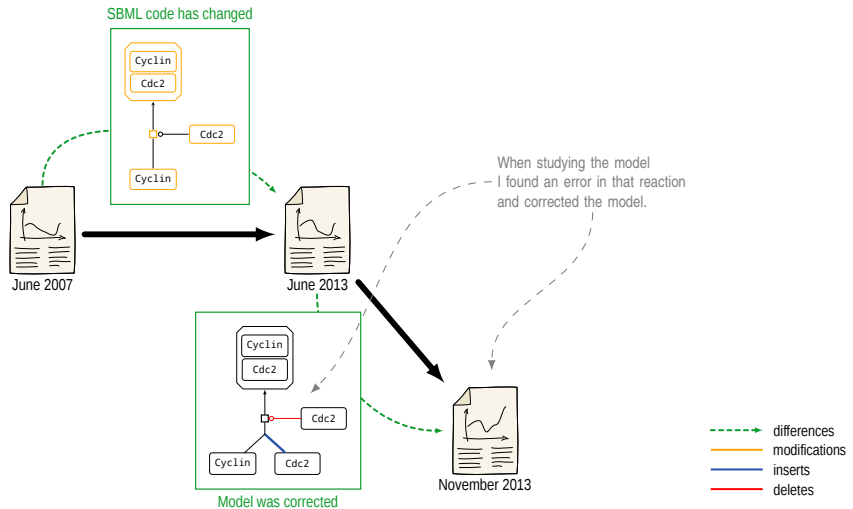
The model with id BIOMD000000107 was published in
– BioModels Database. It encodes the biological system
described by Novak and Tyson in 1993.

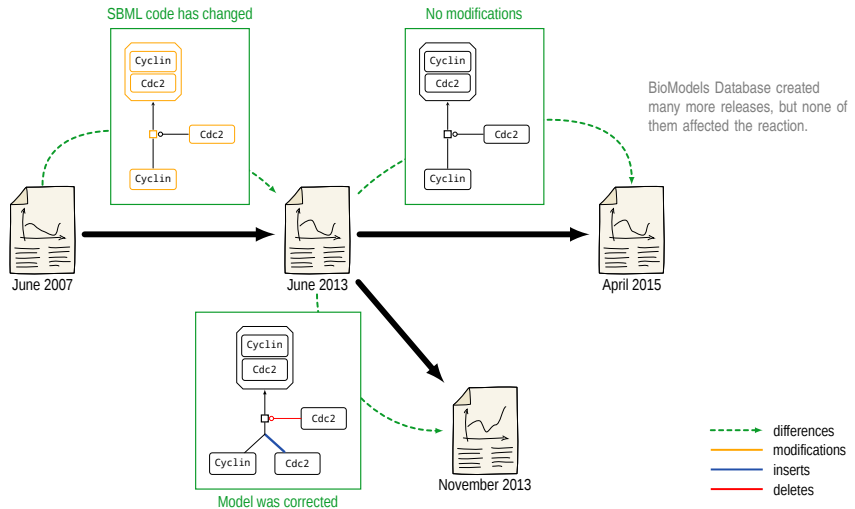


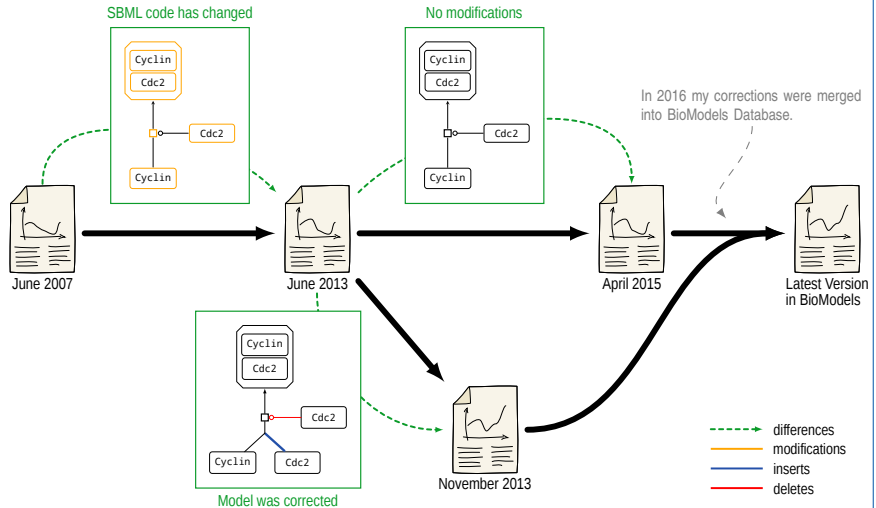
Along with many other models in BioModels Database, the model was released in multiple versions between 2007 and 2013.

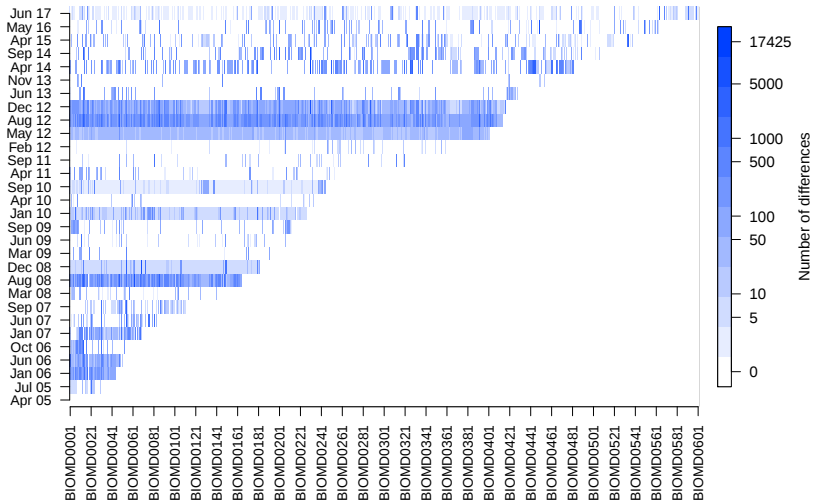


- differences
- modifications
- inserts
- deletes





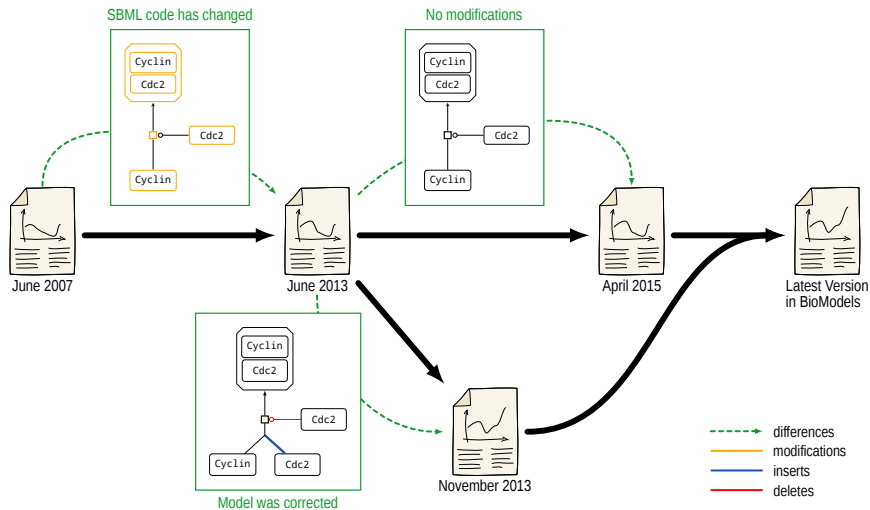


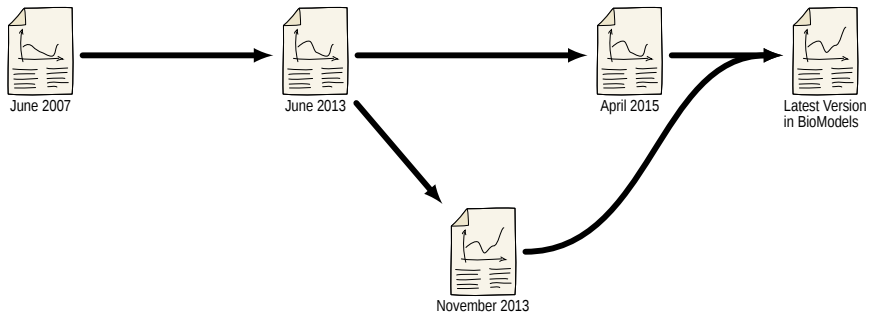


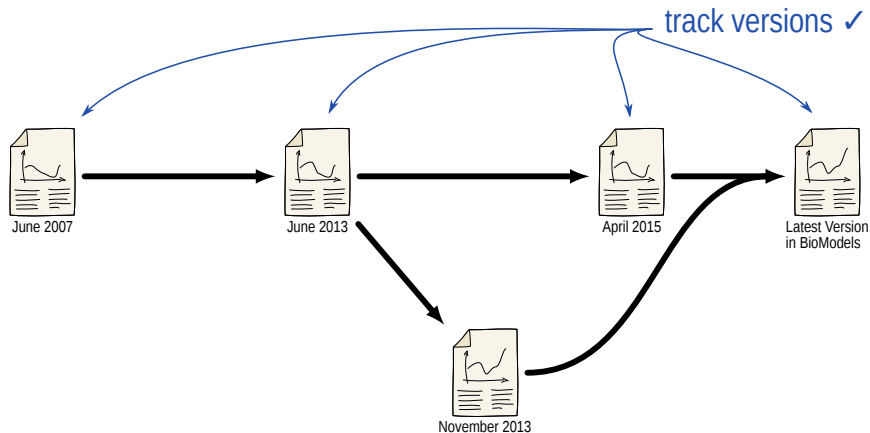
Scharm, Gebhardt, Touré, Bagnacani, Salehzadeh-Yazdi, Wolkenhauer and Waltemath: *Evolution of computational models in BioModels Database and the Physiome Model Repository.* In *BMC Systems Biology* 2018 12:53.

- Requirements of a version control system for computational models:
 - it must be entailed to the structure of model documents,
 - changes must be transparent and versions must be unambiguously identifiable, addressable, and accessible,
 - changes must be justified.
- Only with proper difference detection at hand users are able to grasp a model's history and to identify errors and inconsistencies.

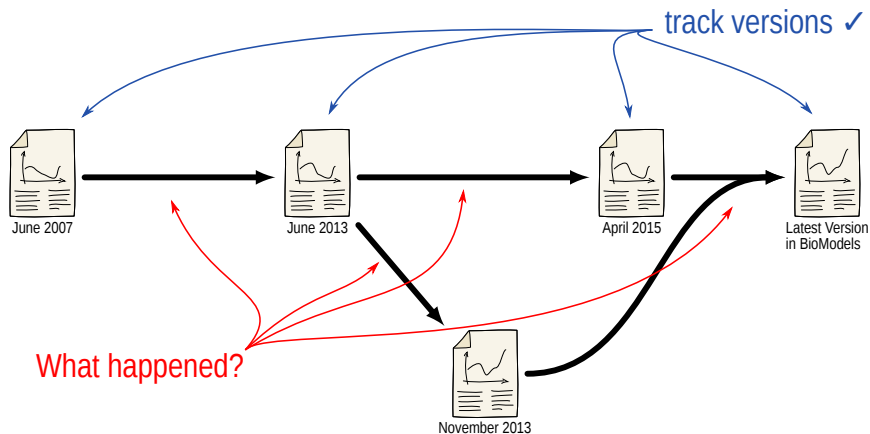
Waltemath, Henkel, Hälke, **Scharm** and Wolkenhauer: *Improving the Reuse of Computational Models through Version Control*.
In *Bioinformatics* 2013 29:6 742–748.







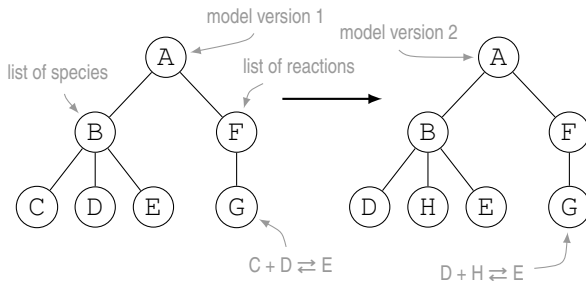
BioModels Database collects 
 Physiome Model Repository focuses on 



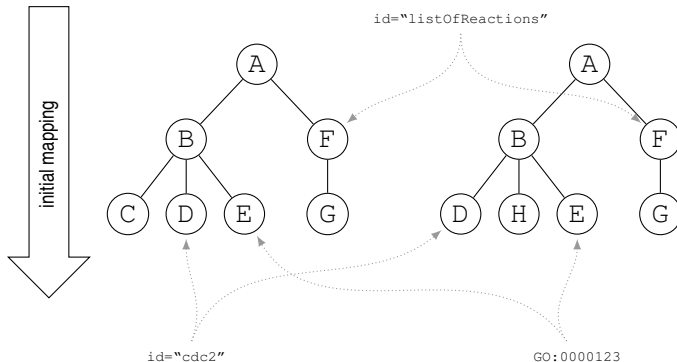
A method to detect and characterise differences in versions of computational models, including

1. an algorithm to detect changes based on the ideas of the XyDiff algorithm,
2. output formats to communicate the changes,
3. an ontology to semantically describe changes.

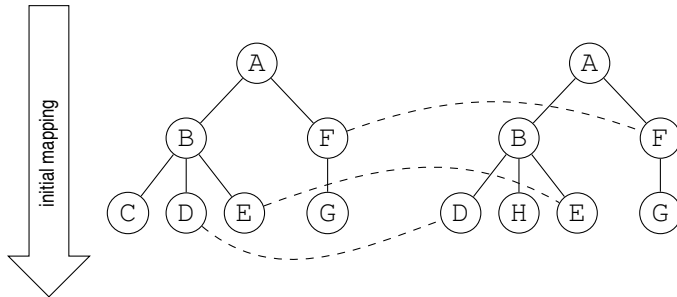
Scharm, Wolkenhauer and Waltermath: *An algorithm to detect and communicate the differences in computational models describing biological systems.* In *Bioinformatics* 2015 32:4 563-570



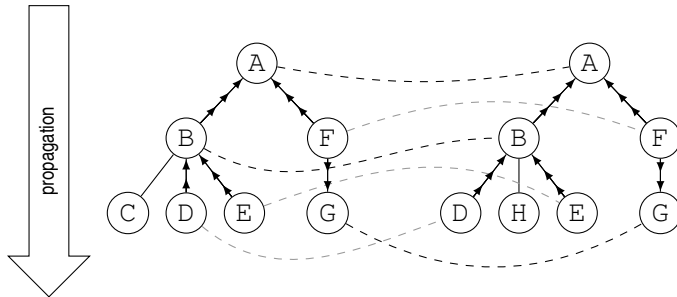
Scharm, Wolkenhauer and Waltemath: *An algorithm to detect and communicate the differences in computational models describing biological systems.* In *Bioinformatics* 2015 32:4 563-570



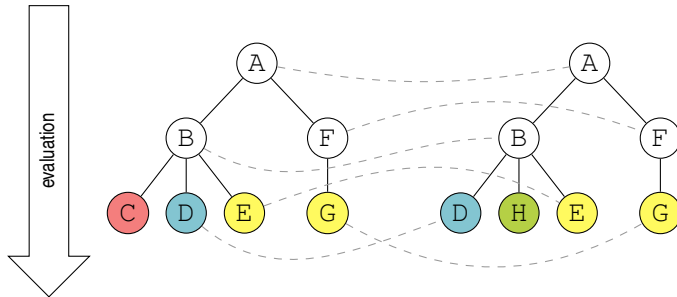
Scharm, Wolkenhauer and Waltemath: *An algorithm to detect and communicate the differences in computational models describing biological systems.* In *Bioinformatics* 2015 32:4 563-570



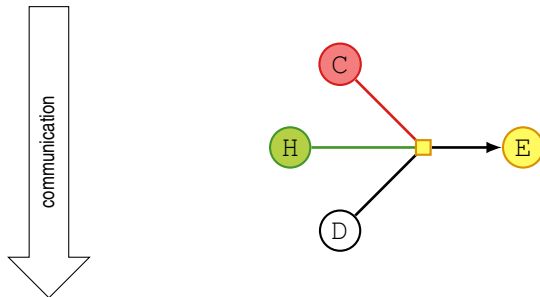
Scharm, Wolkenhauer and Waltemath: *An algorithm to detect and communicate the differences in computational models describing biological systems.* In *Bioinformatics* 2015 32:4 563-570



Scharm, Wolkenhauer and Waltemath: *An algorithm to detect and communicate the differences in computational models describing biological systems.* In *Bioinformatics* 2015 32:4 563-570

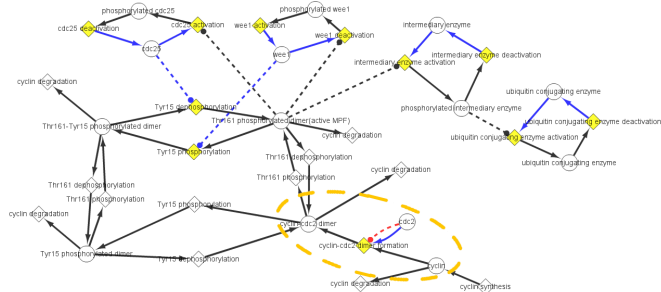


Scharm, Wolkenhauer and Waltemath: *An algorithm to detect and communicate the differences in computational models describing biological systems.* In *Bioinformatics* 2015 32:4 563-570



Scharm, Wolkenhauer and Waltemath: *An algorithm to detect and communicate the differences in computational models describing biological systems.* In *Bioinformatics* 2015 32:4 563-570

Highlighted Reaction Network



```

1 <?xml version="1.0" encoding="UTF-8" standalone="no"?>
2 <bives type="fullDiff">
3   <update />
4   <delete>
5     [...]
6     <node id="6" oldChildNo="1" oldTag="modifierSpeciesReference"
7       oldPath="..../listOfModifiers[1]/modifierSpeciesReference[1]"
8       oldParent="..../listOfModifiers[1]" triggeredBy="5" />
9     <attribute id="7" name="species" triggeredBy="6"
10       oldPath="..../modifierSpeciesReference[1]" oldValue="cdc2" />
11   </delete>
12   <insert>
13     [...]
14     <node id="12" newChildNo="2" newTag="speciesReference"
15       newParent="..../listOfReactants[1]"
16       newPath="..../listOfReactants[1]/speciesReference[2]" />
17     <attribute id="13" name="species" triggeredBy="12"
18       newPath="..../speciesReference[2]" newValue="cdc2" />
19     <attribute id="14" name="metaid" triggeredBy="12"
20       newPath="..../speciesReference[2]" newValue="S18337" />
21   </insert>
22   <move />
23 </bives>

```

Reactions

R13 (Tyr15 dephosphorylation)

- $p_dimer_p \rightarrow dimer_p$
- Modifiers: **cdc25(unknown)**

R12 (Tyr15 phosphorylation)

- $dimer_p \rightarrow p_dimer_p$
- Modifiers: **wee1(unknown)**

R24 (ubiquitin conjugating enzyme deactivation)

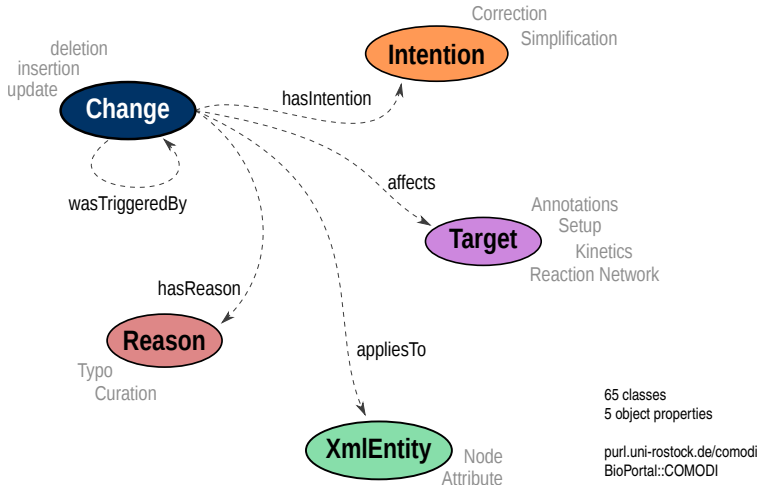
- $UbE_star \rightarrow UbE$

R3 (cyclin-cdc2 dimer formation)

- $cyclin + cdc2 \rightarrow dimer$
- Modifiers: **cdc2(unknown)**

Text-based Report

- A good communication of model changes can increase the trust in a model.
- COMODI — Computational MOdels DIffer.
- The COMODI ontology provides terms to characterise changes in models.



Scharm, Waltemath, Mendes and Wolkenhauer: *COMODI: an ontology to characterise differences in versions of computational models in biology.*
In *Journal of Biomedical Semantics* 2016 7:46.

```
<parameter name="Km1"  
value="0.3"  
units="molesperlitre" />
```

```
<parameter name="Km1"  
value="0.7"  
units="molesperlitre" />
```

```
<parameter name="Km1"  
value="0.3"  
units="molesperlitre" />
```

difference detection

```
<parameter name="Km1"  
value="0.7"  
units="molesperlitre" />
```

```
<update>  
  <attribute id="1" name="value"  
    oldPath="/sbml[1]/../parameter[1]"  
    oldValue="0.3" newValue="0.7"  
  [...] />  
</update>
```

```
<parameter name="Km1"
value="0.3"
units="molesperlitre" />
```

difference detection

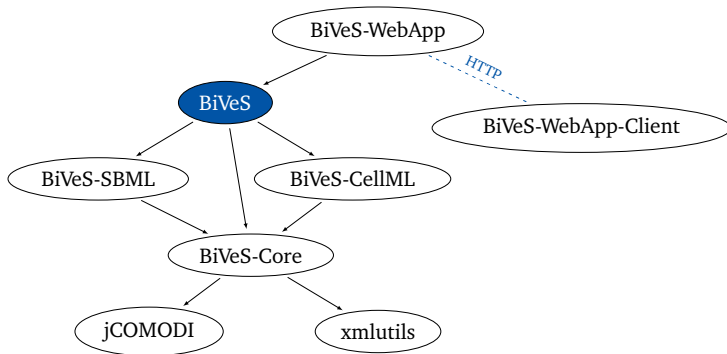
```
<parameter name="Km1"
value="0.7"
units="molesperlitre" />
```

```
<update>
  <attribute id="1" name="value"
    oldPath="/sbml[1]/../parameter[1]"
    oldValue="0.3" newValue="0.7"
  [...] />
</update>
```

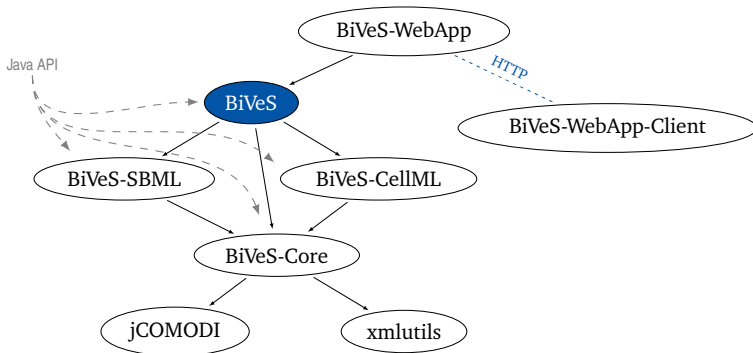
annotation

```
#1 a comodi:Update ;
comodi:appliesTo comodi:XmlAttribute ;
comodi:affects comodi:ParameterSetup ;
comodi:hasIntention comodi:Correction ;
comodi:hasReason comodi:MismatchWithPublication.
```

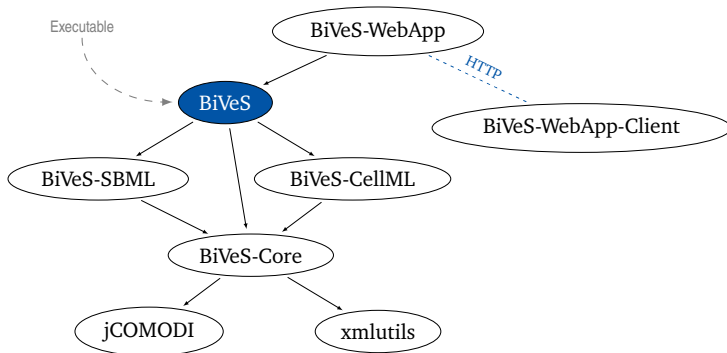
 BiVeS is a framework implementing the method to characterise differences in computational models.



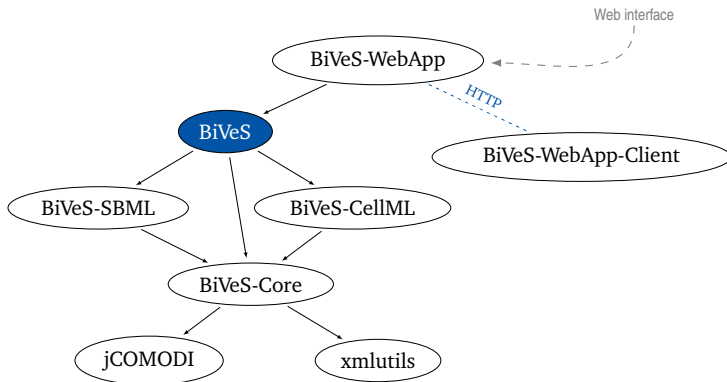
 BiVeS is a framework implementing the method to characterise differences in computational models.

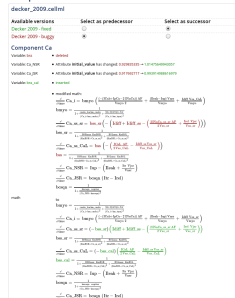
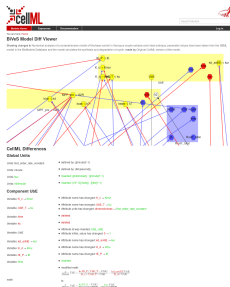
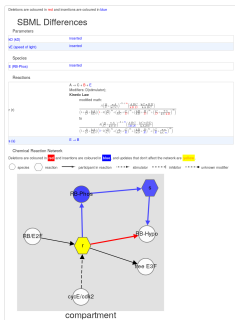


 BiVeS is a framework implementing the method to characterise differences in computational models.



 BiVeS is a framework implementing the method to characterise differences in computational models.





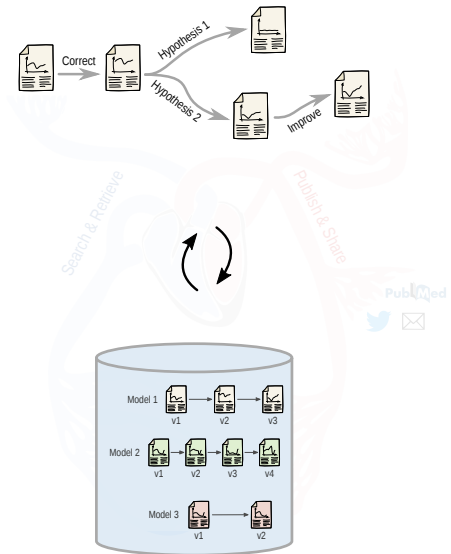
SEEK and the FAIRDOMHub

Physiome Model
Repository

Cardiac Electrophysiology
Web Lab

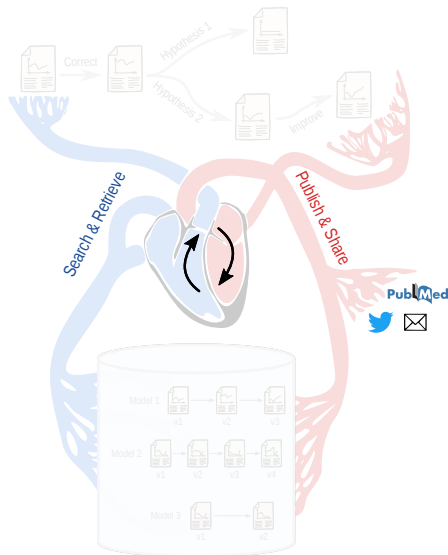
A method to characterise differences in computational models (Chapters 2 and 3)

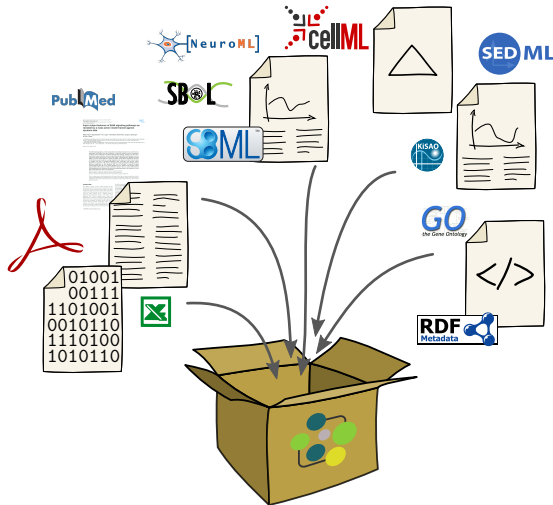
Support for shareable and reproducible simulation studies (Chapter 4)



A method to characterise differences in computational models (Chapters 2 and 3)

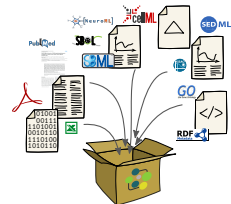
Support for shareable and reproducible simulation studies (Chapter 4)



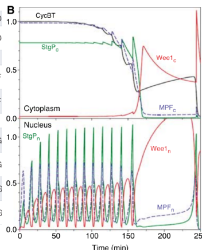


Bergmann, Adams, Moodie, Cooper, Glont and **Scharm** et al.: COMBINE archive and OMEX format: one file to share all information to reproduce a modeling project. In *BMC Bioinformatics* 2014 15:369.

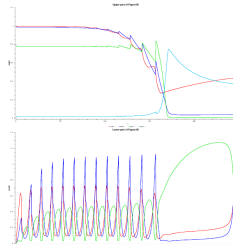
File	Format	Description
manifest.xml	Omx	Skeleton, automatically generated by WebCAT
metadata.rdf	Omx	Skeleton, automatically generated by WebCAT
README.md	Markdown	Human readable information for users stumbling upon the archive
model/		
BIOMD000000144.xml	SBML L2V1	origin: www.ebi.ac.uk/biomodels-main/download?mid=BIOMD000000144
calzone_2007.svg	SVG	origin: models.cellml.org/workspace/calzone_thieffry_tyson_novak_2007
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calzone_thieffry_tyson_novak_2007.cellml	CellML 1.0	origin: models.cellml.org/workspace/calzone_thieffry_tyson_novak_2007
sbgn/Calzone2007.gml	GML	SBGN compliant figure generated using SBGN-ED
sbgn/Calzone2007.graphml	GraphML	SBGN compliant figure generated using SBGN-ED
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sbgn/Calzone2007.sbgn	SBGN-ML	SBGN-ML encoded figure generated using SBGN-ED



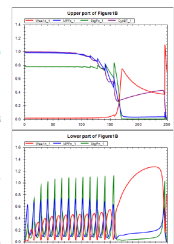
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Calzone2007-simulation-figure-1B.xml	SED
documentation/	
Calzone2007.pdf	PDF
Calzone2007-supplementary-material.pdf	PDF
result/	
Fig1B-bottom-COPASI.svg	SVG
Fig1B-top-COPASI.svg	SVG
Fig1B-bottom-webtools.png	PNG
Fig1B-top-webtools.png	PNG



(a) Figure 1B from the original publication



(b) COPASI



(c) SED-ML Web Tools

Scharm and **Waltemath**: *A fully featured COMBINE archive of a simulation study on syncytial mitotic cycles in Drosophila embryos.*
In *F1000Research* 2016 5:2421.

The Cardiac: Electrophysiology Web Lab

Jonathan C. Smith,¹ Martin Schwan,² and Gary D. Miasen¹
¹University of Illinois at Chicago, Chicago, Illinois, USA; ²University of Bonn, Bonn, Germany

Abstract Electrophysiological recordings within cardiac electrophysiology are a long history, and systems biology include new data and analysis tools. This paper presents a new cardiac electrophysiology web lab that includes a series of modules that allow students to explore the underlying mechanisms and emergent behavior in this system. Students can explore the effects of a single ionic current on the action potential, the effects of multiple ionic currents on the action potential, the effects of changes in the underlying parameters on the action potential, and the effects of changes in the underlying parameters on the action potential. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool.

Introduction The cardiac electrophysiology web lab is a new tool for teaching and learning about the underlying mechanisms and emergent behavior in this system. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool.

Methods The cardiac electrophysiology web lab is a new tool for teaching and learning about the underlying mechanisms and emergent behavior in this system. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool.

Results The cardiac electrophysiology web lab is a new tool for teaching and learning about the underlying mechanisms and emergent behavior in this system. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool.

Conclusions The cardiac electrophysiology web lab is a new tool for teaching and learning about the underlying mechanisms and emergent behavior in this system. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool. The web lab is designed to be used by students in a classroom setting, and it is also available as a self-paced learning tool.

Keywords cardiac electrophysiology, systems biology, web lab, action potential, ionic currents, emergent behavior, classroom setting, self-paced learning tool.

References [1] Smith, J. C., Schwan, M., and Miasen, G. D. (2010). The cardiac electrophysiology web lab: A new tool for teaching and learning about the underlying mechanisms and emergent behavior in this system. *Journal of Computational Science*, 1(1), 1-10.

Footnotes [1] Smith, J. C., Schwan, M., and Miasen, G. D. (2010). The cardiac electrophysiology web lab: A new tool for teaching and learning about the underlying mechanisms and emergent behavior in this system. *Journal of Computational Science*, 1(1), 1-10.

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Correspondence Jonathan C. Smith, University of Illinois at Chicago, Chicago, Illinois, USA. Email: jcs@uic.edu

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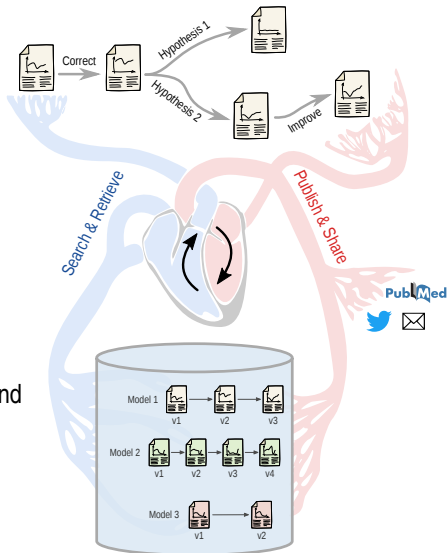
Citation Smith J. C., Schwan M., and Miasen G. D. (2010) The Cardiac: Electrophysiology Web Lab. *Journal of Computational Science* 1(1): 1-10. doi:10.4236/jcs.2010.11001

URL http://www.ccsenet.org/jcs

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The Cardiac
Electrophysiology
Web Lab

- Models are subject to changes.
- A novel method to identify and characterise changes:
 - entailed to the structure of models,
 - changes become transparent,
 - changes can be justified.
- Methods and tools support sharing and reproducing of research results.



Many thanks to...

Olaf Wolkenhauer
Ali Salehzadeh-Yazdi
Holger Hennig
Tom Theile
Sherry Freiesleben
Markus Wolfien
Peggy Sterling
Ulf Liebal
Shailendra Gupta



**SYSTEMS BIOLOGY
BIOINFORMATICS
ROSTOCK**

Icedove	Java	CellML
Iceweasel	Maven	SBML
OpenSSH	Docker	COPASI
Tomcat	Debian, GNU/Linux	FAIRDOM
Eclipse	Stack Exchange	Inkscape
Okular	Git, SVN, Hg	L ^A T _E X
Zsh	Python, Perl, PHP	Texstudio
R	Trac, Git(Hub Lab), Wiki*	Protégé



SEMS
simulation experiment management system

Dagmar Waltemath
Martin Peters
Tom Gebhardt
Vasundra Touré
Mariam Nassar
Fabienne Lambusch
Ron Henkel
Vivek Garg
Srijana Kayastha
Jenny Fabian



Jonathan Cooper
Stian Soiland-Reyes
Natalie Stanford
Matthew Gamble
Gary Mirams
Carole Goble
Pedro Mendes
Tommy Yu
Frank Bergmann
Olga Krebs
Falk Schreiber

...the audience!