Identifying, Interpreting, and Communicating Changes

in XML-encoded Models of Biological Systems





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RB-Hypo

We here present tools for version control for computational models, which help to:

- Gain insights in the modelling process, thereby increasing confidence in models [3].
- Improve reproducibility of model-based scientific results in life science.
- Extend, improve, and correct existing models.
- Find related models.

BiVeS

Biomodel **Ve**rsion Control **S**ystem [1]:

- Java library to map hierarchically structured content.
- Compares models encoded in standardised formats (currently: SML [4] and to [5]).
- Matches unchanged or moved entities in model documents.
- Identifies "inserts" and "deletes".
- Constructs a diff (in XML format).
- Interprets identified changes and filters for biologically and mathematically relevant differences.



BiVeS evaluates

the mapping

modified by moving subtrees around the document.



simulation experiment management system

BiVeS's Algorithm

After the document trees have been preprocessed, the algorithm proceeds in three major steps:

- Identical entities are mapped onto each other.
- This initial mapping is propagated into the tree.
- The resulting mapping is evaluated and modifications are classified.

In addition, BiVeS is able to understand the impact of detected modifications and exports the differences in various formats, such as the



The diff, produced by BiVeS, can be used to grasp the changes which occurred between two versions of a model.

BudHat

The BudHat [2] web interface demonstrates the capabilities of BiVeS, by displaying the detected differences in various formats:

- The XML-encoded delta.
- A reaction network highlighting the changes using CytoscapeWeb [6], CytoscapeJS [7], or Graphene [8].
- A human readable report listing all modifications relevant to the model.



highlighted chemical reaction network or a text based summary. These outputs can easily be integrated in existing tools to increase the benefit for the users.

There are three different ways of integrating BiVeS:

Integration of BiVeS

Report Component Hierarchy XML Patch CellML Differences Component COMPUTE_ICa_ICaK Variable: • deleted PCa_max • deleted • modified math: $FK = Pscale (-7)PCa = \begin{cases} Pscale PCa_max & if so = 0 \\ 1.5 Pscale PCa_max & otherwise \end{cases} VF_over_RT = \frac{V}{RT_over_F}$ VFsq_over_RT = 1000 Faraday VF_over_RTaL_Ca = .3? ² VF_over_RT - Cao 0.341a2_Ca = ? ² VF_over_RT - 1 ICamax = $\frac{PCa + VFsq_over_RTaL_Ca}{a_2Ca}$ ICa = ICamax yCa OpenIcabar = $\begin{cases} 0 & ifICamax ?0 \\ ICamax & otherwise \end{cases} FK prime = \frac{PK}{1+\frac{Icabar}{ICabaff}}$ $a_LK = Ki ?^{VF_over_RT} - Koa2_K = ?^{VF_over_RT} - 1ICaK = \frac{PK prime OpenyCa VFsq_over_RT aL_K}{a_2K}$ math	The uses l the m websi	Function BiVeS's W nodification te.	Functional Curation Project [11 iVeS's Web Service to track odifications of models on their e.	
$F_{R} = Pscale (-7)PCa = \begin{cases} Pscale (-4) & if iso = 0 \\ 1.5 Pscale (-4) & otherwise \end{cases} VF_over_RT = \frac{V}{RT_over_F}VFsq_over_RT = 1000 Faraday VF_over_RT \\ al_Ca = -3?^{2}VF_over_RT - Cao 0.341a2_Ca = ?^{2}VF_over_RT - 1ICamax = \frac{PCa 4 VFsq_over_RT al_Ca}{a2_Ca}ICa = ICamax yCa Open \\ Icabar = \begin{cases} 0 & ifICamax ?0 \\ ICamax & otherwise \end{cases} PKprime = \frac{PK}{1 + \frac{Icabar}{ICahalf}}al_K = Ki ?^{VF_over_RT} - Koa2_K = ?^{VF_over_RT} - 1 \\ ICaK = \frac{PKprime Open yCa VFsq_over_RT al_K}{a2_K} \\ inserted - deleted - moved - updated \end{cases}$	Yellow pages Experim Data files Models SOF Log in / Register Login: Password:	Find, share and exchange Data, Models and Process ment details Assets Activities Scales Documentation Ps Publications Biosamples Biosamples Home > Models Index > My Teusink > Compare versions A summary of the differences in the SBML between version 2 and version 1 for the files Teusink (1) xml and Teusink(1) Deletions are coloured in red and insertions are coloured in blue SBML Differences		
	Remember me: Alternatively Log in using d*OpenID Log in Need an account? Sign up	Both documents have same Leve Species GLCi (GLCi) G6Px (G6P) - G6P (G6P)	el/Version: L2V1 Attribute <i>initialConce</i> Attribute <i>id</i> has chang	ntration has changed: 0.097 – 0.087 ed: G6Px – G6P
The ቚ SEEK platform [12] uses BiVeS's	Forgotten password? Tags [show all] Biochemistry Bioinformatics	Prb (Prbx) - Prb (Prb) Reactions	Attribute name has ch	nanged: Prbx – Prb
compare the models in the database	Data Management Databases Fermentation Genetics Mathematical modelling Matlab Metabolomics Microbiology Molecular Biology parameter	vGLYCO (vGLYCO) vTreha (vTreha)	G6Px + Prb + G6P - Glyc $2G6Px + 2G6P + Prb - Trh$ $GLCi + Prb - G6Px + G6P$ Kinetic Law	
compare me models in me database.	estimation Proteomics SBML Software Engineering Systems Biology Taverna testing Transcriptomics		modified math: VmGLK	$\left(-\frac{GeP}{\left(SUMAXP+\left(SUMAXP^{2}-2SUMAXPPrb+sKeqAKSUMAXPPrb}{(1-4KeqAK)KeqGLK}\right)}\right)$

Results

<XML>

</XML>

Diff

We developed an algorithm that identifies the differences be-

BiVeS provides a **sophisticated API** to compare models and then visualise

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Models from BioModels Database

tween versions of a computational model and implemented it in our Java library BiVeS. Using BiVeS we analysed the versions of publicly available models. Models are subject to continual modifications, as seen in the figure on the left, and we recognised a pattern in the updates. We distinguish between model related modifications (corrections, improvements, extensions) and format specific updates. Taken together, our solution provides novel insights into the evolution of computational models. For the first time we are able to automatically compare computational models and export the differences in human readable formats.

the results. This API is, for example, used by BudHat.

Discover the benefits yourself at **budhat.sems.uni-rostock.de**!

References

[1] http://sems.uni-rostock.de/bives/ [2] http://sems.uni-rostock.de/budhat/ [3] Waltemath et al.: Improving the reuse of computational models through version control Bioinformatics, 2013 [4] Hucka et al.: The Systems Biology Markup Language (SBML): A medium for representation and exchange of biochemical network models Bioinformatics, 2003 [5] Lloyd et al.: CellML: its future, present and past Progress in Biophysics and Molecular Biology, 2004 [6] Lopes et al.: Cytoscape Web: an interactive web-based network browser Bioinformatics, 2010 [7] http://cytoscape.github.io/cytoscape.js/ [8] http://stanleygu.com/graphene-sems/ [9] Lloyd et al.: The CellML Model Repository Bioinformatics, 2008 [10] Li et al.: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models BMC Systems Biology, 2010 [11] Cooper et al.: High-throughput functional curation of cellular electrophysiology models Progress in Biophysics and Molecular Biology, 2011 [12] Wolstencroft et al.: The SEEK: a platform for sharing data and models in systems biology Methods Enzymol, 2011



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