Universität Rostock Traditio et Innovatio

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Model Meta-Information

Dagmar Waltemath

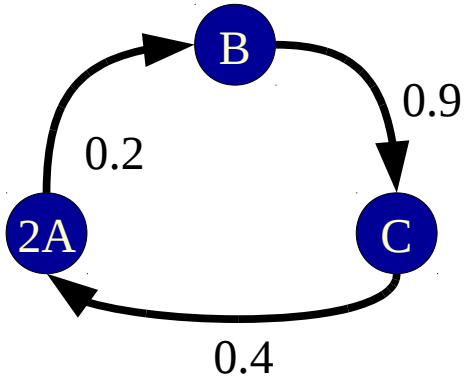
Workshop on

Ontology in Modeling and Simulation of Neuronal Systems

Rostock, 26th of May, 2010

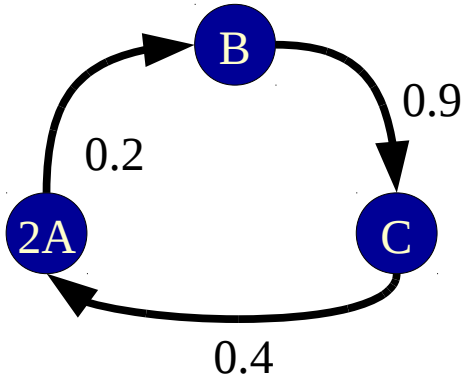
Part 1: Meta-Information and annotations

Model structure vs meta-information



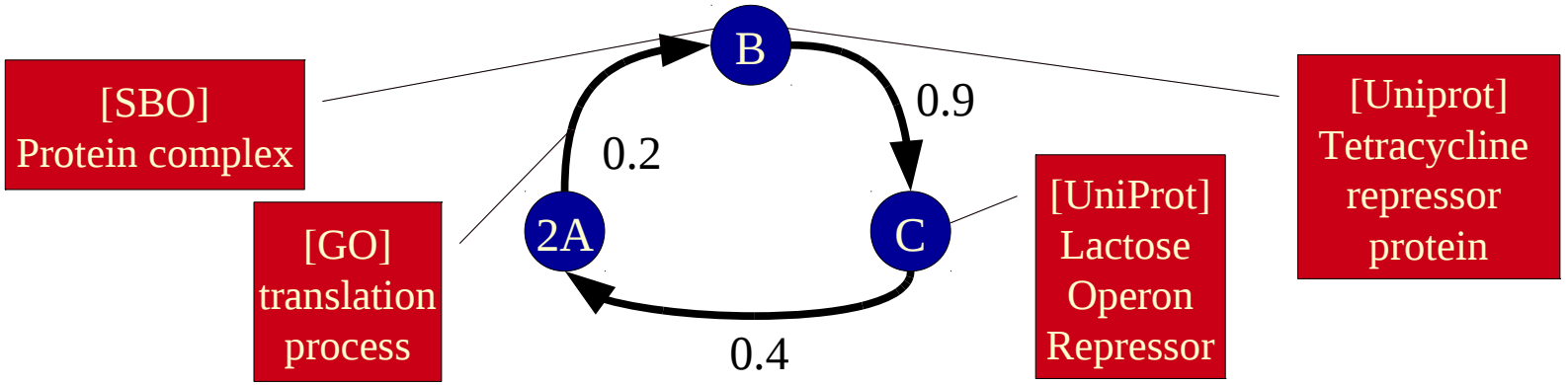
- Model structure, e.g. SBML, CellML
  - Encodes the network, e.g. of biochemical reactions
  - Necessary mathematical information for simulation/execution of a model

Model structure vs meta-information



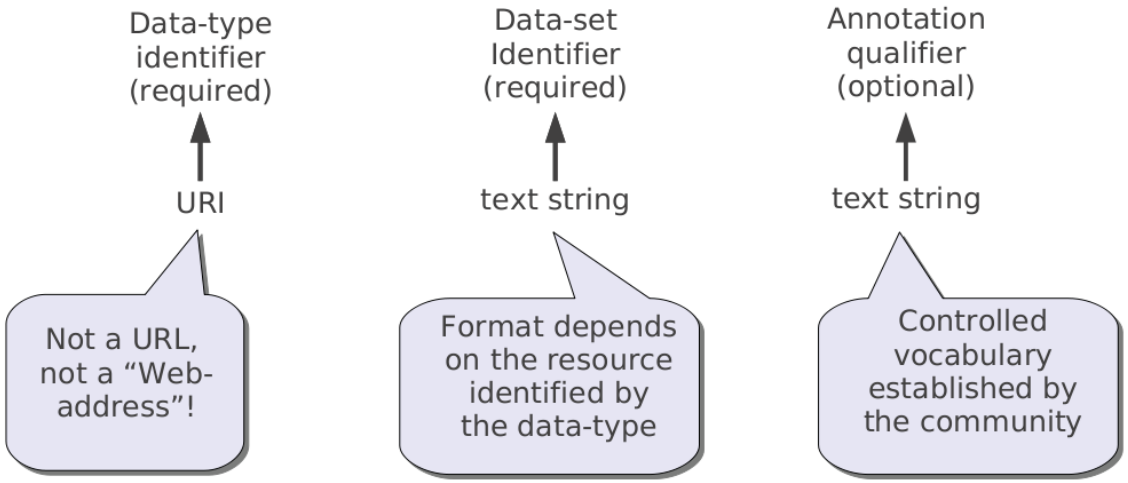
- Models not only are one-time encodings of the mathematics of a biological system
  - Model reuse (expansion, teaching, collaborations ...)
  - Model search & browsing
  - Model visualisation
  - Model merging ...

Model structure vs meta-information



- Model meta-information helps “understanding” the model
  - _ MIRIAM (Minimum Information Requested in the Annotation of Models)
  - _ Use of controlled annotation, particularly ontologies, including Gene Ontology, Systems Biology Ontology, UniProt, CheBi ...

Model meta-information encoding

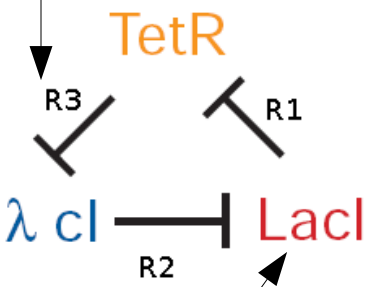


- **MIRIAM standard** on MIRIAM resources
- Makes meta-information computer-processable
- Ensures permanent links to information and knowledge

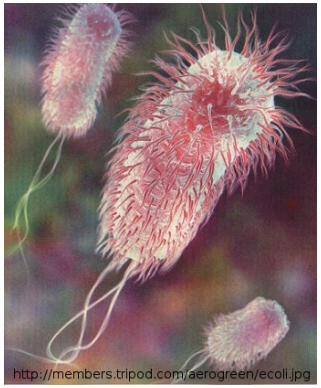
http://www.ebi.ac.uk/miriam/main/ and http://www.biomodels.net/qualifiers/

Possible types of meta-information

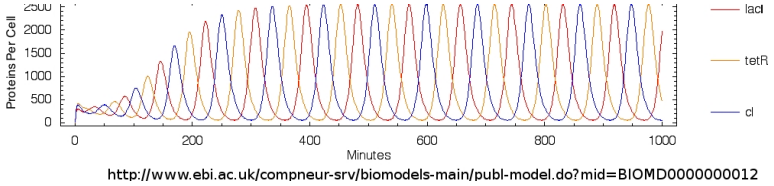
Reaction:
degradation of TetR transcripts
(GO:0006402)



Species:
transcript Lactose operon repressor (UniProtKB:P03023),
is versionOf
mRNA (CHEBI:33699),
located in the cell (GO:0005623)



Organism:
E-Coli (UniProt:562)
Compartment:
Cell (GO:0005623)
Publication:
pubmed:10659856
Format: SBML
(SED-ML:type="SBML")



Behavior: Oscillation (TEDDY_0000006)
SimulationAlgorithm: Gillespie (KiSAO:000029)

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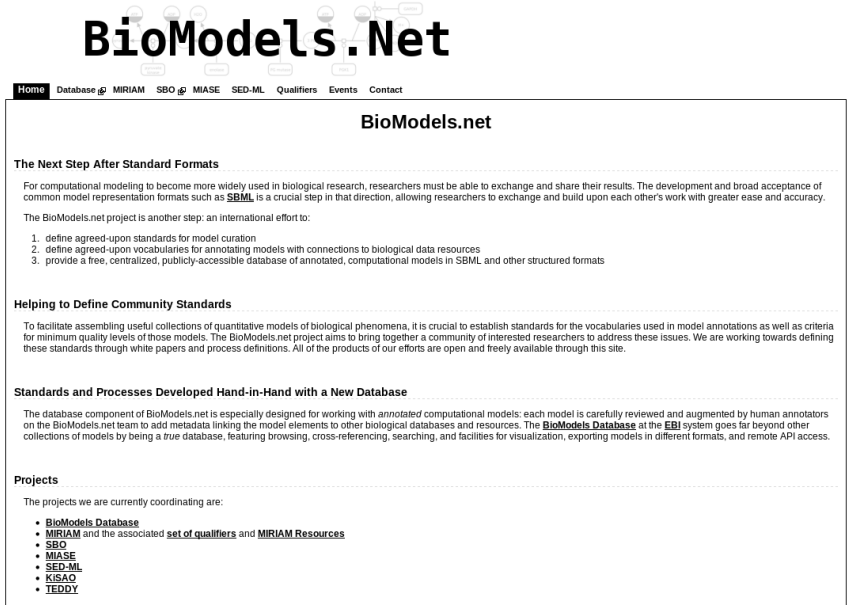
Biomodels.net initiative



Minimum Information Requested In the Annotation of Models (**MIRIAM**)

- Systems Biology Ontology (**SBO**)

Minimum Information About a Simulation

- Experiment (**MIASE**)
- Simulation Experiment Description Markup Language (**SED-ML**)
- Kinetic Simulation Algorithm Ontology (**KiSAO**)
- Terminology for the Description of Dynamics (**TEDDY**)
-

http://www.biomodels.net

Summary

- Use cases and software for model annotation
  → follow-up presentation Ron Henkel
- Further information on model meta-information
  - Metadata For Systems Biology, Juty (2009)
    http://videolectures.net/mlsb09_juty_mfsb/
  - Minimum information requested in the annotation of biochemical models (MIRIAM), *Le Novère, Finney, Hucka et al. , Nature (2006)*
    http://www.nature.com/nbt/journal/v23/n12/abs/nbt1156.html

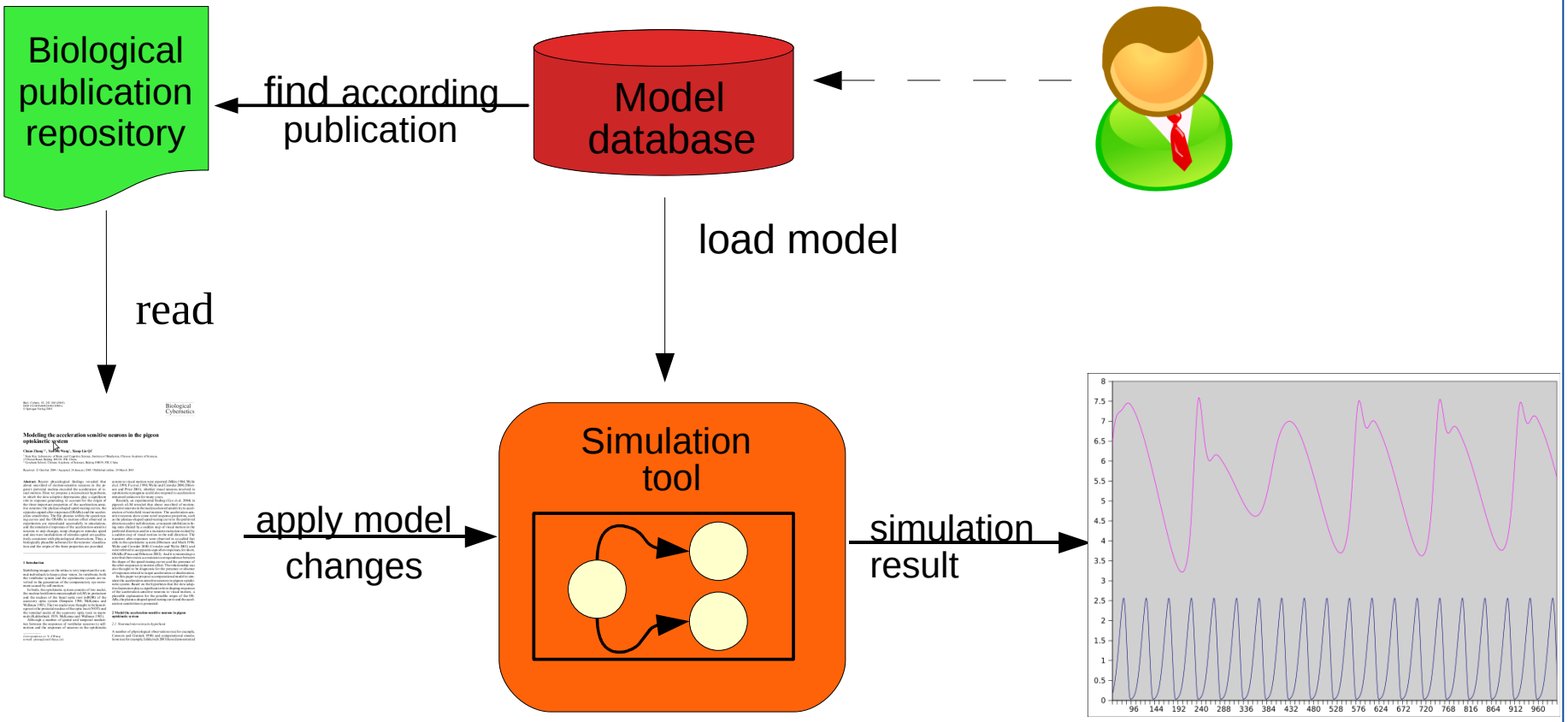
Part 2: Simulation experiment descriptions

Part 2: Simulation experiment descriptions

SED-ML: A format proposal for the storage and exchange of simulation experiments

(as one particular type of meta-information)

Motivation


Biological publication repository
find according publication
Model database
load model
read
Simulation tool
apply model changes
simulation result
Biological Cybernetics
Modeling the acceleration sensitive neurons in the pigeon optokinetic system
8
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4
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3
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1
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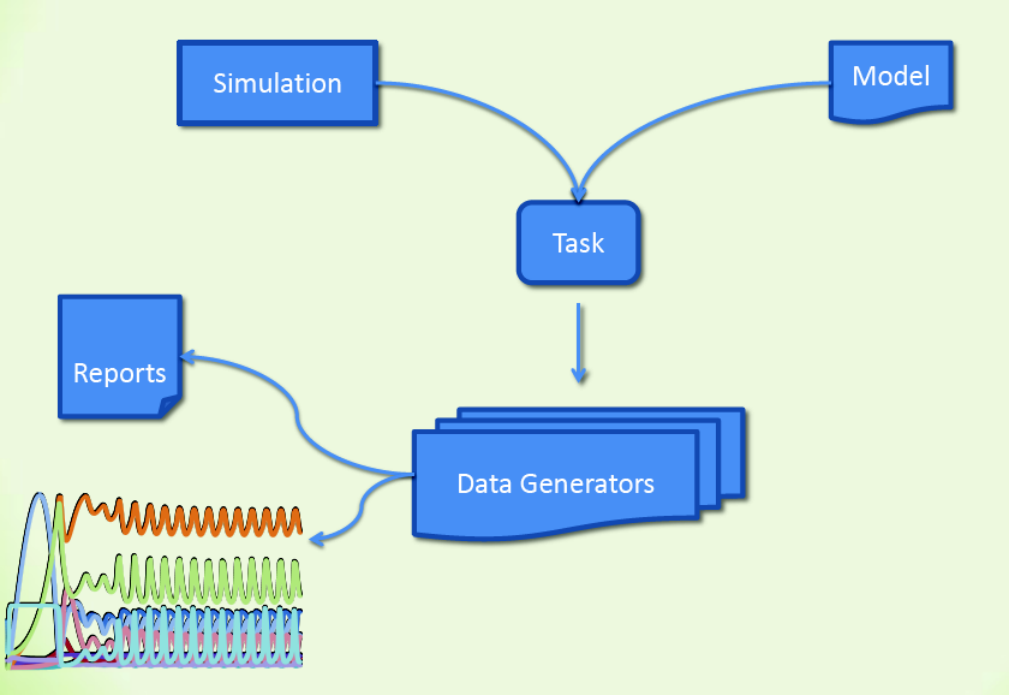
96 144 192 240 288 336 384 432 480 528 576 624 672 720 768 816 864 912 960

SED-ML

- Simulation Experiment Description Markup Language
  - Community project since 2007
  - XML Format / XML Schema / UML Object model
  - Main parts:
    - Pre-processing
    - Model references
    - Simulation settings
    - Post-processing

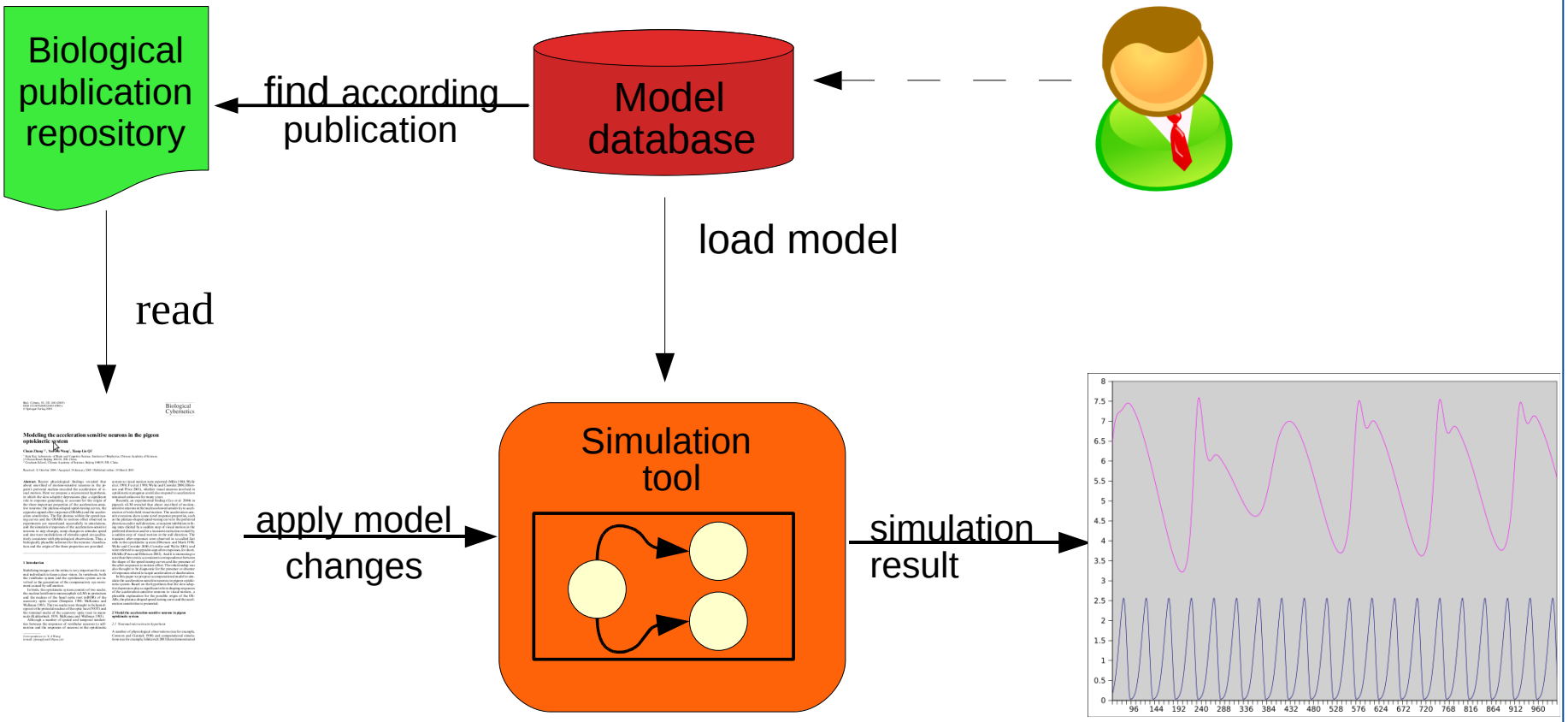
SED-ML



(Figure by Frank Bergmann, biomodels.net 2010)

- Model
- Simulation
- Task
- DataGenerator
- Output

SED-ML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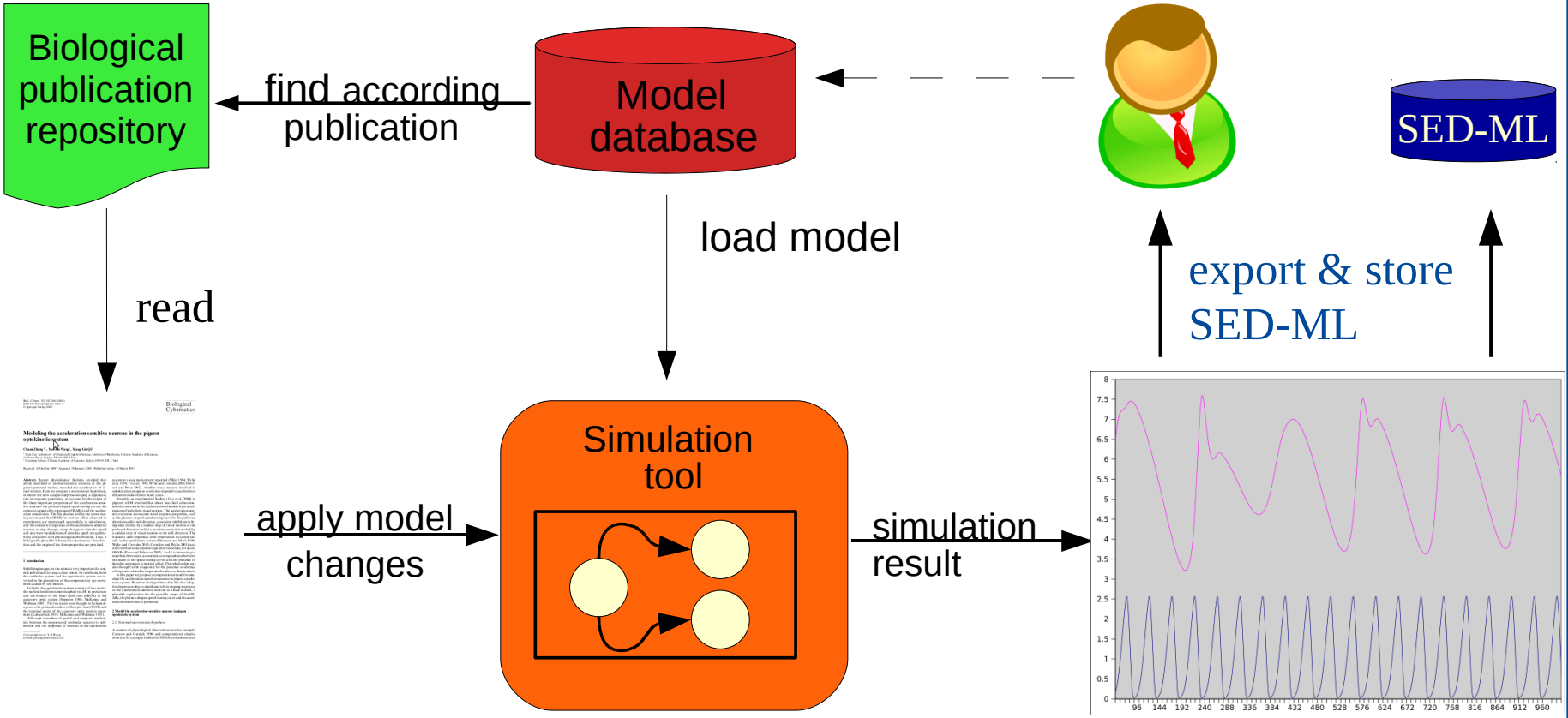
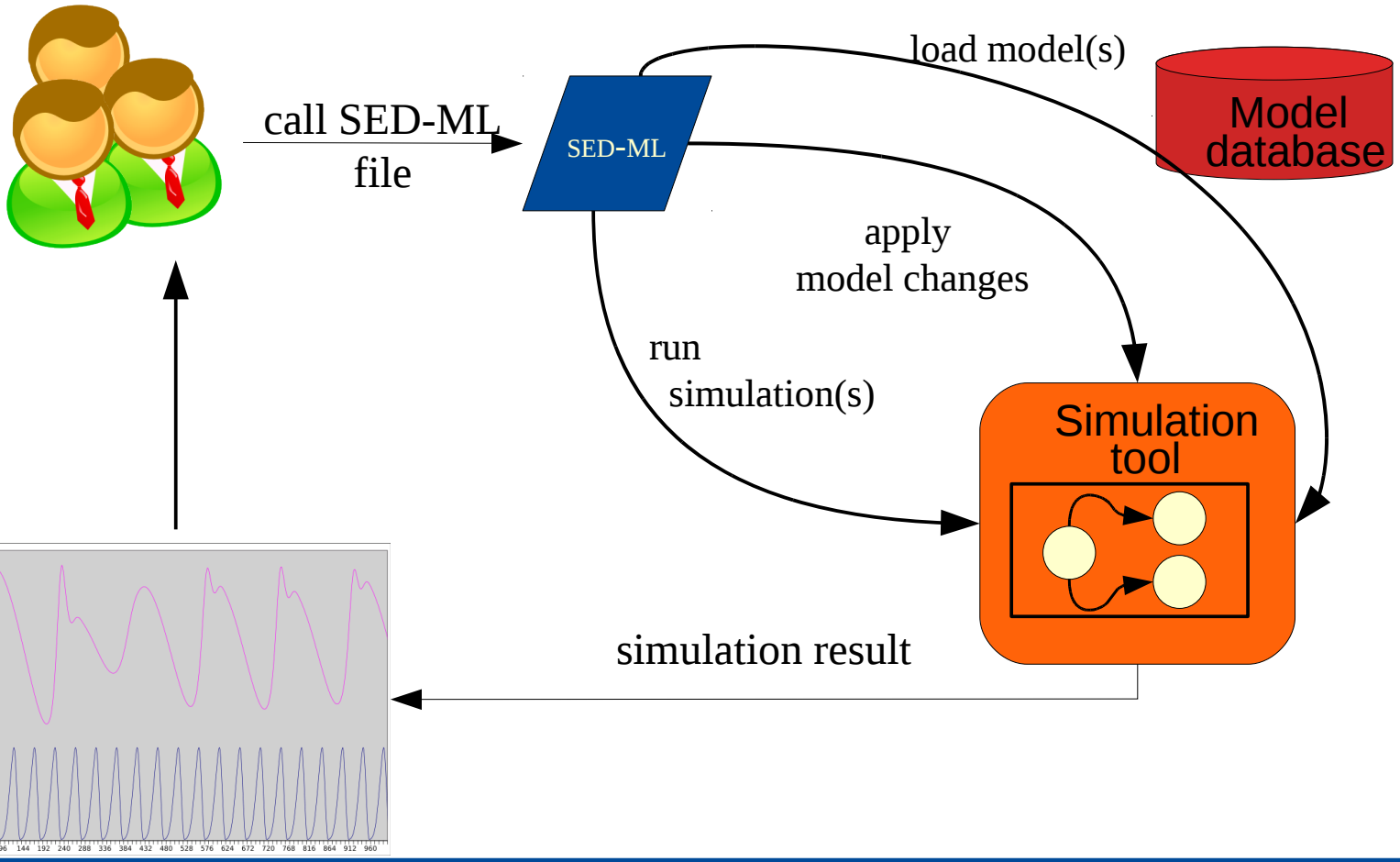
SED-ML


Biological publication repository
find according publication
Model database
SED-ML
load model
read
export & store SED-ML
Simulation tool
apply model changes
simulation result

SED-ML


load model(s)
call SED-ML file
SED-ML
Model database
apply model changes
run simulation(s)
Simulation tool
simulation result

SED-ML Specification & Implementation

- SED-ML L1 V1 Specification
  - _ under development
  - _ preliminary version available from Sourceforge
- SED-ML Implementation
  - _ Libsedml & examples
  - _ Jlibsedml
  - _ SED-ML validator

Simulation Experiment Description Markup Language (SED-ML) : Level 1 Version 1

April 29, 2010

Editors

Dagmar Waltemath — *Rostock University, Germany*
Nicolas Le Novère — *European Bioinformatics Institute, UK*
Frank T. Bergmann — *University of Washington, Seattle, USA*

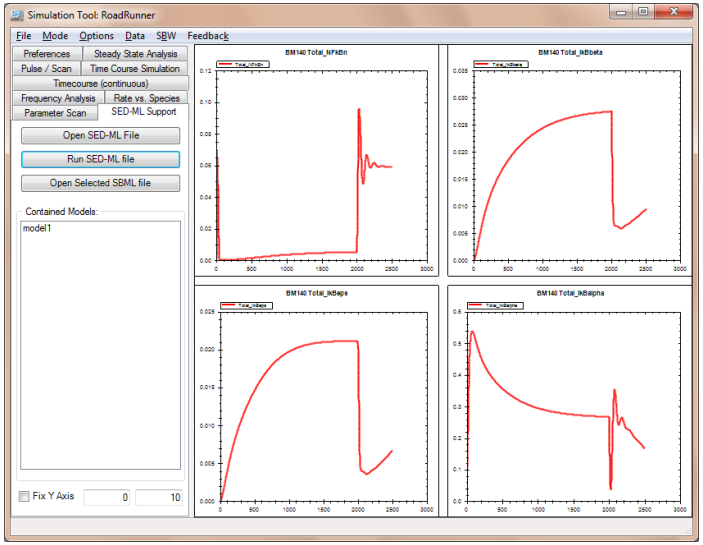
To discuss any aspect of the current SED-ML specification as well as language details, please send your messages to the mailing list sed-ml-discuss@lists.sourceforge.net. *To get subscribed to the mailing list, please write to the same address* sed-ml-discuss@lists.sourceforge.net. *To contact the authors of the SED-ML specification, please write to* dagmar.waltemath@uni-rostock.de

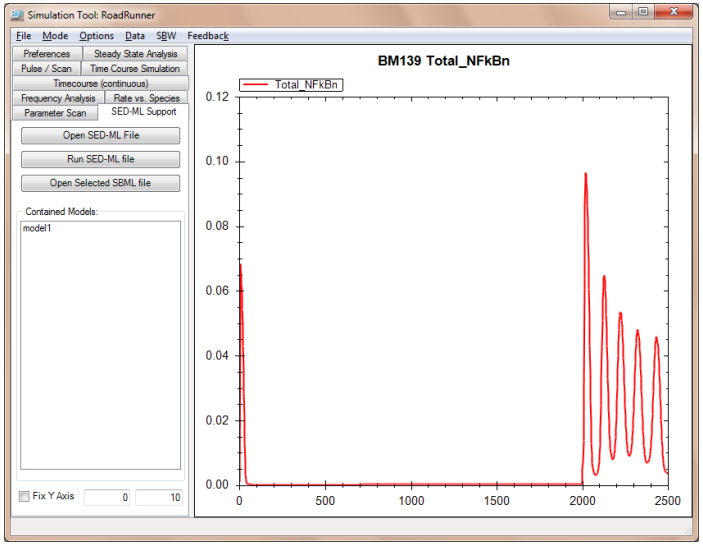
Use Cases

- Storage simulation experiment
  - independently from a simulation tool
  - in a reusable and exchangeable manner
- Import simulation experiment
  - collaborative work
  - teaching
  - curation
- Simulation using several models
  - in different formats → coupling?
- Simulation experiment using different settings

Example

"I normally use Copasi but most of the time it shows errors and/or warnings when I tried to import SBML models in it. For an example in Biomodel database the model BIOMD0000000139 and BIOMD0000000140 are *two different models* and they are *supposed to show different results*. Unfortunately simulating them in Copasi gives *same result for both the models*. Moreover different versions and curated model also cause problem. " (arvin mer on sbml-discuss)





(Figures produced by Frank Bergmann in SBW Workbench)

Summary

- Community
  - **Nicolas Le Novère** (EBI)
  - **Frank Bergmann** (SBW Workbench, libsedml)
  - Richard Adams (SED-ML validator, jlibsedml)
  - Ion Moraru (Virtual Cell)
  - ...
- Further Information
  - http://sourceforge.net/projects/sed-ml/
  - http://biomodels.net/sed-ml
- Getting involved
  - sed-ml-discuss@lists.sourceforge.net

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Example:
What we learn from meta-information and simulation descriptions …

IEEE TRANSACTIONS ON NEURAL NETWORKS, VOL. 14, NO. 6, NOVEMBER 2003

Simple Model of Spiking Neurons

Eugene M. Izhikevich

***Abstract*—A model is presented that reproduces spiking and bursting behavior of known types of cortical neurons. The model combines the biologically plausibility of Hodgkin–Huxley-type dynamics and the computational efficiency of integrate-and-fire neurons. Using this model, one can simulate tens of thousands of spiking cortical neurons in real time (1 ms resolution) using a desktop PC.**

***Index Terms*—Bursting, cortex, Hodgkin–Huxley, PCNN, quadratic integrate-and-fire, spiking, thalamus.**

BIOMD0000000127 - Izhikevich2003_SpikingNeuron

SBML formats | Other formats | Actions | Submit Model Comment

Model | Overview | Math | Physical entities | Parar

Reference Publication

Publication ID: 18244602

IEEE Trans Neural Netw 2003;14(6):1569-72.
Simple model of spiking neurons.
Izhikevich EM.
The Neurosciences Inst., San Diego, CA, USA. [more]

Model

Original Model: *BIOMD0000000127.xml.origin*

Submitter: Enuo He

Submission ID: MODEL4880479792

Submission Date: 28 Jul 2007 04:22:14 UTC

Last Modification Date: 22 Apr 2009 00:46:12 UTC

Creation Date: 16 Jul 2007 17:41:14 UTC

Encoders: Enuo He

set #1	bqbiol:isVersionOf	Gene Ontology regulation of action potential Gene Ontology regulation of membrane pote Gene Ontology regulation of action potential
set #2	bqmodel:isDescribedBy	DOI 10.1109/TNN.2003.820440
set #3	bqbiol:is	Taxonomy Mammalia

Notes

The model is according to the paper *Simple Model of Spiking Neurons* In this paper, a simple spiking model is preser yet as computationally efficient as the integrate-and-fire model. Known types of neurons correspond to different value Figure2RS,IB,CH,FS,LTS have been simulated by MathSBML.

RS: a=0.02, b=0.2, c=-65, d=8.

IB: a=0.02,b=0.2,c=-55,d=4

CH: a=0.02,b=0.2,c=-50,d=2

FS:a=0.1b=0.2c=-65,d=2

LTS:a=0.02,b=0.25,c=-65,d=2

Information in the SBML model

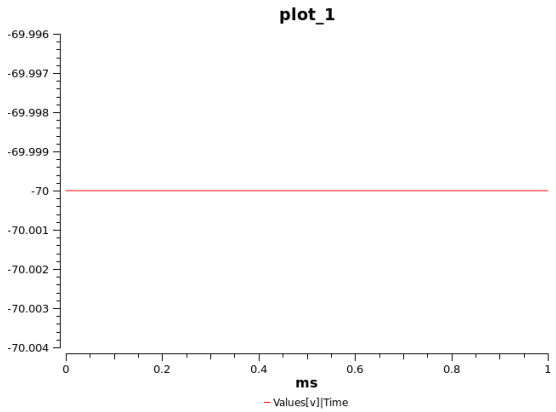
- 1 compartment
- 1 standard species
- No reactions
- 8 global quantities (parameters)
- 2 rate rules
- 2 events

Information in the model annotation

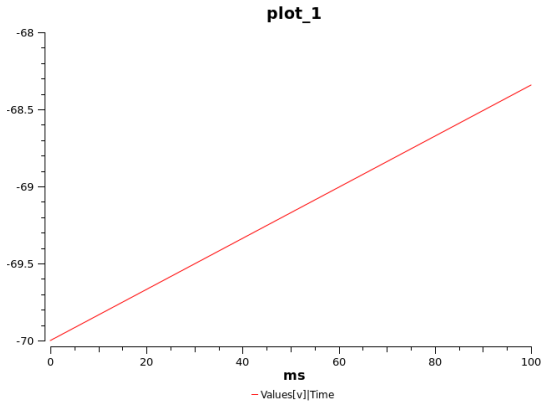
- **Model** reference urn:miriam:biomodels.db:BIOMD0000000127
- **Publication** reference urn:miriam:pubmed:18244602
- Model is on **organism** mammals urn:miriam:taxonomy:40674
- **Compartment** is version of a cellular compartment urn:miriam:obo.go:GO%3A0005623
- Has a standard **species** *not annotated in the model*
- Encodes 2 rate rules: the regulation of membrane potential (variable **v**) urn:miriam:obo.go:GO%3A0042391, the positive regulation of potassium ion transport (variable **U**) urn:miriam:obo.go:GO%3A0043268
- No **reactions**
- 8 global quantities (**parameters**) *not annotated in the SBML model*
- Has 2 **events**: a version of the stabilization of membrane potential (event **event_0000001**) urn:miriam:obo.go:GO%3A0030322, and the detection of electrical stimulus (event **Stimulus**) urn:miriam:obo.go:GO%3A0050981

Information in the SED-ML file

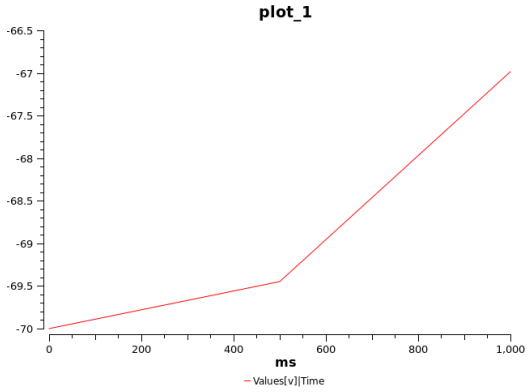
- First tries (COPASI, time course on **v**, initial parametrisation)



1 ms



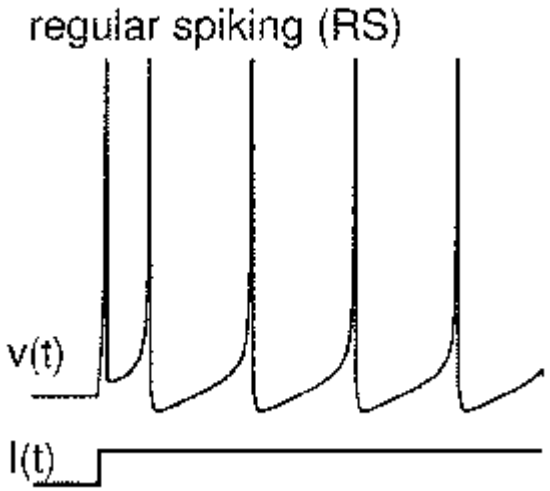
100ms



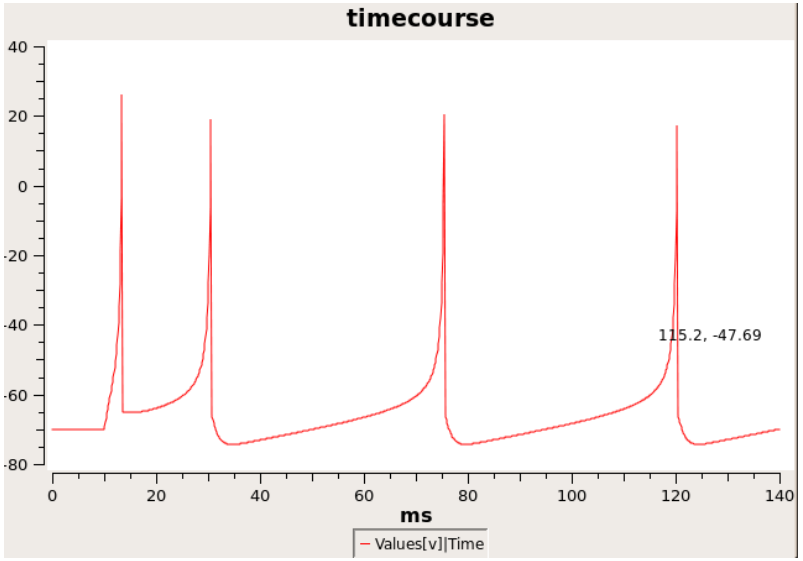
1000ms

Information in the SED-ML file

- Adjusting simulation step size and duration



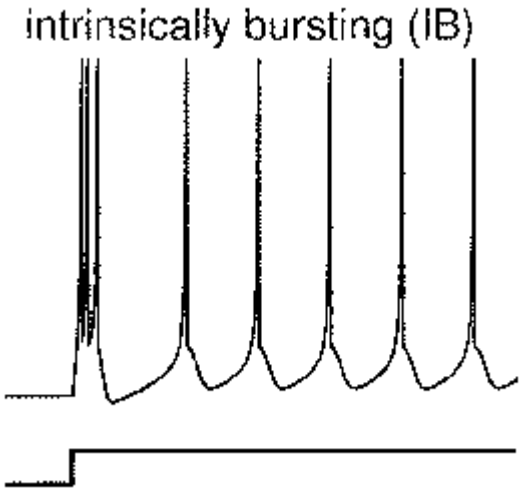
publication



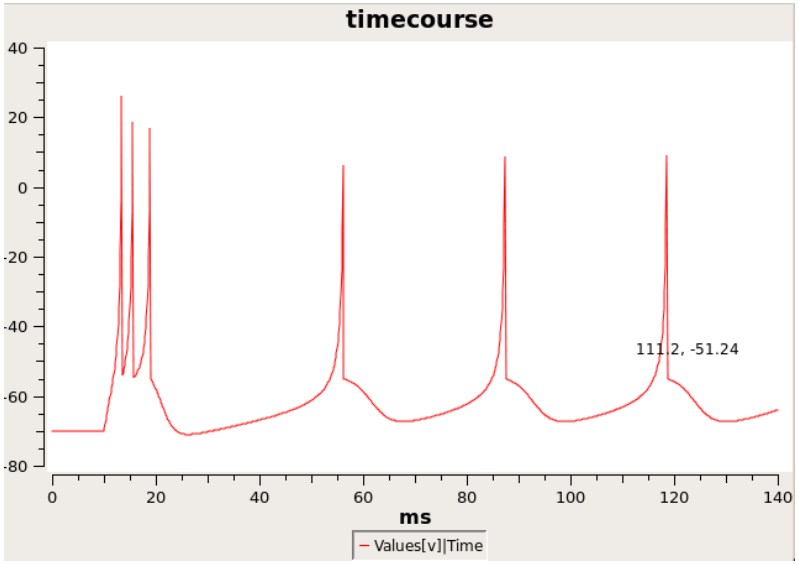
COPASI, duration: 140ms, step size: 0.14

Information in the SED-ML file

- Updating initial model parameters



Publication



COPASI, adjusted parameter values
(a=0.02, b=0.2 **c=-55, d=4**)

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Thank you for your attention!

dagmar.waltemath@uni-rostock.de

sed-ml-discuss@lists.sourceforge.net