David Nickerson

CellML Workshop 2012

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

Reproducible simulation experiments with SED-ML

13.03.2012

Dagmar Waltemath

SYSTEMS BIOLOGY
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Universität
Rostock

Traditio et Innovatio

The necessity for reproducible science

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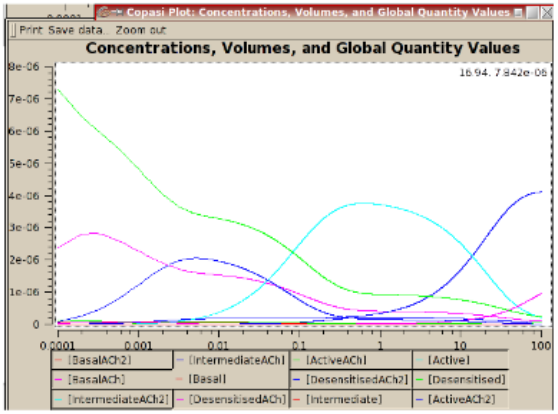
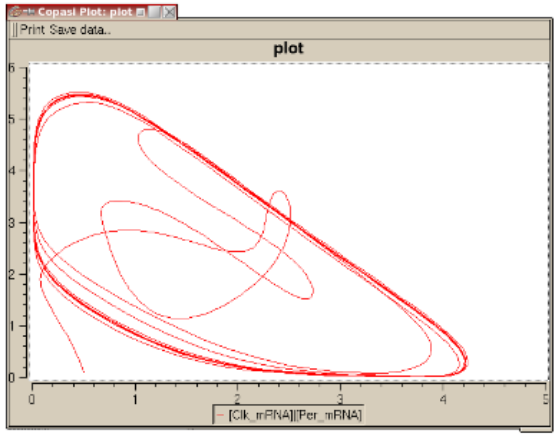
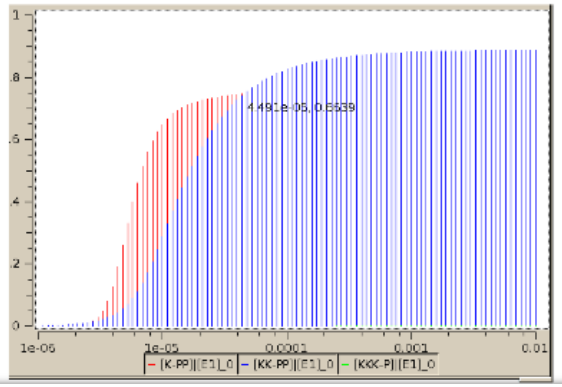
Edelstein et al 1996 (BIOMD0000000002)



Ueda, Hagiwara, Kitanol 2001 (BIOMD0000000022)



Huang & Ferrell (BIOMD0000000009)



Bornheimer et al 2004 (BIOMD0000000086)

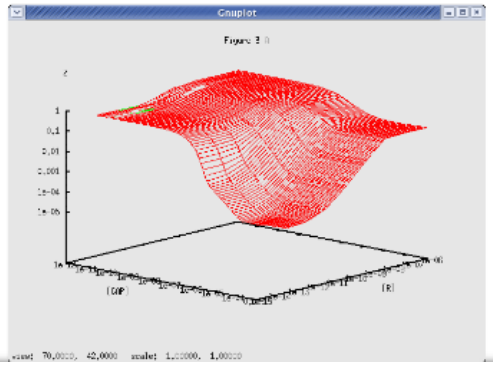
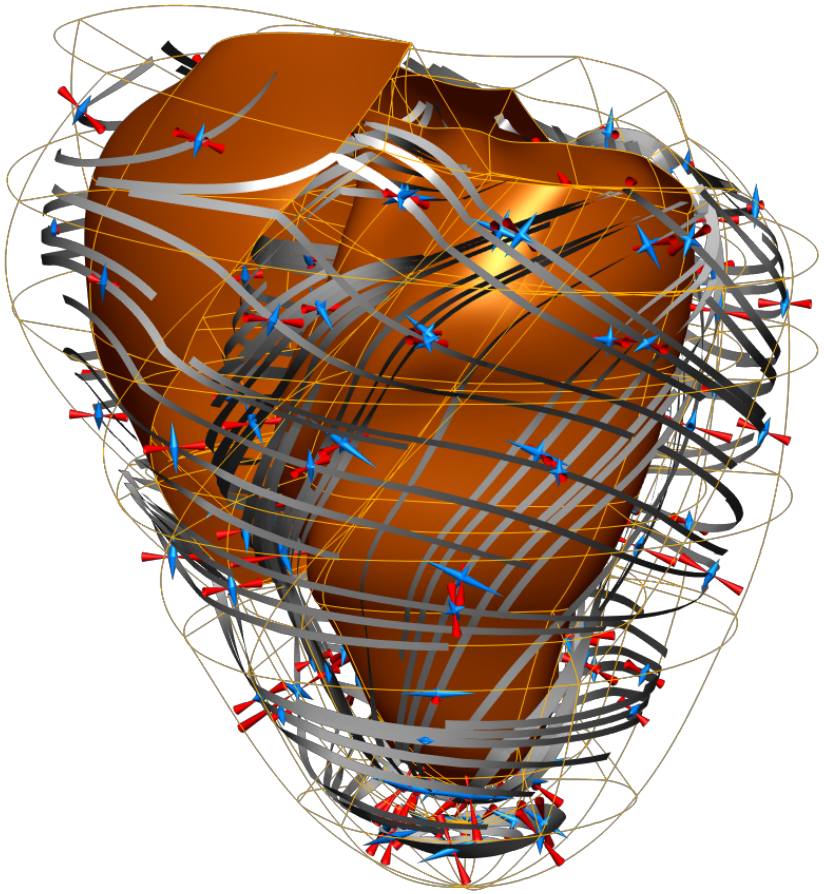


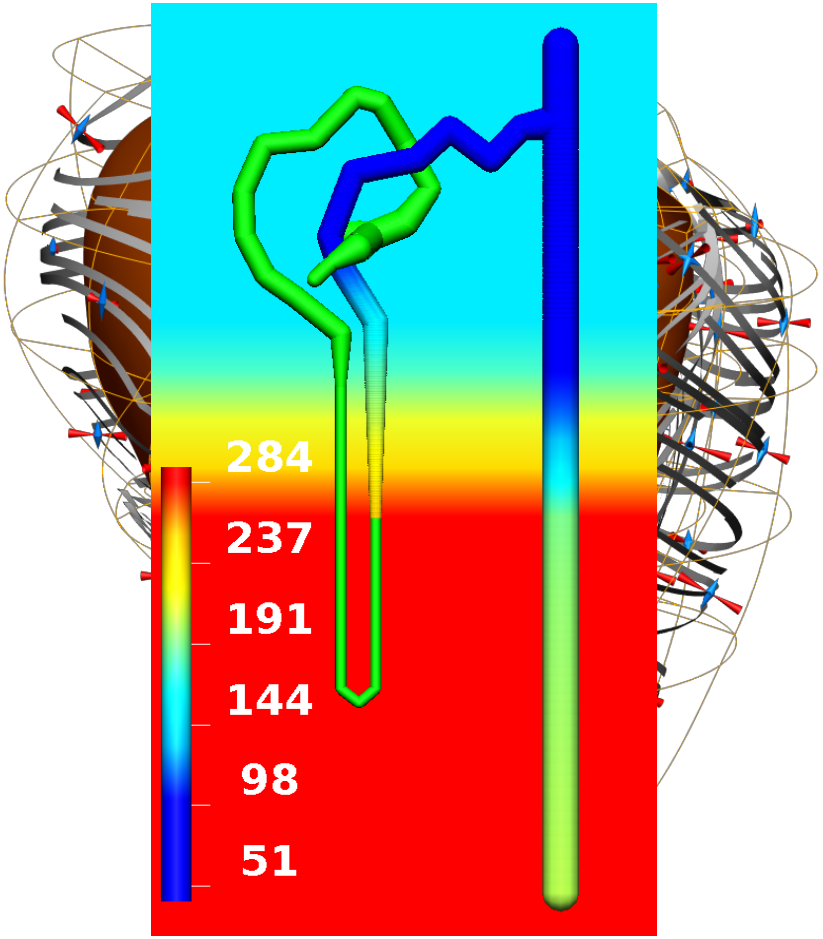
Fig.: Example simulation results (Le Novère, *Neuroinformatics (2010)*)

Similarly for complex models!



× time
× patient
× drug dose
× …

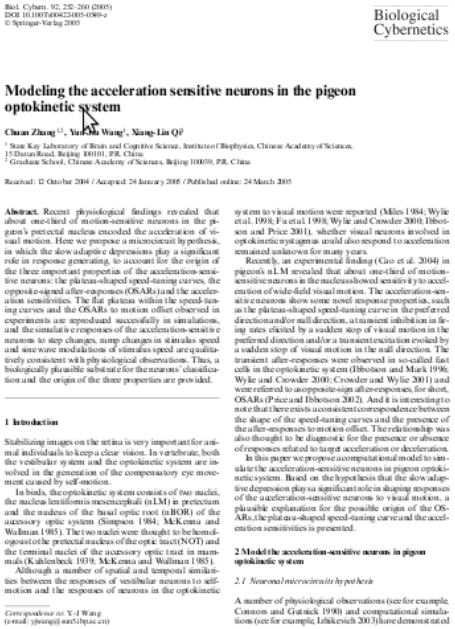
Similarly for complex models!



× time
× patient
× drug dose
× …

SED-ML Motivation

Biological publication repository



Modeling the acceleration sensitive neurons in the pigeon optokinetic system

Chuan Zhang, Yun-Shu Wang, Xiang-Lin Qi

Simulation tool

models

?

Simulation result

SED-ML Motivation

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"[..] in Biomodels 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. [..] "
(arvin mer on sbml-discuss)

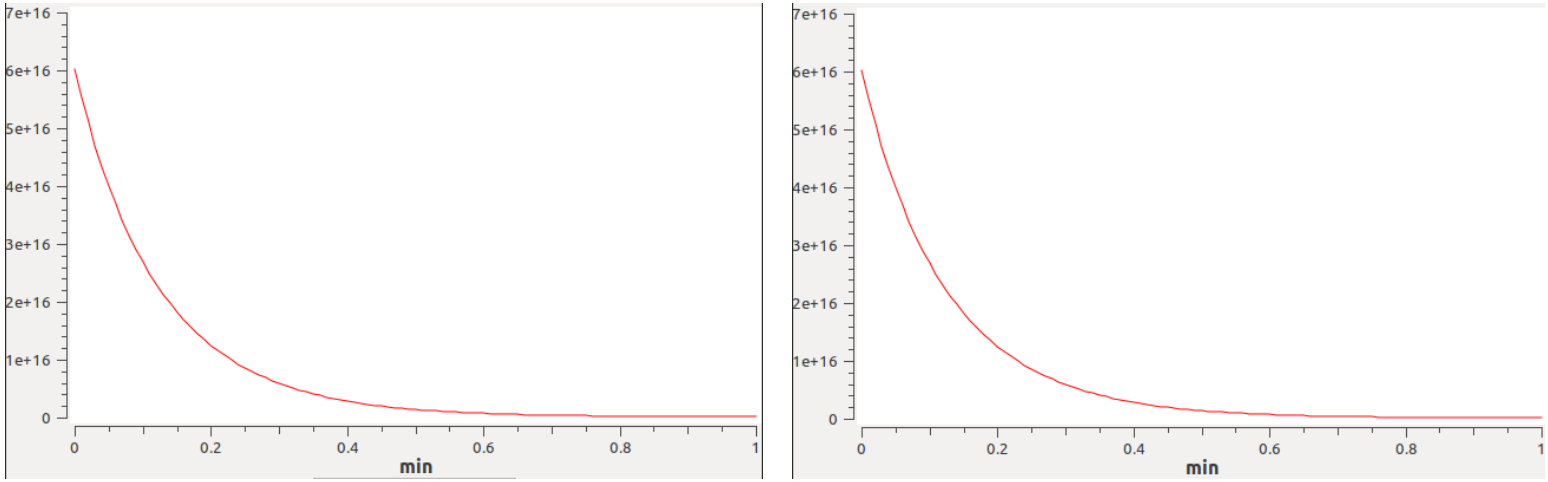

Fig.: running model files (COPASI simulation tool)

SED-ML Motivation

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"[..] in Biomodels 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. [..] "
(arvin mer on sbml-discuss)

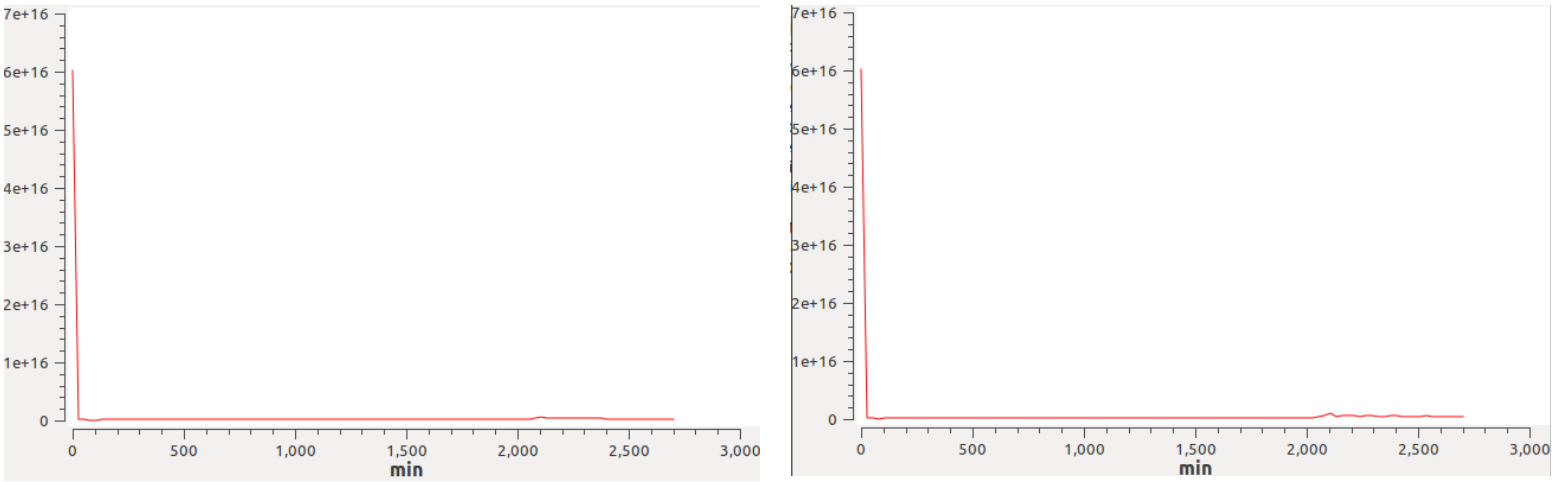
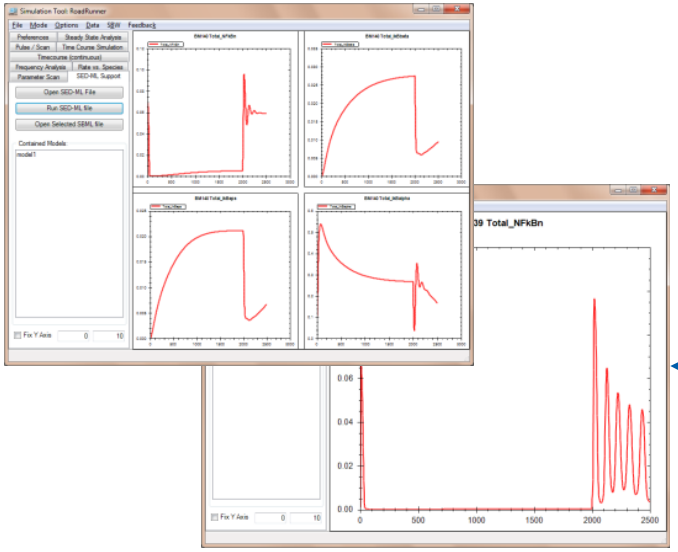


Fig.: running model files (COPASI simulation tool)

SED-ML Motivation

BIOMD0000000139 , BIOMD0000000140



Simulation results (SBW Workbench)

SED ML

Simulation

Systems Biology Workbench

models

BioModels

SED-ML Level 1 Version 1

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Levels: *major revisions containing substantial changes*

Versions: *minor revisions containing corrections and refinements*

Editorial board: *coordinates SED-ML development (elected by sed-ml-discuss members)*

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

March 25, 2011

Editors

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

The latest release of the Level 1 Version 1 specification is available at
http://sed-ml.org/

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
sed-ml-editors@lists.sourceforge.net

SED-ML Level 1 Version 1:

- multiple models
- multiple simulation setups
- time course simulations
- no “nested simulation”
- only explicit model entities can be addressed (XPath)

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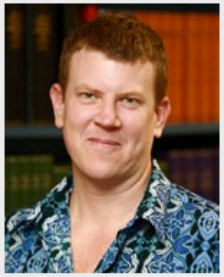
sed-ml.org/about.html

The SED-ML specification is written by an editorial board consisting of five editors. They are elected by the SED-ML community (members of the sed-ml-discuss mailing list) and serve for 3-year terms as volunteers.

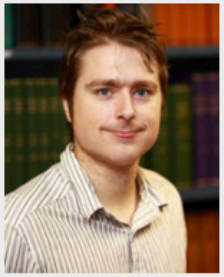
Frank Bergmann (editor, elected 2011-*2014*)
Frank T. Bergmann (PhD in Computational and Systems Biology) is a researcher at the **California Institute of Technology** where his primary interest is in standardization efforts around **SBML**. He is also the lead developer of the **Systems Biology Workbench** along with the **LibSEDML library**.

Dagmar Waltemath (editor, elected 2011-*2014*)
Dagmar Waltemath (Diploma degree in Computer Science) is guest researcher at the **Systems Biology and Bioinformatics group, Rostock**. She works on the standardisation of simulation experiment descriptions in Computational Biology (**MIASE**).

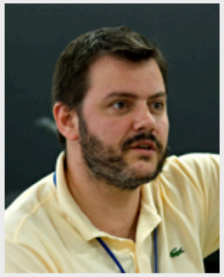
Richard Adams (editor, elected 2011-*2013*)
Richard Adams (PhD in Cell Biology) is software project manager at the **Centre for Systems Biology, Edinburgh**. He works on the **SBSI systems biology software framework**, SED-ML tools and the jlibsedml Java library for SED-ML.



David Nickerson (editor, elected 2011-*2013*)
David Nickerson is a Research Fellow in the Auckland Bioengineering Institute where he leads the Auckland Kidney Physiome project. David is also involved in many aspects of the CellML project as well as various cardiac modeling projects. He also develops several CellML-related software tools.



Andrew Miller (editor, elected 2011-*2012*)
Andrew Miller is a researcher at the **Auckland Bioengineering Institute**. His research interests focus around the representation of mathematical models; he is involved in the development of tools for processing **CellML** models, including SProS, a SED-ML processing service that forms part of the CellML API.



Nicolas Le Novère (editorial advisor)
Nicolas Le Novère is a group leader at the **EMBL-European Bioinformatics Institute**. His research unfolds along two axis: 1) modelling neuronal signalling, at the molecular, sub-cellular and cellular levels, and 2) developing tools and resources for systems biology, in particular including standards.

Main building blocks

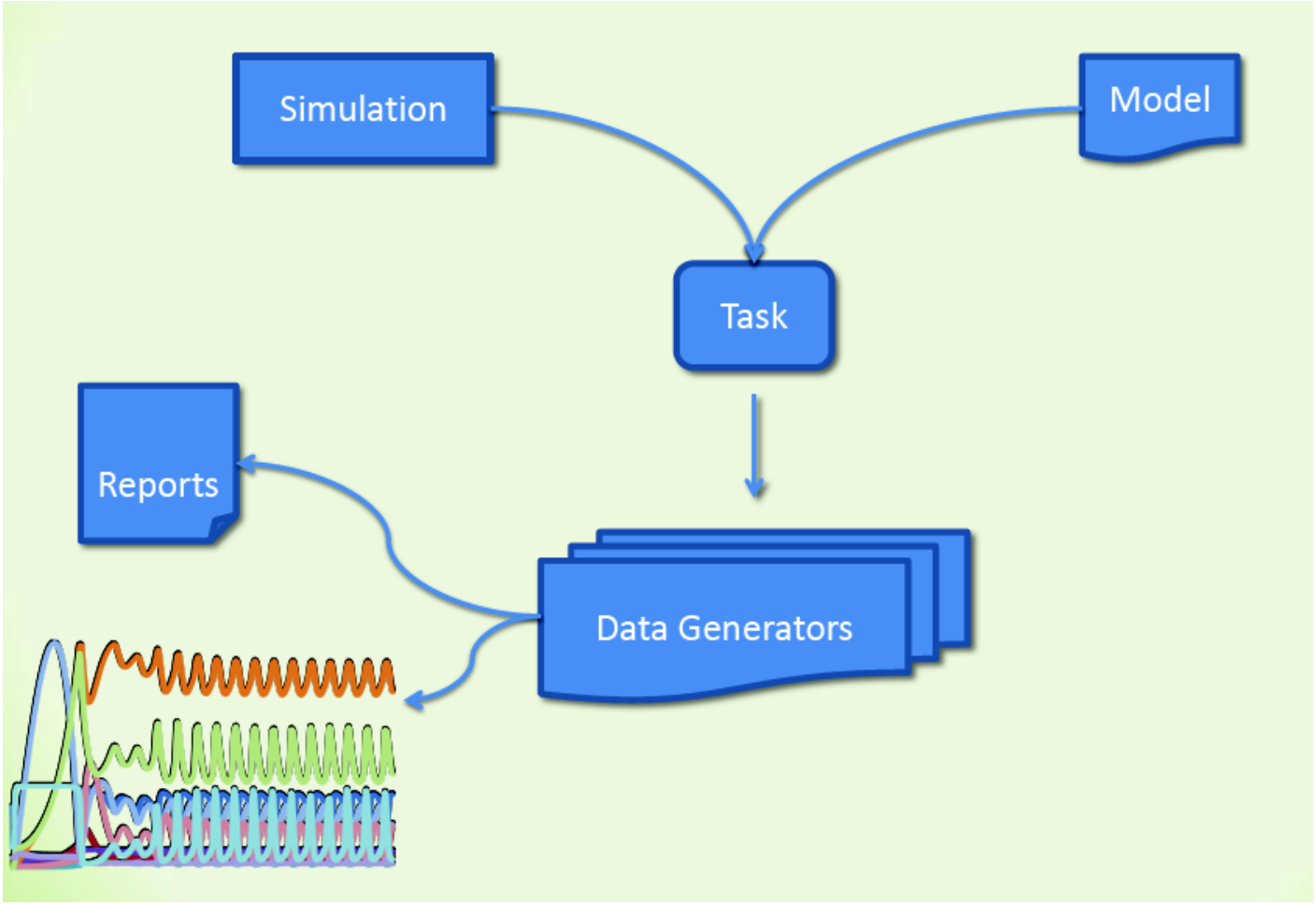


Figure: SED-ML structure *(Waltemath et al., 2011)*

SED-ML – What does it look like?

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                outputStartTime="0" outputEndTime="1000" numberOfPoints="1000">
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        <model id="model1" name="Repressilator-regular oscillations"
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                <notes>
        <p xmlns="http://www.w3.org/1999/xhtml">
        This is the unmodified model.
        </p>
        </notes>
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                language="urn:sedml:language:sbml.level-2.version-3" source="model1">
                        <notes>
        <p xmlns="http://www.w3.org/1999/xhtml">
        This variant produces damped oscillations.
        </p>
```

SED-ML – What does it look like?

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<listOfSimulations>
        <uniformTimeCourse id="simulation1" initialTime="0"
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                        <notes>
        <p xmlns="http://www.w3
        This variant produces damped oscillations.
        </p>
```
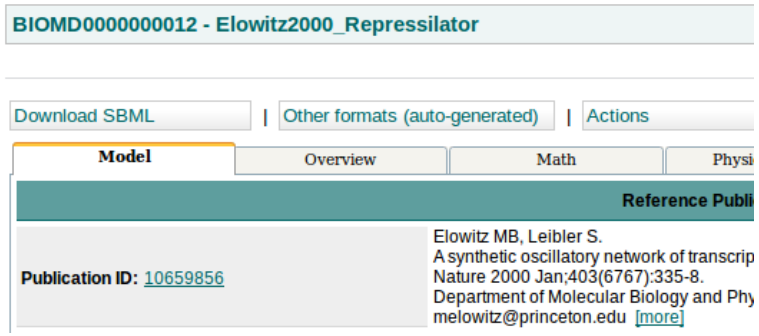

KiSAO

next reaction method

SBML



Example: Running a simple model of spiking neurons

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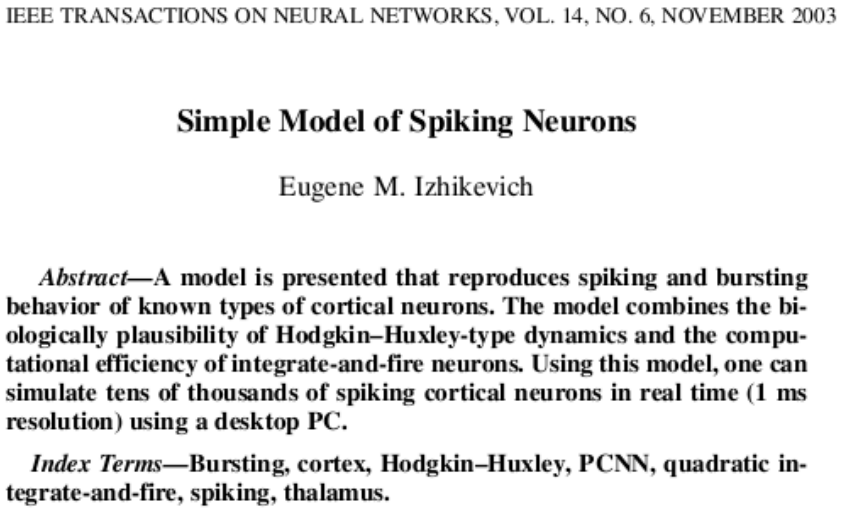


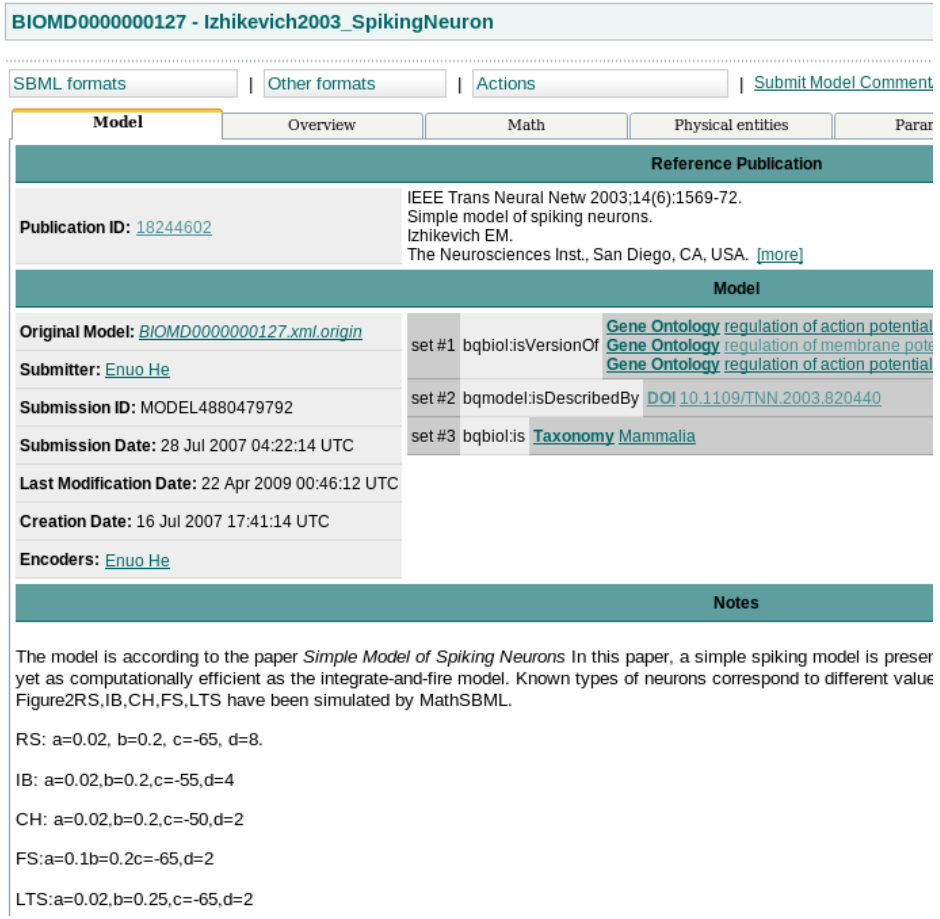
IEEE TRANSACTIONS ON NEURAL NETWORKS, VOL. 14, NO. 6, NOVEMBER 2003

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

Example: What is encoded in the model

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

Example: What is encoded in the model

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Model available from **BioModels DB**:
urn:miriam:biomodels.db:BIOMD0000000127
Representing the **Simple model of spiking neurons** published by **Izhikevich (2003)** in urn:miriam:pubmed:18244602
Model is for organism **mammals** urn:miriam:taxonomy:40674

1 compartment is version of

a **cellular compartment** urn:miriam:obo.go:GO%3A0005623

1 standard species

No reactions

8 global quantities (parameters)

2 rate rules encoded: 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

2 events encoded: 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

Example: What happens if I just simulate?

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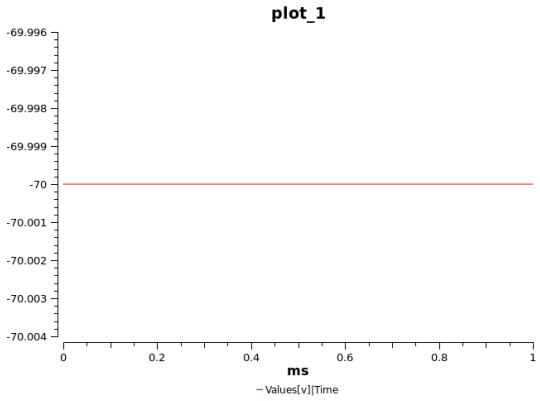
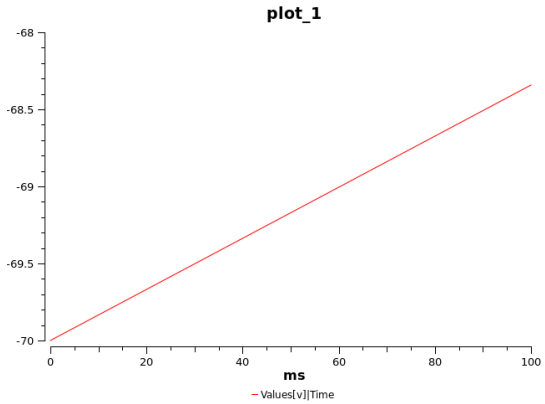
First attempt to run the model, measuring the spiking rate *v* over time

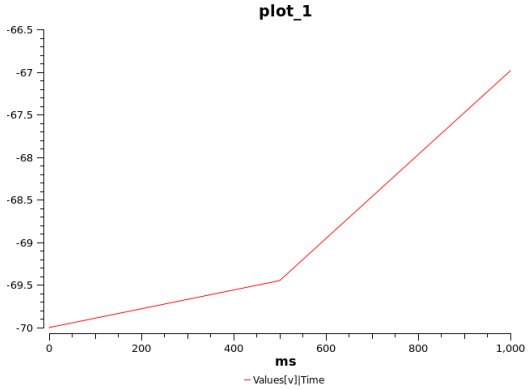
- load SBML into the simulation tool COPASI
- use parametrisation as given in the SBML file
- define output variables (**v**)
- run the time course



1 ms (standard)



100ms



1000ms

Example: What happens if I just simulate?

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Second attempt to run the model, adjusting simulation step size and duration

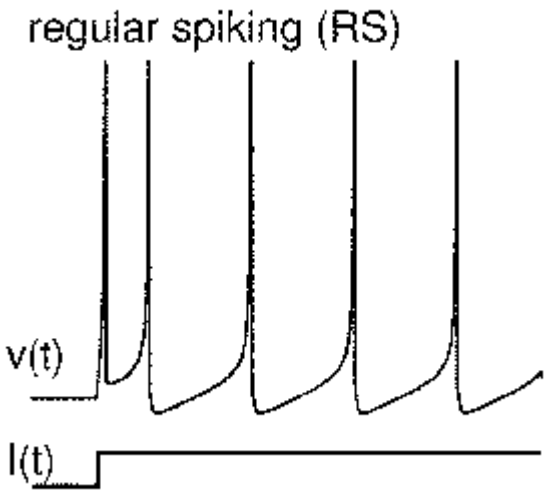

Fig: reference publication

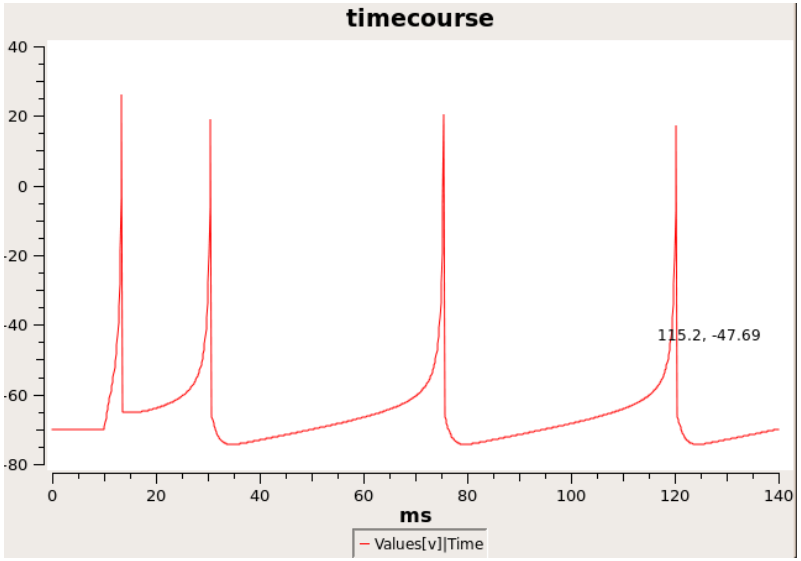

Fig.: COPASI simulation, duration: 140ms, step size: 0.14

Example: What happens if I just simulate?

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Third attempt to run the model, updating initial model parameters

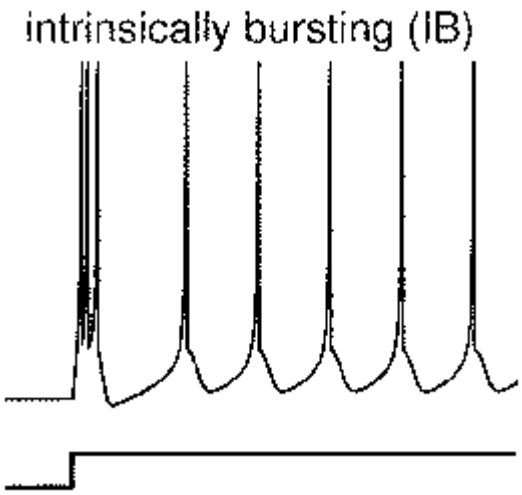

Fig.: reference publication

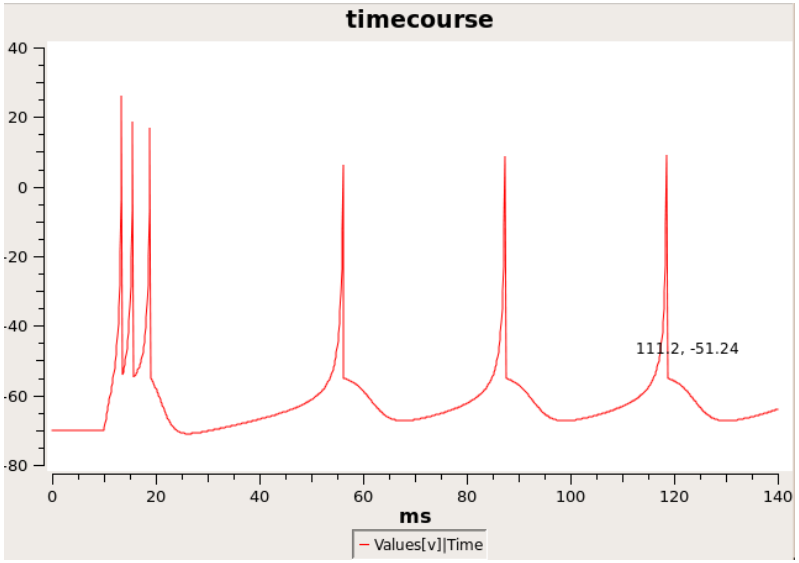

Fig.: COPASI, adjusted parameter values (a=0.02, b=0.2 **c=-55, d=4**)

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models.cellml.org/e/71/view

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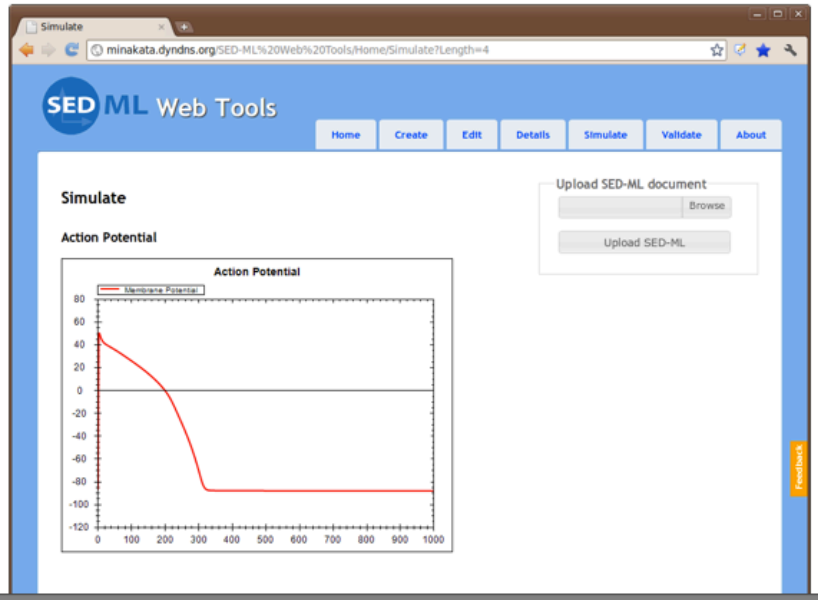
The ORd human ventricular action potential model

This workspace houses a CellML 1.0 encoding of the 2011 O'Hara, Virág, Varró, & Rudy 2011 human cardiac ventricular action potential model (ORd). The original article is available at: http://www.ncbi.nlm.nih.gov/pubmed/21637795. This model was encoded based on the Matlab version of the code available from: http://rudylab.wustl.edu/research/cell/.

The CellML 1.0 encoding of the ORd model was contributed by Steven Niederer. While the units in the CellML encoding are not yet perfect, it is a match for the Matlab code and matches the simulation output for a single beat perfectly. The figure below shows the output of the simulation experiment action-potential.xml encoded in SED-ML using the original version of the model from Steve. This output is generated by running the simulation experiment using the SED-ML Web Tools.



Model Curation

Curation Status:

Source

Derived from workspace An encoding of the human ORd model by Steve Neiderer at changeset a96ef0c61614.

Downloads

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Navigation

Ohara_Rudy_2011.cellml

action-potential.xml

cellML

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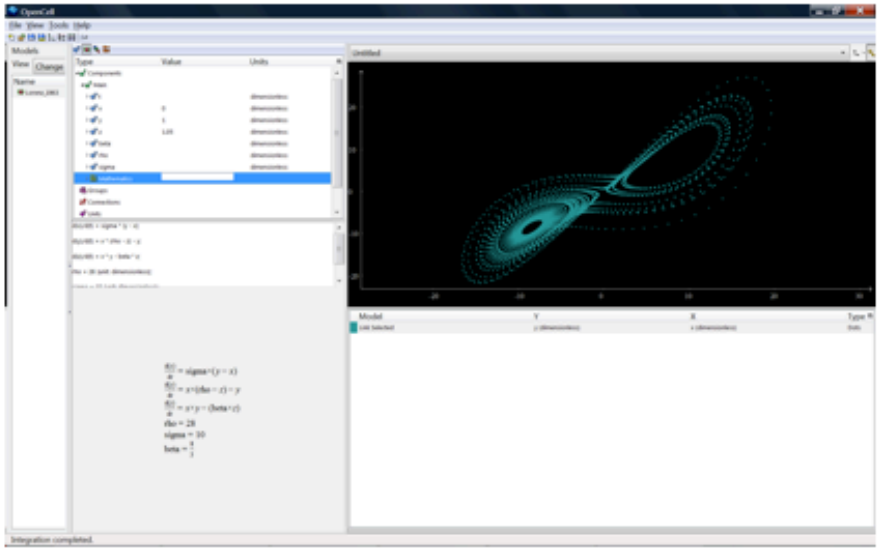
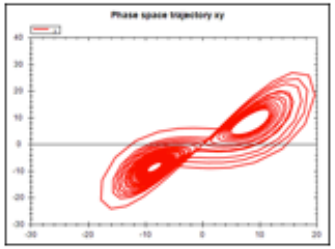
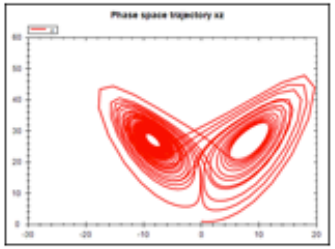
The Lorenz Attractor, a classical mathematical model

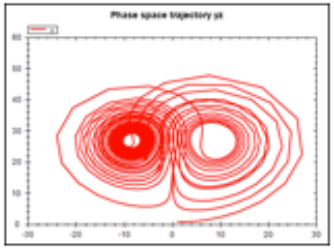
This workspace houses a CellML encoding of the 1963 Lorenz model which became a well-known demonstration of deterministic chaos. The original article DOI is 10.1175/1520-0469(1963)020<0130:DNF>2.0.CO;2. This model was encoded based on the Octave code available in the related Wikipedia article.

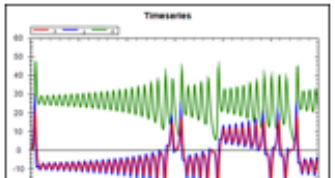
An OpenCell 0.8 session file is available. SED-ML can also be used to simulate this model, the simulation description is in Lorenz_1963_sedml.xml, and the simulation experiment can be run using the SED-ML Web Tools. The figures below show the results fro OpenCell and from using SED-ML.











Model Curation

Curation Status: ☆☆☆

OpenCell: ★☆☆

Source

Derived from workspace Deterministic Nonperiodic Flow at changeset 1cdf5c612924.

Downloads

Complete Archive as .tgz

Navigation

The Lorenz Attractor, a classical mathematical model

How to contribute to SED-ML

SYSTEMS BIOLOGY
BIOINFORMATICS
ROSTOCK

1. Have a look at the current SED-ML
   Specification document on http://sed-ml.org

2. Try out some of the existing examples
   http://sed-ml.org and http://sourceforge.net/projects/libsedml

3. Identify what is missing for you to encode your simulation experimental setups - What can you not express?

4. Submit a feature request & post it on the list

feature request tracker: http://sourceforge.net/projects/sed-ml

mailing list: sed-ml-discuss@lists.sourceforge.net

1. … submit a proposal with example files and prototype

proposal tracker: http://sourceforge.net/projects/sed-ml