# Introduction to SED-ML – the Simulation Experiment Description Markup Language

**BrainScaleS CodeJam/NeuroML workshop, Edinburgh**

13th March 2012

Dagmar Waltemath

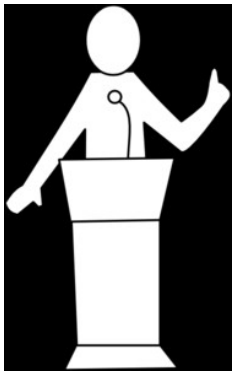

SYSTEMS BIOLOGY
BIOINFORMATICS
ROSTOCK

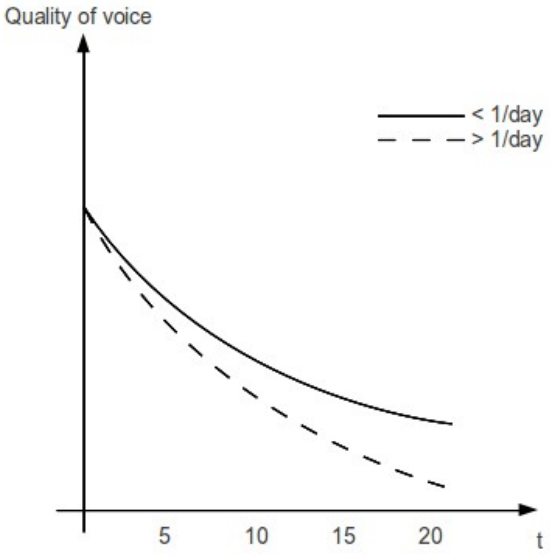
Universität
Rostock


Traditio et Innovatio

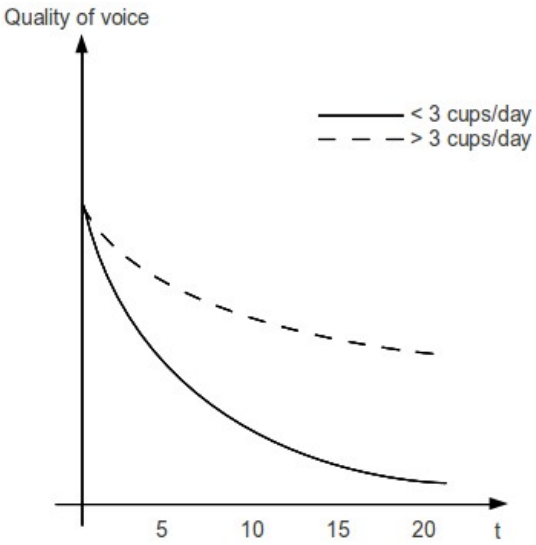
# Motivation

[a probably copy-righted Whisky image] & [a probably copy-righted honey image] =

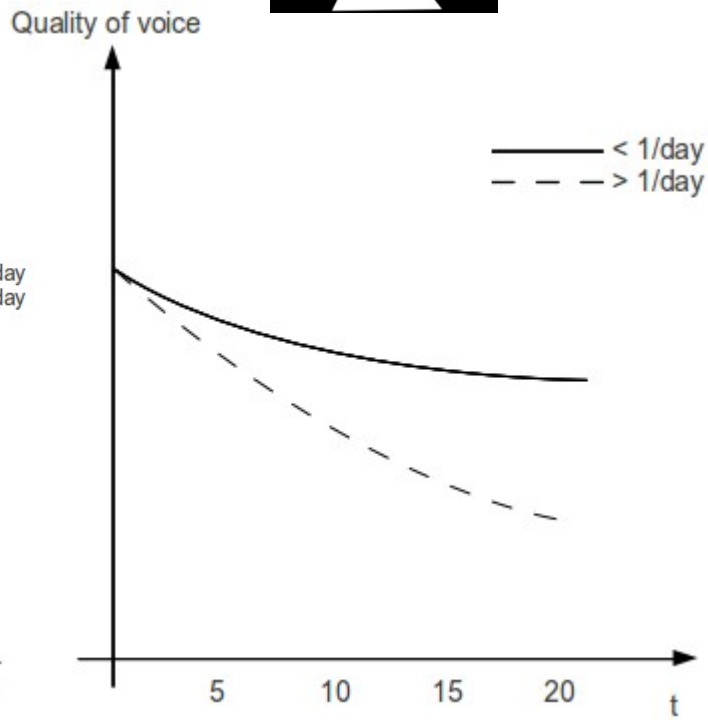





whisky




honey




combined

# Motivation



Biological publication repository

Biological Cybernetics

Modeling the acceleration sensitive neurons in the pigeon optokinetic system

Chuan Zhang [1], Yu-Mei Wang [1], Xiang-Lin Qi [2]

[1] State Key Laboratory of Brain and Cognitive Science, Institute of Biophysics, Chinese Academy of Sciences, 15 Datun Road, Beijing 100101, P.R. China
[2] Graduate School, Chinese Academy of Sciences, Beijing 100039, P.R. China

Received: 12 October 2004 / Accepted: 24 January 2005 / Published online: 24 March 2005

Abstract. Recent physiological findings revealed that about one-third of motion-sensitive neurons in the pigeon's pretectal nucleus encoded the acceleration of visual motion. Here we propose a microcircuit hypothesis, in which the slow adaptive depressions play a significant role in response generating, to account for the origin of the three important properties of the acceleration-sensitive neurons: the plateau-shaped speed-tuning curves, the opposite-signed after-responses (OSARs) and the acceleration sensitivities. The flat plateau within the speed-tuning curves and the OSARs to motion offset observed in experiments are reproduced successfully in simulations, and the simulative responses of the acceleration-sensitive neurons to step changes, ramp changes in stimulus speed and sine wave modulations of stimulus speed are qualitatively consistent with physiological observations. Thus, a biologically plausible substrate for the neurons' classification and the origin of the three properties are provided.

1 Introduction

Stabilizing images on the retina is very important for animal individuals to keep a clear vision. In vertebrate, both the vestibular system and the optokinetic system are involved in the generation of the compensatory eye movement caused by self-motion.

In birds, the optokinetic system consists of two nuclei, the nucleus lentiformis mesencephali (nLM) in pretectum and the nucleus of the basal optic root (nBOR) of the accessory optic system (Simpson 1984; McKenna and Wallman 1985). The two nuclei were thought to be homologous to the pretectal nucleus of the optic tract (NOT) and the terminal nuclei of the accessory optic tract in mammals (Kahlenbeck 1939; McKenna and Wallman 1985).

Although a number of spatial and temporal similarities between the responses of vestibular neurons to self-motion and the responses of neurons in the optokinetic system to visual motion were reported (Miles 1984; Wylie et al. 1993; Fu et al. 1993; Wylie and Crowder 2000; Ibbotson and Price 2001), whether visual neurons involved in optokinetic nystagmus would also respond to acceleration remained unknown for many years.

Recently, an experimental finding (Gao et al. 2004) in pigeon's nLM revealed that about one-third of motion-sensitive neurons in the nucleus showed sensitivity to acceleration of wide-field visual motion. The acceleration-sensitive neurons show some novel response properties, such as the plateau-shaped speed-tuning curve in the preferred direction and/or null direction, a transient inhibition in firing rates elicited by a sudden stop of visual motion in the preferred direction and/or a transient excitation evoked by a sudden stop of visual motion in the null direction. The transient after-responses were observed in so-called fast cells in the optokinetic system (Ibbotson and Mark 1996; Wylie and Crowder 2000; Crowder and Wylie 2001) and were referred to as opposite-sign all on-responses, for short, OSARs (Price and Ibbotson 2002). And it is interesting to note that there exists a consistent correspondence between the shape of the speed-tuning curves and the presence of the after-responses to motion offset. The relationship was also thought to be diagnostic for the presence or absence of responses related to target acceleration or deceleration.

In this paper we propose a computational model to simulate the acceleration-sensitive neurons in pigeon optokinetic system. Based on the hypothesis that the slow adaptive depression plays a significant role in shaping responses of the acceleration-sensitive neurons to visual motion, a plausible explanation for the possible origin of the OSARs, the plateau-shaped speed-tuning curve and the acceleration sensitivities is presented.

2 Model the acceleration-sensitive neurons in pigeon optokinetic system

2.1 Neuronal microcircuits hypothesis

A number of physiological observations (see for example, Connors and Gutnick 1990) and computational simulations (see for example, Ishikevich 2003) have demonstrated

Correspondence to: Y.-J. Wang (e-mail: yjwang@sun5.ibp.ac.cn)

Simulation tool

models

cellML biology. math. data. knowledge.

SBML

NeuroML

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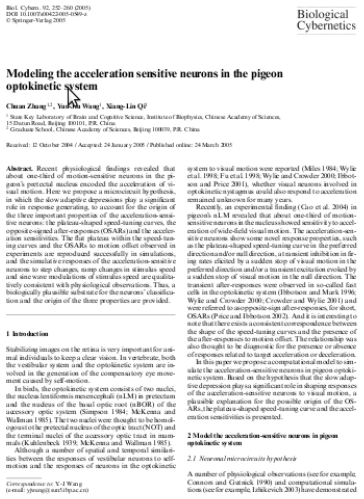
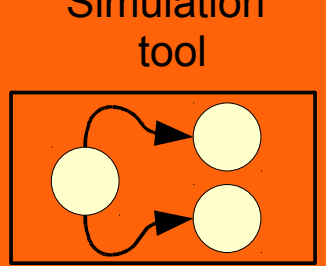


Biological Cybernetics

Modeling the acceleration sensitive neurons in the pigeon optokinetic system

Simulation tool



models

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SBML

[NeuroML]

?

Simulation results

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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)

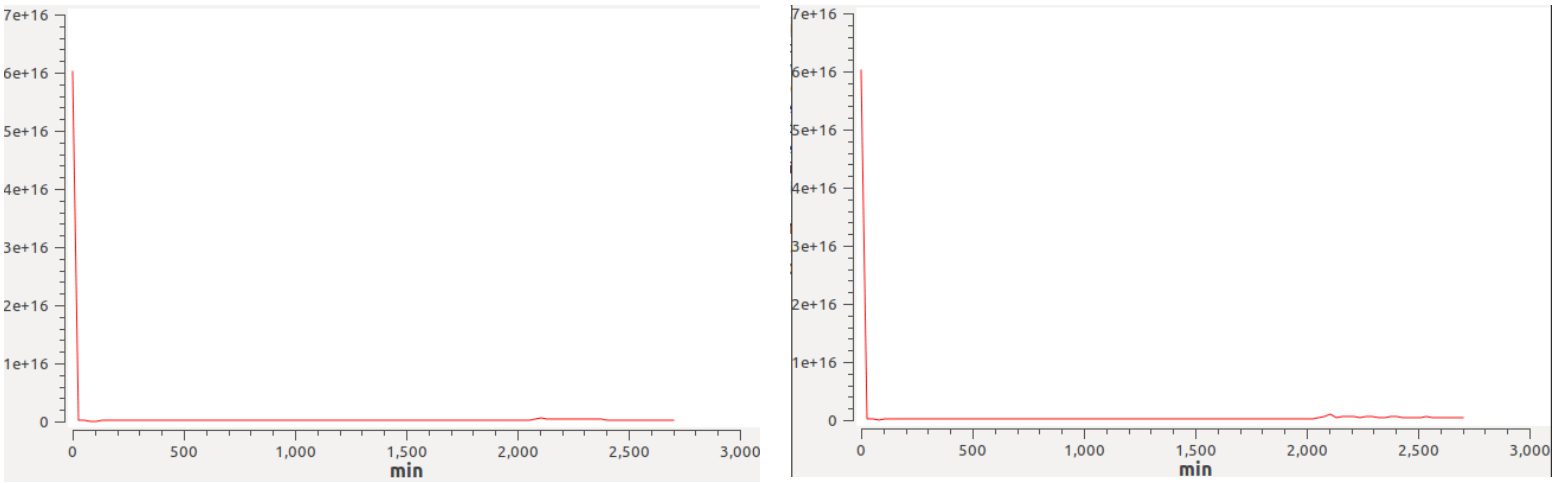


Fig.: running model files (COPASI simulation tool)

# Motivation

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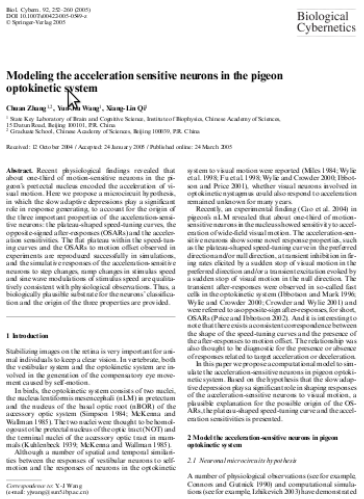


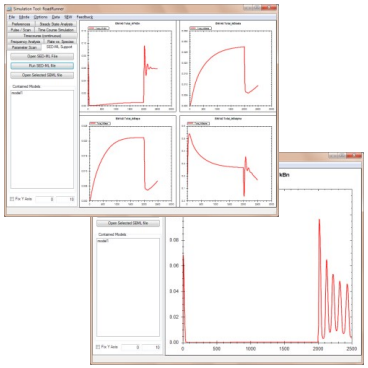

Simulation results
(SBW Workbench)

Simulation tool

Systems Biology Workbench

models

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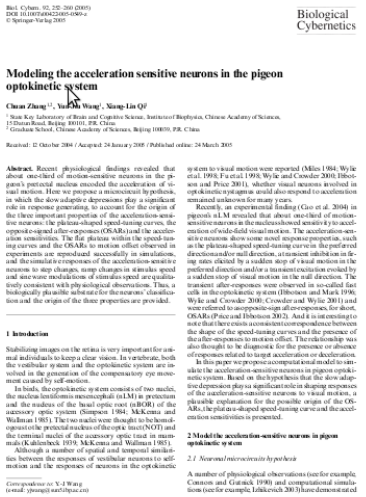
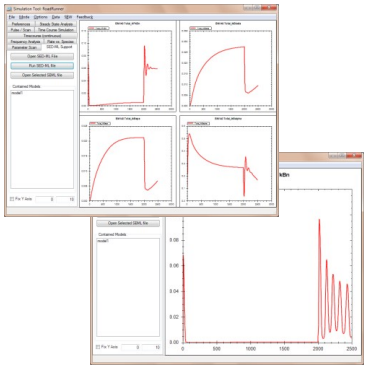
NeuroML

# Motivation



Biological publication repository

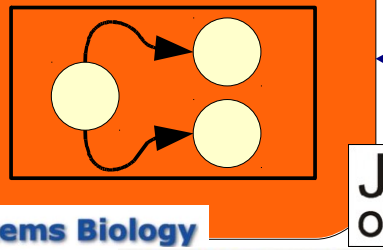


Simulation results
(SBW Workbench)

SED ML

Simulation tool



JWS online

models

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[NeuroML]

Systems Biology Workbench

CellDesigner.org

# 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)*

SED-ML Level 1 Version 1:

- multiple models
- multiple simulation setups
- time course simulations

**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

# Major building blocks



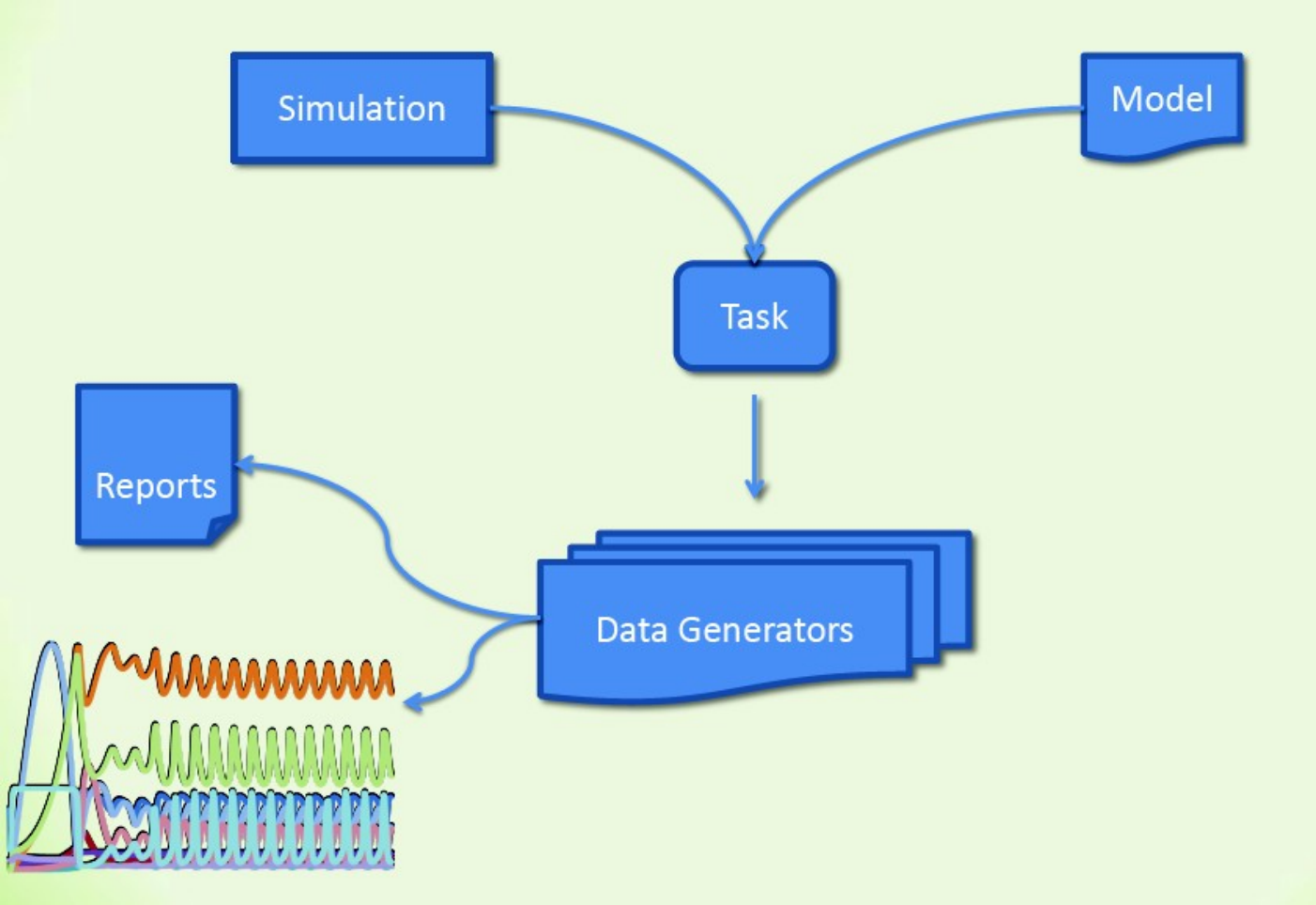


Fig.: SED-ML structure *(Waltemath et al., 2011)*

# Model Class: defining the models used in the experiment set-up

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- Ideally: link that unambiguously defines a model in an open repository
- Optionally: model preprocessing

  e.g., updated or additional model parameter, substituted mathematical function...

```
<model id="model1" name="spiking neuron"
  language="urn:sedml:language:sbml.level-2.version-3"
  source="urn:miriam:biomodels.db:BIOMD0000000127">
    <listOfChanges>
      <changeAttribute
        target="/sbml/model/listOfParameters/parameter
        [@name='c']/@value" newValue="-55">
      </changeAttribute>
    </listOfChanges>
</model>
```

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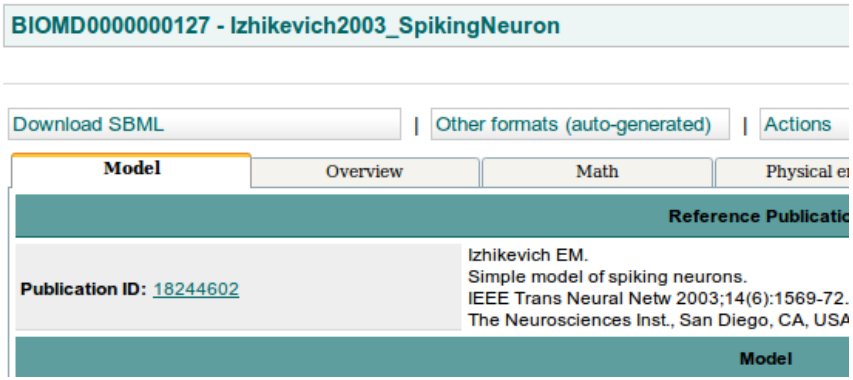

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# Simulation Class: setting up the simulation

SYSTEMS BIOLOGY BIOINFORMATICS ROSTOCK

- Defining the type of simulation
- Defining the simulation algorithm to apply and its settings
  - Reference: Kinetic Simulation Algorithm Ontology
    http://www.biomodels.net/kisao/

```
<uniformTimeCourse id="simulation1"
 initialTime="0"
 outputStartTime="0"
 outputEndTime="1000"
 numberOfPoints="1000">
  <algorithm kisaoID="KISAO:0000088" />
</uniformTimeCourse>
```

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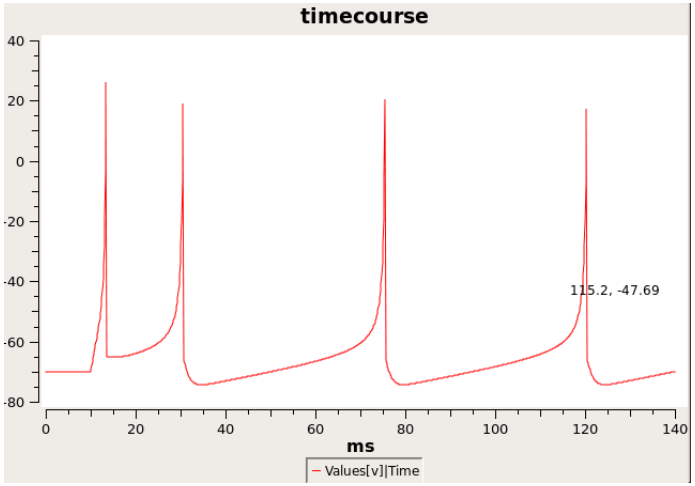


Fig.: COPASI simulation tool

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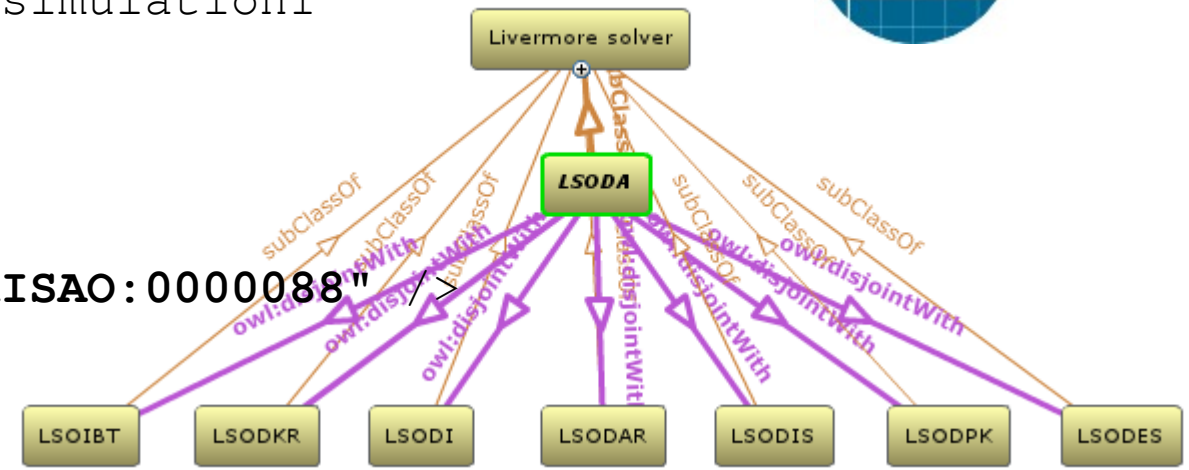

# TaskClass: grouping models and simulations

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- Assigning 1 simulation to 1 model at a time
- Multiple tasks

```
<listOfTasks>
  <task id="task1" name="spiking with initial
   parameters" modelReference="model1"
   simulationReference="simulation1" />
  <task id="task2" name="spiking with updated
   parameters" modelReference="model2"
   simulationReference="simulation1" />
</listOfTasks>
```

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```

# DataGenerator Class: Post-processing

SYSTEMS BIOLOGY BIOINFORMATICS ROSTOCK

- Defining all entities needed in the outputs
- Processing of result data after simulation
- Only on explicitly defined model entities
- ...and on predefined implicit variables,
  e.g., time

```
<dataGenerator id="v" name="voltage">
  <listOfVariables>
    <variable id="v1" taskReference="task1"   target="/sbml/
     model/listOfParameters/parameter[@id='v']"/>
  </listOfVariables>
  <math:math>
    <math:ci>v1</math:ci>
  </math:math>
</dataGenerator>
```

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SYSTEMS BIOLOGY BIOINFORMATICS ROSTOCK

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  </listOfVariables>
  <math:math>
    <math:ci>v1</math:ci>
  </math:math>
</dataGenerator>
```

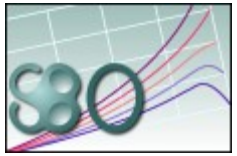

“voltage”

# Output Class: defining the simulation output

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- Defining an output type
- Defining what is to be stored/plotted for the output

```
<plot2D id="plot1_Basic" name="voltage change over time">
  <listOfCurves>
    <curve id="c1" logX="false" logY="false"
     xDataReference="timeDG" yDataReference="v" />
  </listOfCurves>
</plot2D>
```

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SYSTEMS BIOLOGY BIOINFORMATICS ROSTOCK

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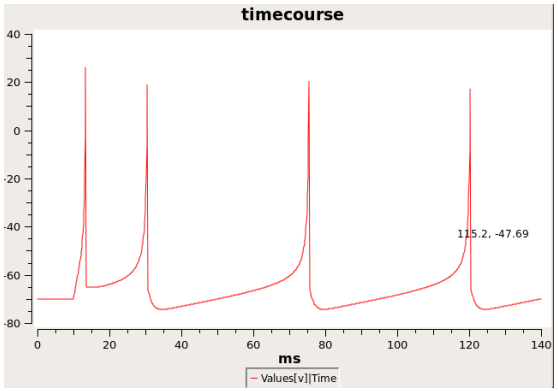


Fig.: COPASI simulation tool

# Example: SED-ML in Computational Biology

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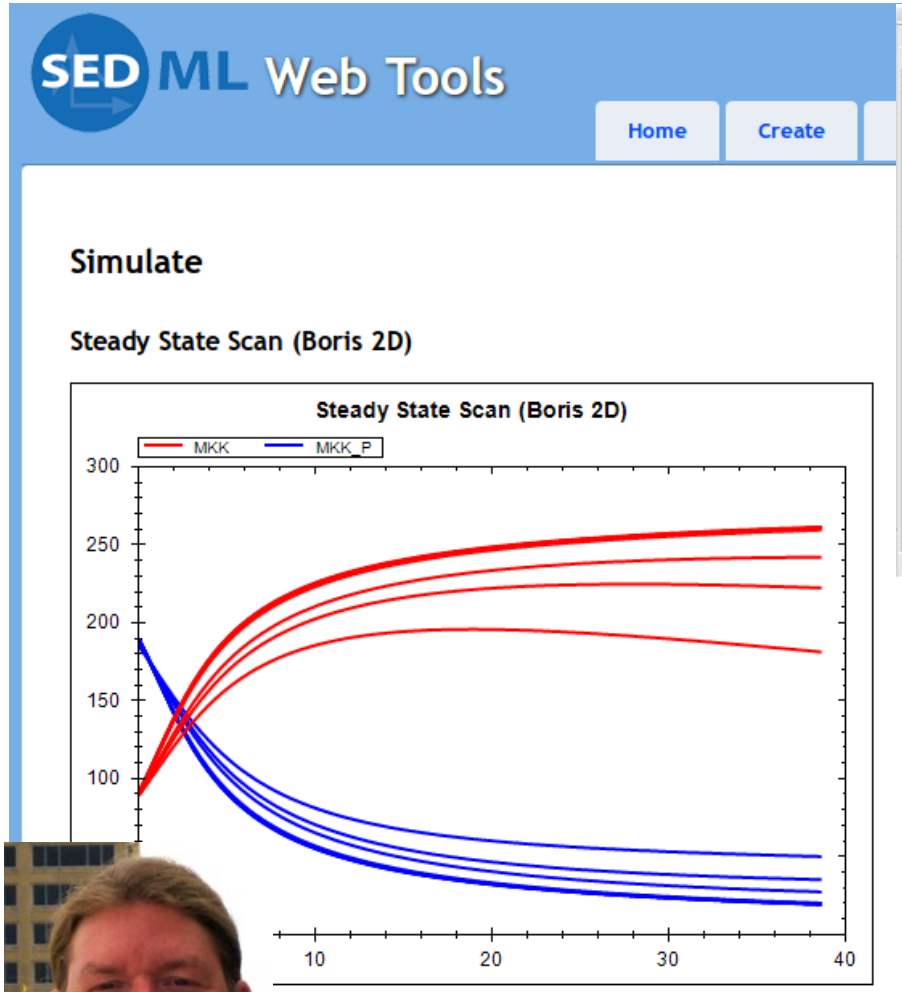
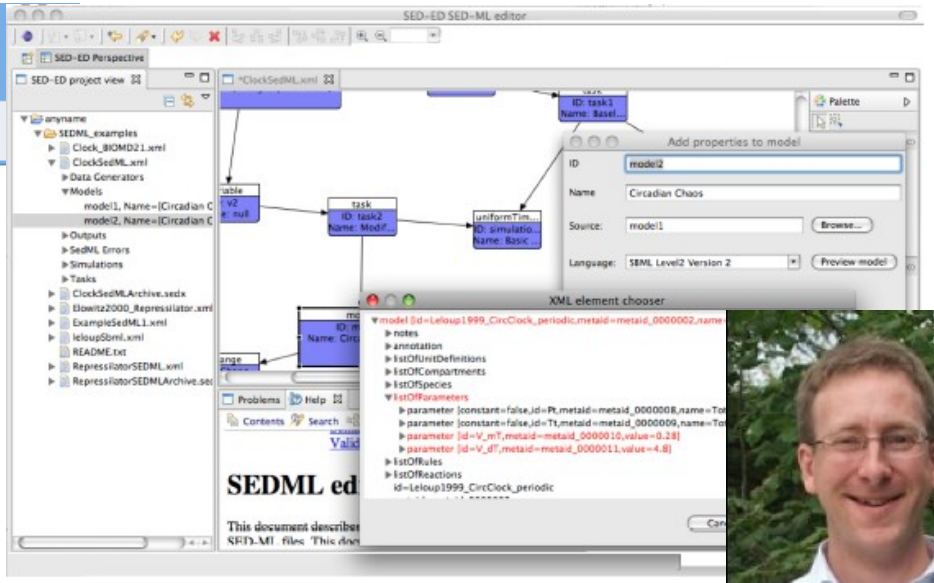
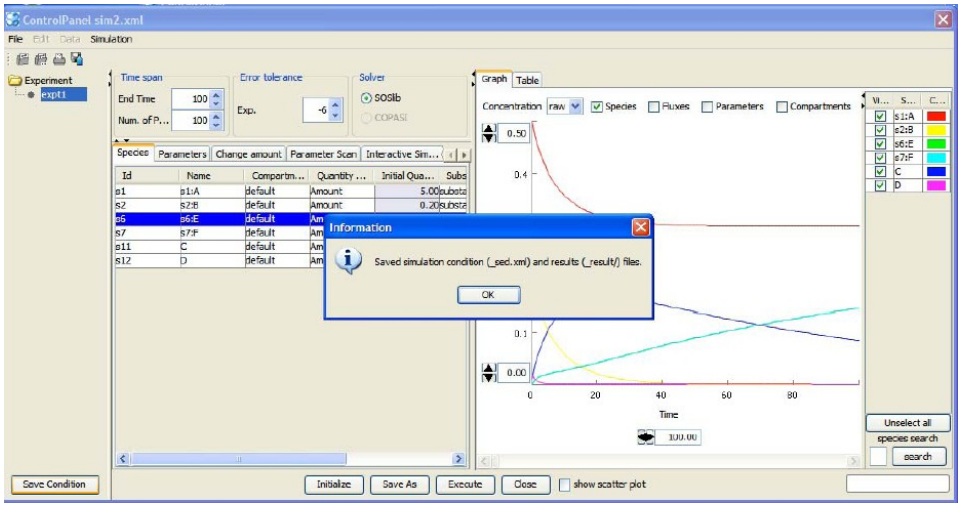





SED-ED (Bioinformatics. 2012 Feb 25)




http://sysbioapps.dyndns.org/SED-ML_Web_Tools

Fig.:SED-ML import/export in CellDesigner

# Example: SED-ML and the CellML repository

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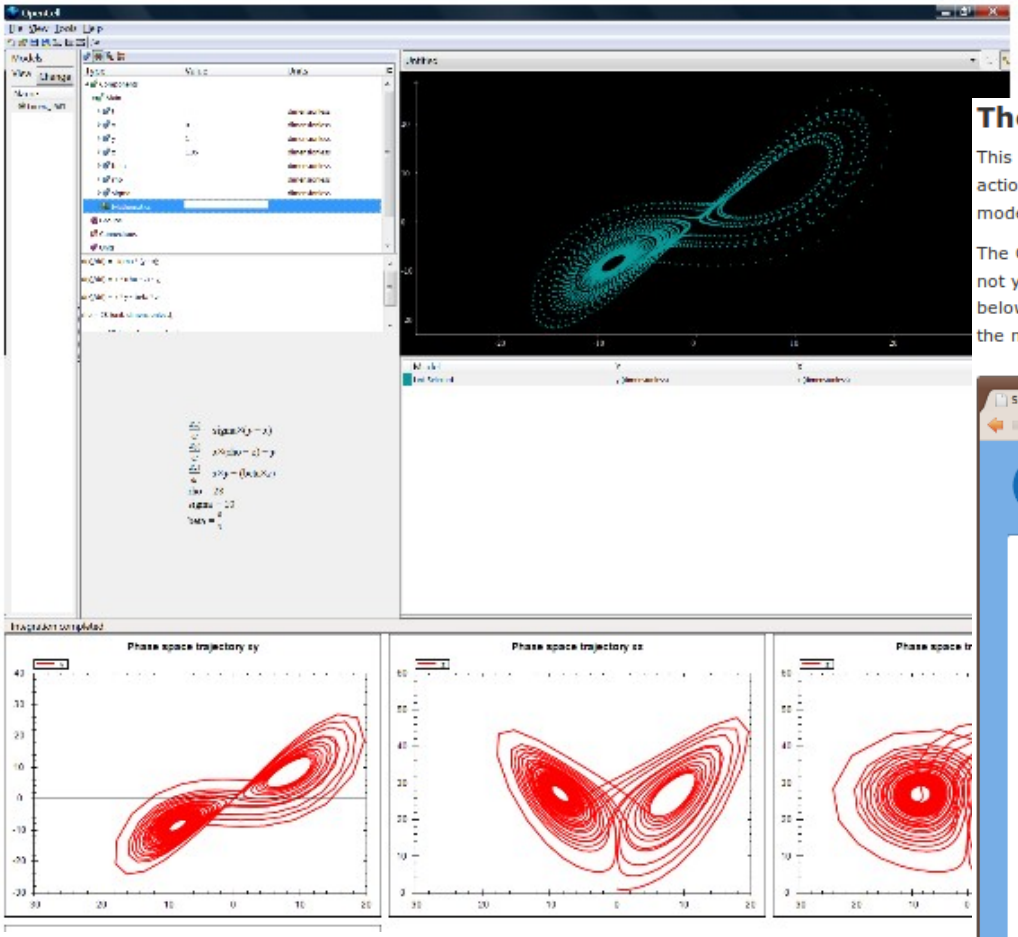
An OpenCell 0.8 session file is available. SED-ML can also be used to simulate this model, the simulation description is in Lorenz_1963_sedml.xml, and the simulation experiment can be run using the SED-ML Web Tools. The figures below show the results fro OpenCell and from using SED-ML.




## 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
action potential model (ORd). The original article is available at: http://www.ncbi.nlm.nih.gov/pubmed
model was encoded based on the Matlab version of the code available from: http://rudylab.wustl.edu

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

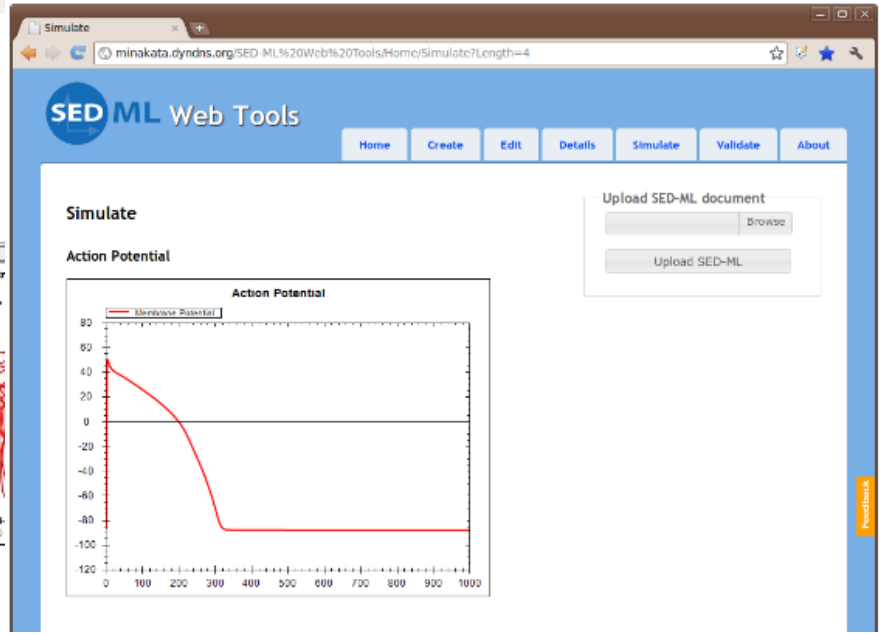



Fig.: CellML models with supplement SED-ML files. (CellML model repository)

# Example: SED-ML for computational neuroscience

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J Neurosci. 2002 Nov 1;22(21):9475-89.

**Response of neurons in the lateral intraparietal area during a combined visual discrimination reaction time task.**

Roitman JD, Shadlen MN.

Program in Neurobiology and Behavior, Department of Physiology and Biophysics, and Regional Primate Research Center, University of Washington, Seattle, Washington 98195-7290, USA.

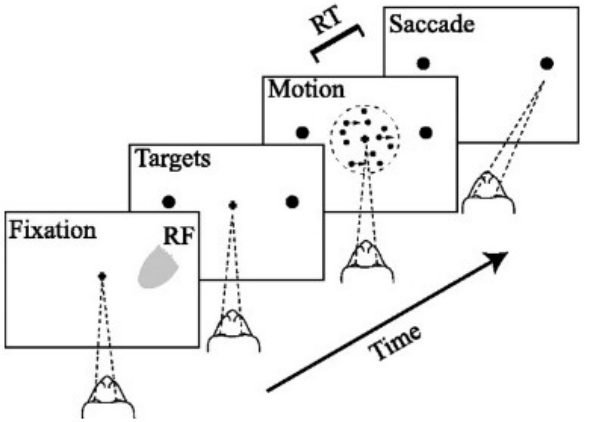
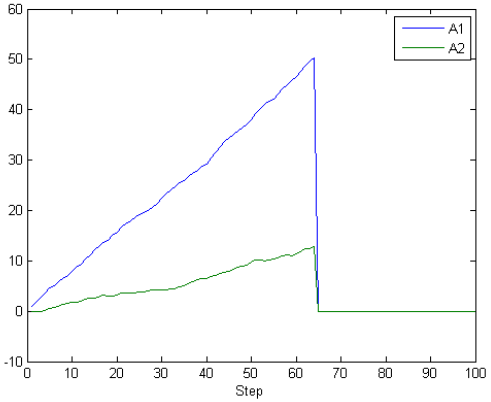
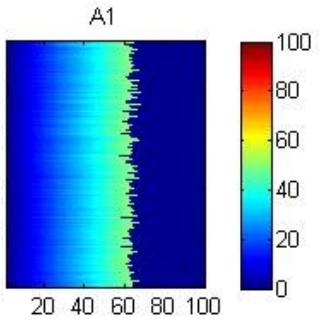
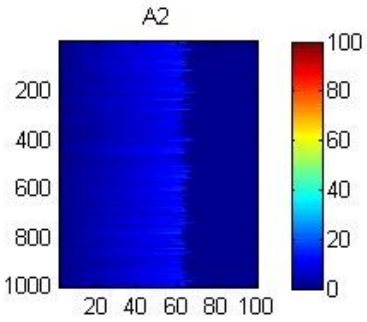
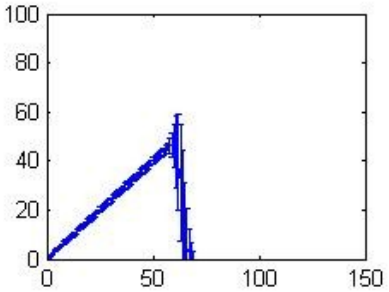


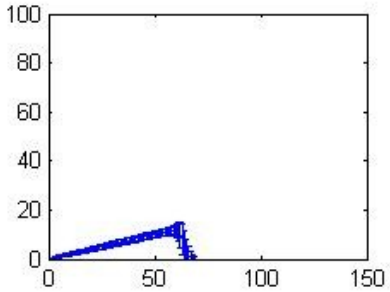

Fig.: *Roitman, Shadlen (2002)*





http://ars.informatik.uni-rostock.de/

# How to contribute to SED-ML

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1. Have a look at the current SED-ML L1 V1

   Specification document on http://sed-ml.org

2. Try out some of the existing examples

   http://sed-ml.org, 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

5. … submit a proposal with example files and prototype

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

# Thank you for your attention!

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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**.

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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.

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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.

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**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.

http://sed-ml.org