Model Meta-Information

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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

UniProt and P62158 (human calmodulin)

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)

\[ \lambda \text{cl} \xrightarrow{R_2} \text{TetR} \xrightarrow{R_1} \text{LacI} \xrightarrow{R_3} \]

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)
Biomodels.net initiative

Minimum Information Requested In the Annotation of Models (MIRIAM)
- Systems Biology Ontology (SBO)
- Minimum Information About a Simulation (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

1. Biological publication repository
2. Find according publication
3. Read
4. Load model
5. Apply model changes
6. Simulation tool
7. Simulation result
8. Publication repository
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

- Model
- Simulation
- Task
- DataGenerator
- Output

(Figure by Frank Bergmann, biomodels.net 2010)
SED-ML

1. Read biological publication repository
2. Find according publication
3. Load model
4. Apply model changes
5. Simulation tool
6. Simulation result
SED-ML

Biological publication repository

find according publication

Model database

load model

Simulation tool

apply model changes

simulation result

export & store SED-ML

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Rostock, 2010
SED-ML

Model database

load model(s)

apply model changes

Simulation tool

run simulation(s)

simulation result

call SED-ML file

SED-ML
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
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
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.
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_00000001**) 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

COPASI, duration: 140ms, step size: 0.14
Information in the SED-ML file

- Updating initial model parameters

intrinsically bursting (IB)

Publication

COPASI, adjusted parameter values
(a=0.02, b=0.2 c=-55, d=4)
Thank you for your attention!

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