

## Formal description and visual modeling of complex biological systems using BioUML workbench and BioUML Network Edition

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BioUML (<http://www.biouml.org>) – Biological Universal Modeling Language – is integrated extensible Java workbench that adopts visual modeling approach for formal description and simulation of complex biological systems (Figure 1). The other distinctive feature of BioUML workbench is tight integration with databases on biological pathways.

The core of BioUML is a meta-model that provides an abstract layer (compartmentalized attributed graph) for comprehensive formal description of wide range of biological and other complex systems. Content of databases on biological pathways, SBML and CellML models, as well as biological pathways in BioPAX format can be expressed in terms of the meta model and used by BioUML workbench. This formal description can be used both for visual depiction and editing of biological system structure and for automated code generation to simulate a model behavior. Meta-model is problem domain neutral and splits the system description into 3 interconnected levels:

1. graph structure - the system structure is described as compartmentalized graph;
2. database level - each graph element can contain reference to some database object;
3. mathematical model - any graph element can be element of mathematical model.

BioUML supports following mathematical elements: variable, formula, equation, event, state and transition.

BioUML workbench provides two alternative simulation engines:

1) Java simulation engine - workbench automatically generates and compiles Java code on the base of visual model (diagram) of a biological system.

2) MATLAB simulation engine - workbench automatically generates code for MATLAB and invokes MATLAB engine to simulate a model behavior using JMatlink library (Patterson and Spiteri, 2003).

Both simulations engines pass 100% SBML semantic test suite that provides a set of valid SBML models with a simulated time course data (Finney, 2004). Test details are available at: [http://www.biouml.org/sbml\\_tests/overview.html](http://www.biouml.org/sbml_tests/overview.html).

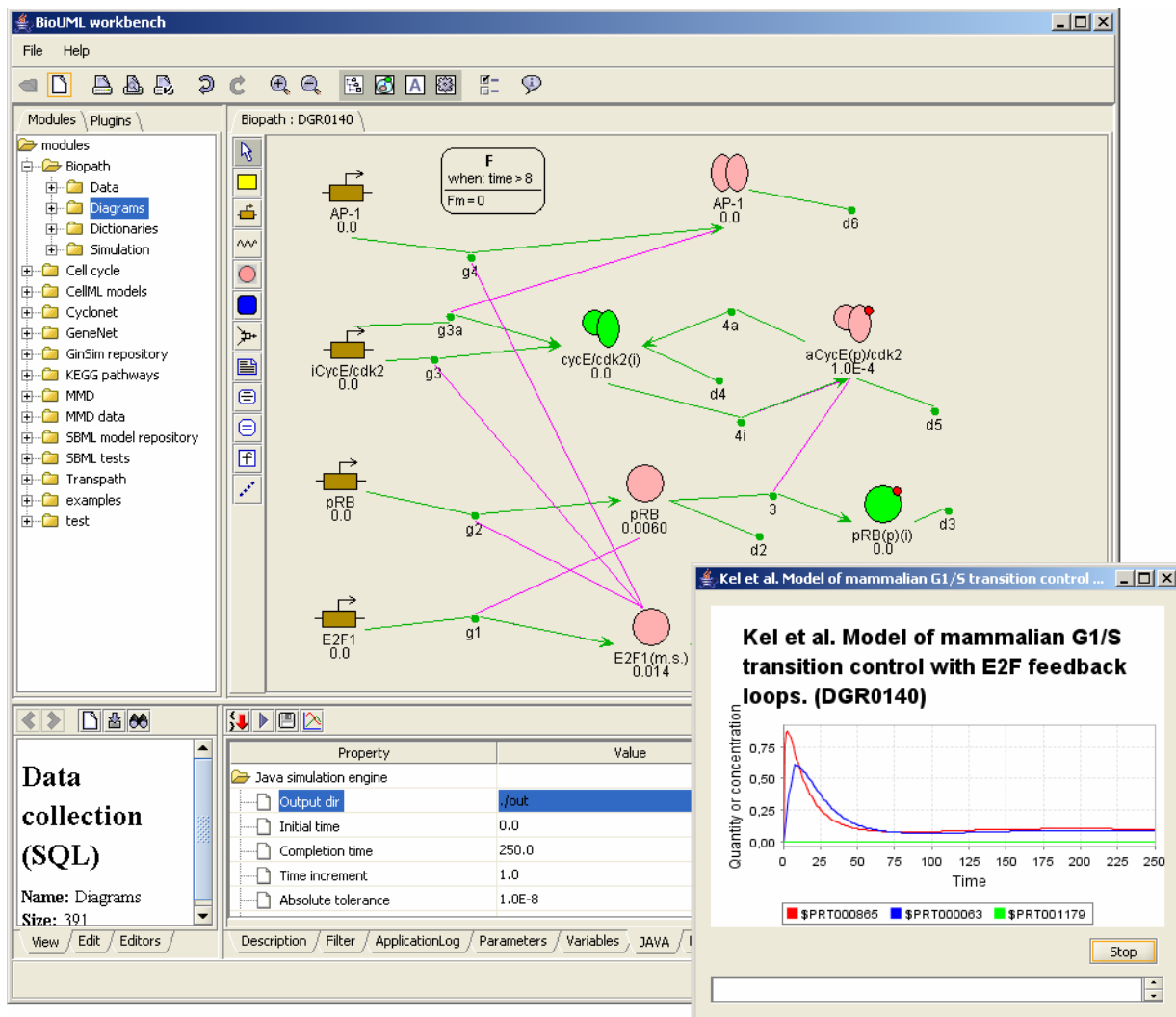


Figure 1: Example of cell cycle model visualization and simulation by BioUML workbench.

New version BioUML Workbench and BioUML Network Edition provides new possibilities for formal description and visual modeling of complex biological systems:

- import/export data in BioPAX format
- import data in OBO format
- full text search using Lucene search engine
- new graph search engine and improved graph layout algorithms
- possibility of seamless integration of external databases into user's database. For example, Ensembl database can be used as gene catalogue in the user's database
- graphic notation editor – allows user to create their own graphic notation and corresponding diagram types
- arterial tree diagram type – used for simulation blood flow

- composite diagram – a mechanism to combine several models into one bigger model using the same mathematical formalism
- agent-based diagram - a mechanism to combine several models into one bigger model using different mathematical formalism. For example, one model is described by system of PDE and other model is described by system of ODE. Additionally, models composition is dynamical – models (agent) can appear, disappear (die) and move in space
- BioUML server – provides high level protocol for BioUML workbench for data access on server side, as well as for data search (full text search, graph search)
- publishing BioUML data using BeanExplorer Enterprise Edition technology
- ru.biosoft.bsa plug-in – BioSequence Analyses – provides visualization and analyses of biological (mainly nucleotide) sequences. This is updated version of library that is core of TRANSPLOERER tool
- org.openscience.cdk plug-in – Chemical Development Kit – allows to visualize structural formulas for chemical substances on diagrams.

BioUML workbench and BioUML Network Edition are used for development of several databases:

- BMOND (<http://bmond.biouml.org>) – Biological MOdels aNd Diagrams database
- Cyclonet (<http://cyclonet.biouml.org>) - an integrated database on cell cycle regulation and carcinogenesis (Kolpakov et al., 2007)
- LipidNet (<http://demo.developmentontheedge.com/lipidnet>) - Lipidomics knowledge base

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