

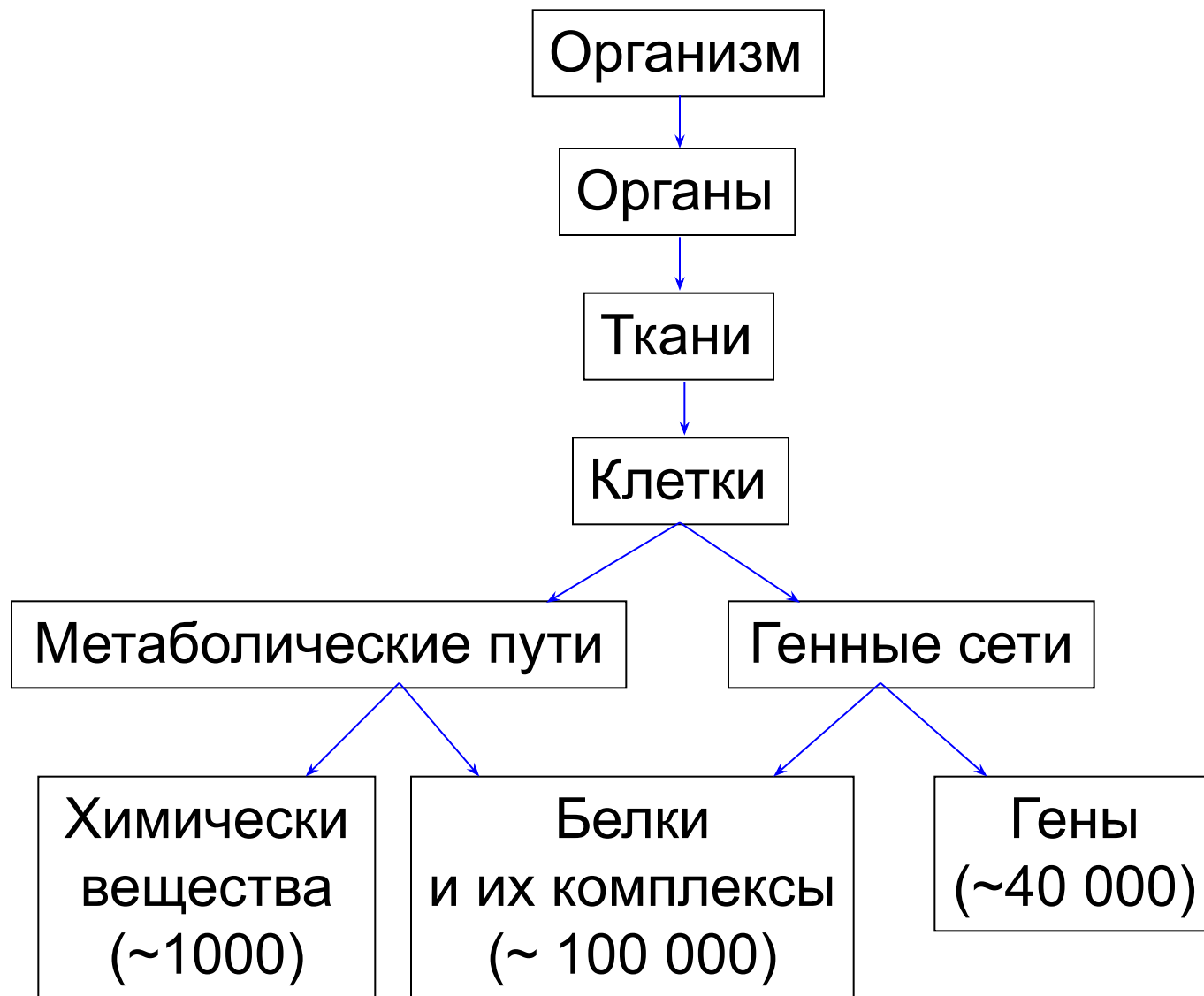
**Комплексный подход для
формального описания,
графического представления и
моделирования
широкого круга биологических и
других сложных систем**

Biosoft.Ru

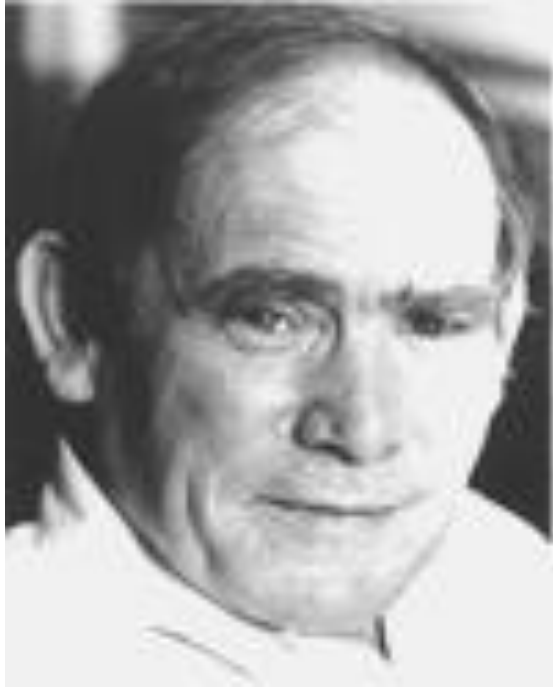
DevelopmentOnTheEdge.com

Лаборатория Биоинформатики КТИ ВТ СО РАН

<http://www.biouml.org>



Базы данных
(более 500 баз данных, общий объем сотни гигабайт)



Сидней Бреннер,
лауреат Нобелевской
премии 2002 года в
области медицины

Сейчас у нас есть беспрецедентная возможность собирать и накапливать данные о природе, тем не менее в современной биологии развивается кризис, который состоит в том что полностью неструктурированные данные не улучшают нашего понимания. Нам нужна система (framework) в которую мы могли бы поместить все эти знания и данные – это то и становится проблемой в биологии.

Мы достигли уровня когда мы больше не можем разговаривать друг с другом – мы стали слишком специализированы. Нам нужна система, используя которую люди могли бы сказать: “Да, я понял.”. Создание такой системы является действительно большим вызовом.

Sydney Brenner, 2003

BioUML - Biological Unified Modeling Language

The screenshot displays the BioUML framework interface, which is used for modeling biological systems. The main window is titled "BioUML framework" and contains several panels:

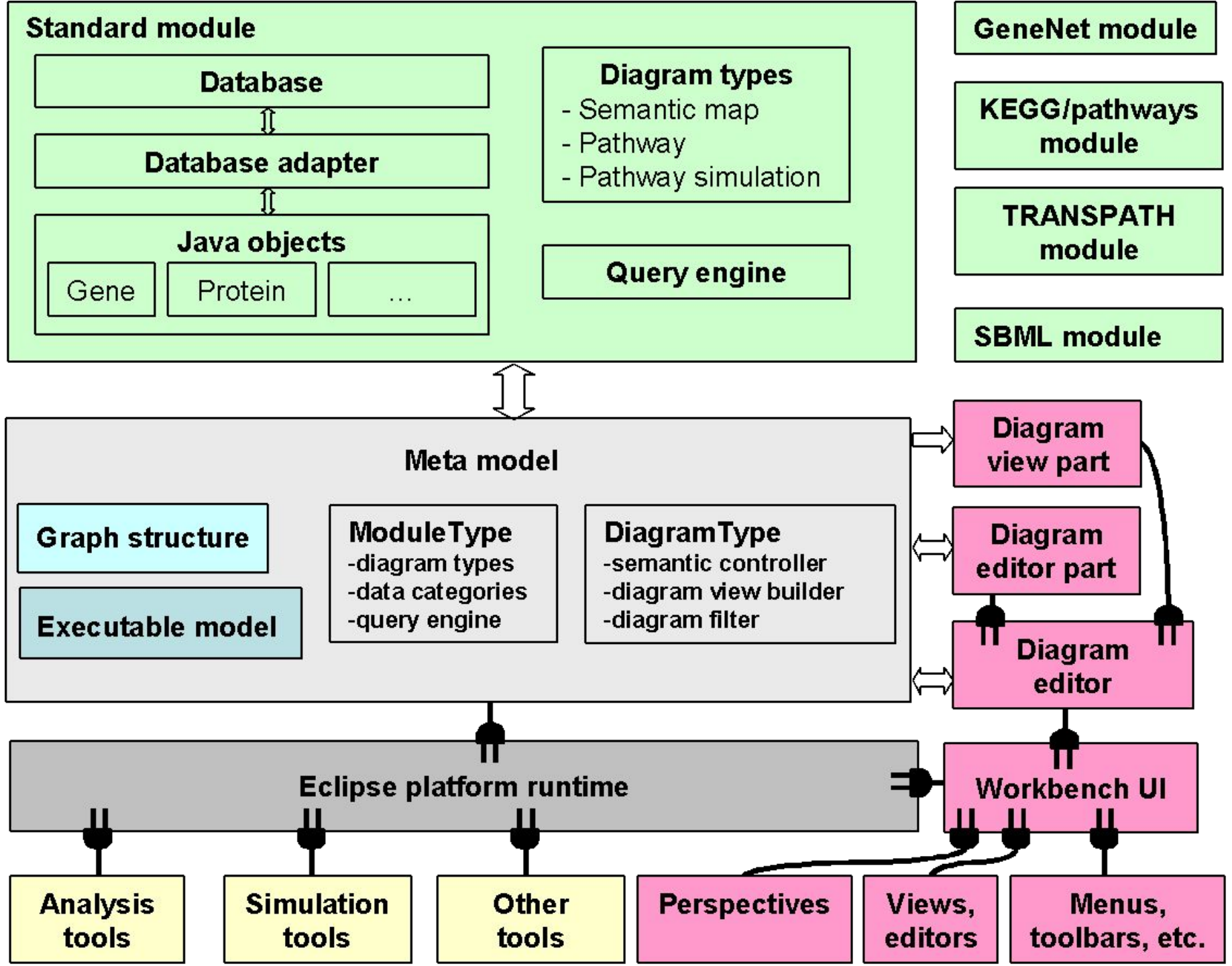
- Modules/Plugins:** A tree view on the left shows the "SBML model repository" containing various models, with "CellCycle-1991Gol.xml" selected.
- SBML model repository: CellCycle-1991Gol.xml:** A central diagram showing a network of reactions (Reaction1-7) involving species C (red circle), M (red circle), X (red circle), and EmptySet (blue square) within a "cytoplasm" boundary.
- Figure No. 1:** A plot titled "Solving Goldbeter problem" showing the time evolution of variables C (blue), M (green), and X (red) over time (0 to 100). The plot shows oscillatory behavior.
- Property Table:** A table showing the properties of the selected reaction (Reaction5):

Property	Value
Node	
Title	Reaction5
Comment	
Data	
Identifier	Reaction5
Name	Reaction5
Reversible	<input type="checkbox"/>
Fast	<input type="checkbox"/>
Kinetic law	
Formula	(Reaction5_VM3...
Time units	
Substance u	
- Minimal Mitotic Oscillator:** A text panel providing citation and description for the model.

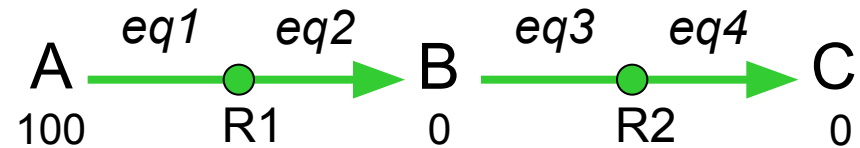
Citation
Goldbeter, A. A minimal cascade model for the mitotic oscillator involving cyclin and cdc2 kinase. Proc. Natl. Acad. Sci. USA 88: 9107-1101 (1991). <http://www.pnas.org/cgi/content/abstract/88/20/9107>

Description
This is a widely cited minimal (3-variable) model for a mitotic oscillator. The three variables represent Cyclin (C), inactive cdc-2 Kinase (M) and an active cdc-2 Kinase (X).
<http://www.pnas.org/cgi/content/abstract/88/20/9107>

Rate constant **Reaction**
K1 = 0.1 (hill khalf) Comp[M] -> M



Пример двух последовательных химических реакций



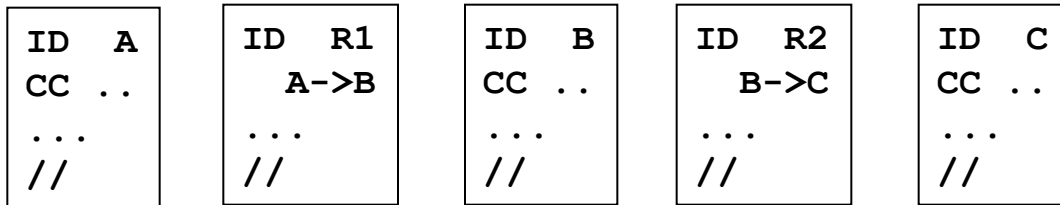
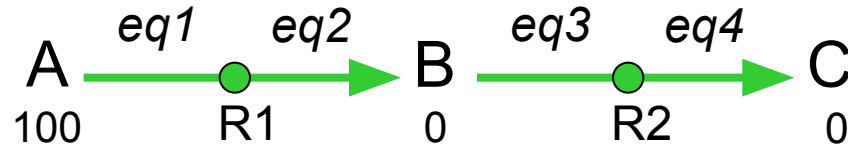
Соответствующая ему математическая модель

$$\frac{dA}{dt} = eq1$$

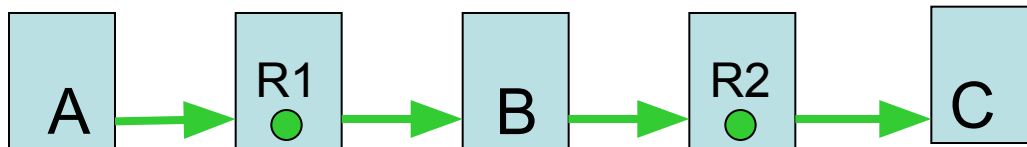
$$\frac{dB}{dt} = eq2 + eq3$$

$$\frac{dC}{dt} = eq4$$

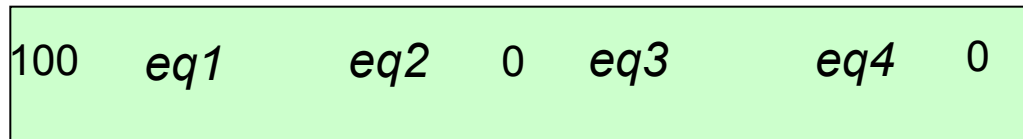
BioUML мета-модель позволяет описать сложную систему на 3 уровнях



Описание компонентов системы в базе данных

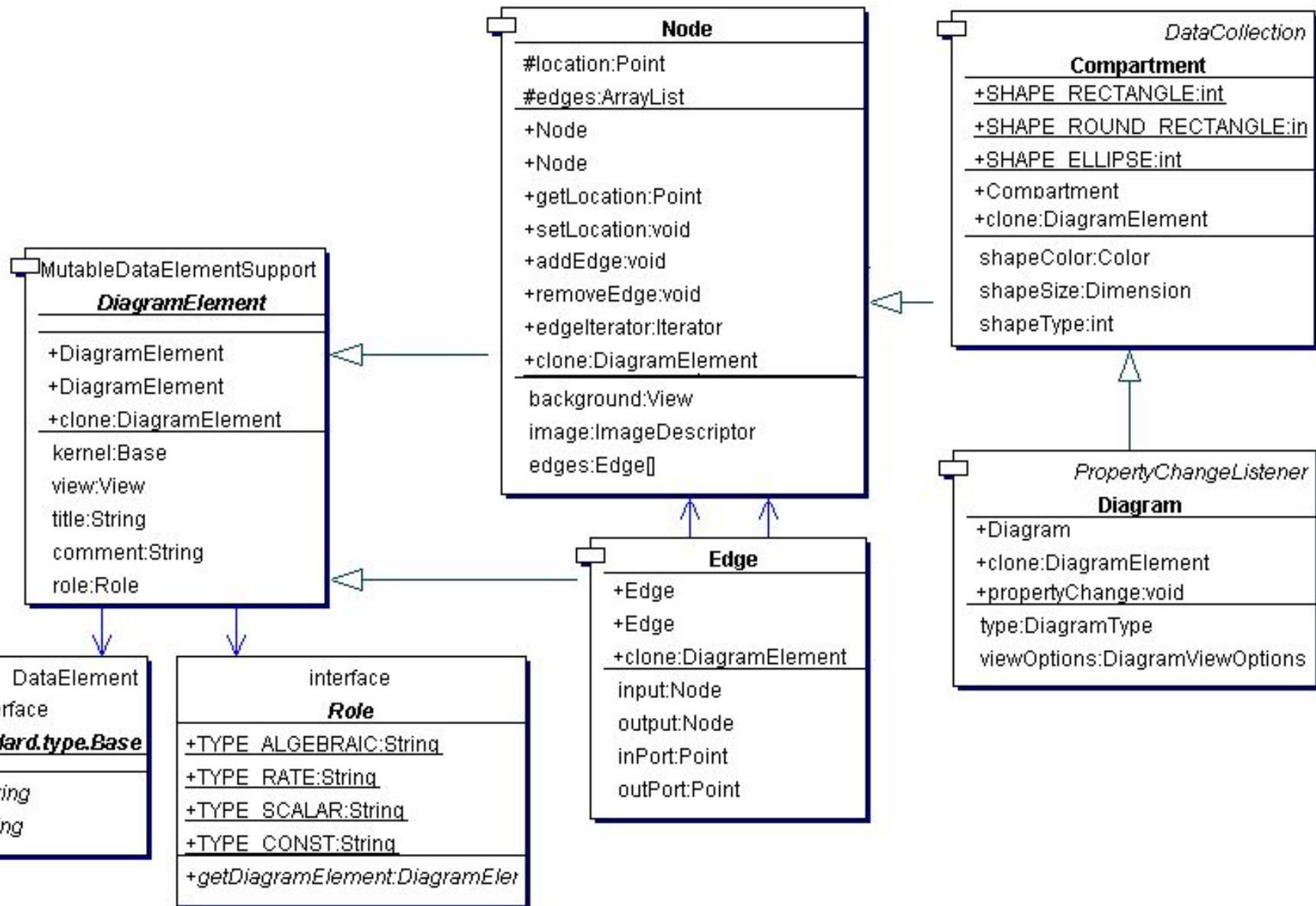


Описание структуры системы в виде графа

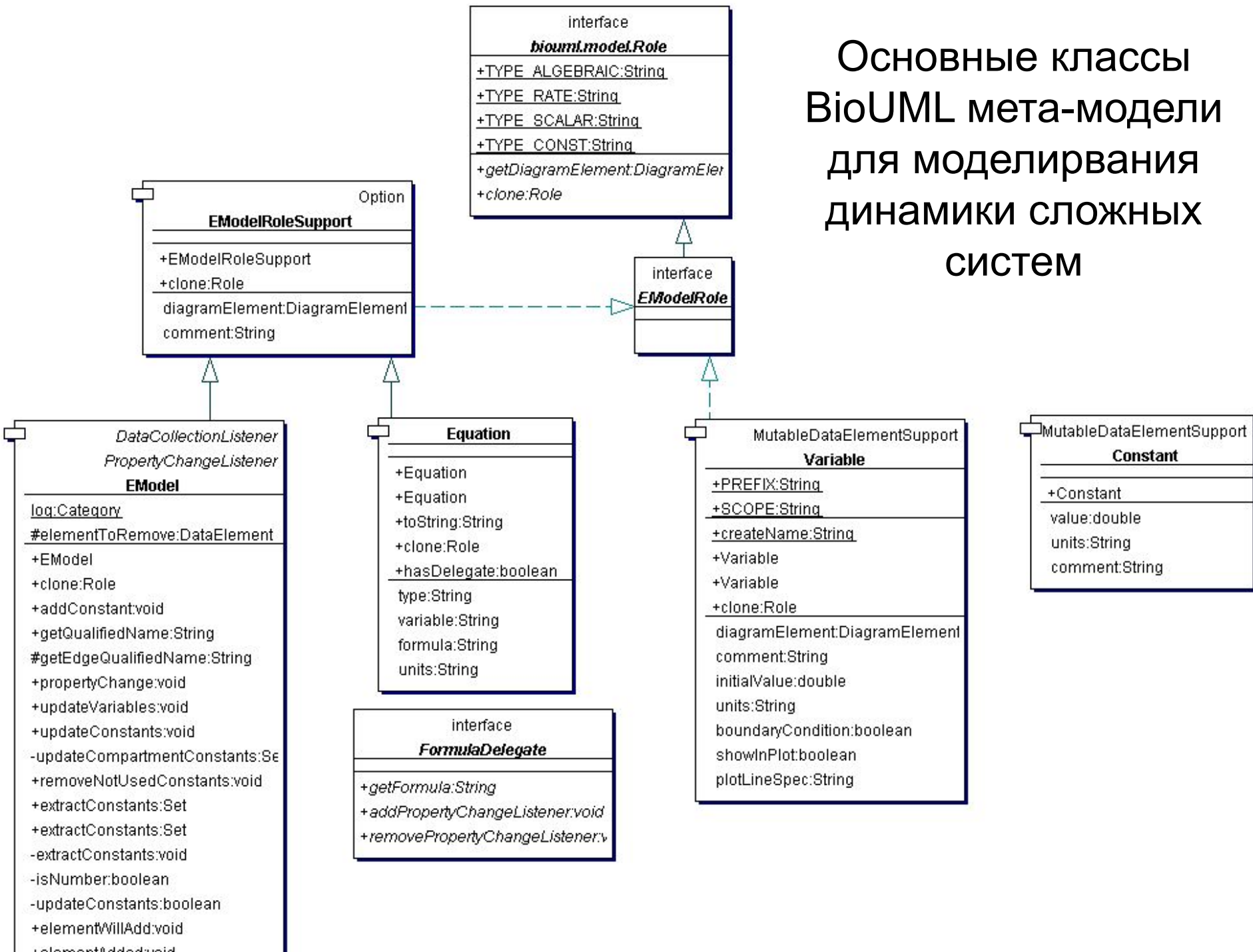


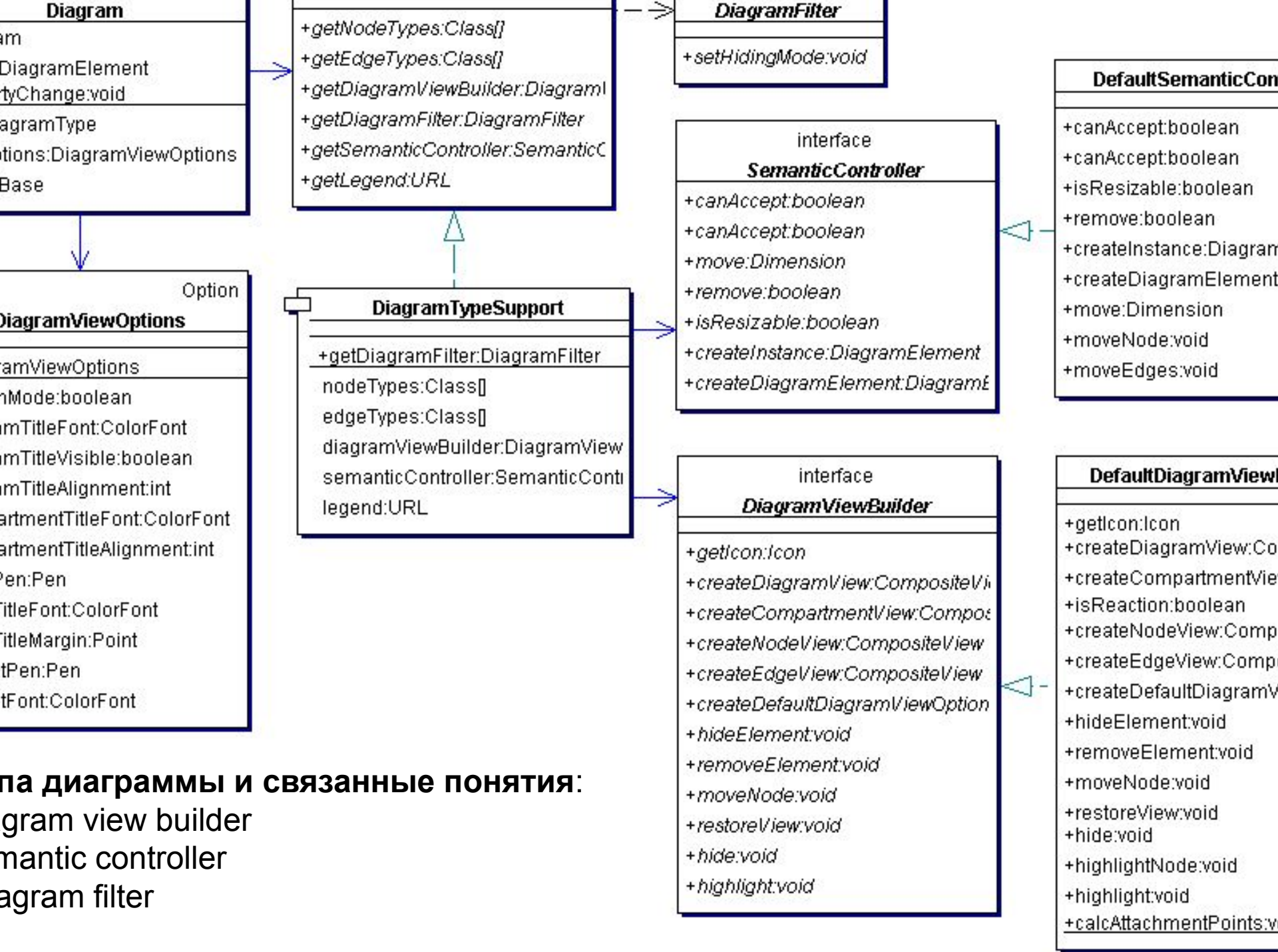
Математическая модель системы

Основные классы BioUML мета-модели для описания структуры графа

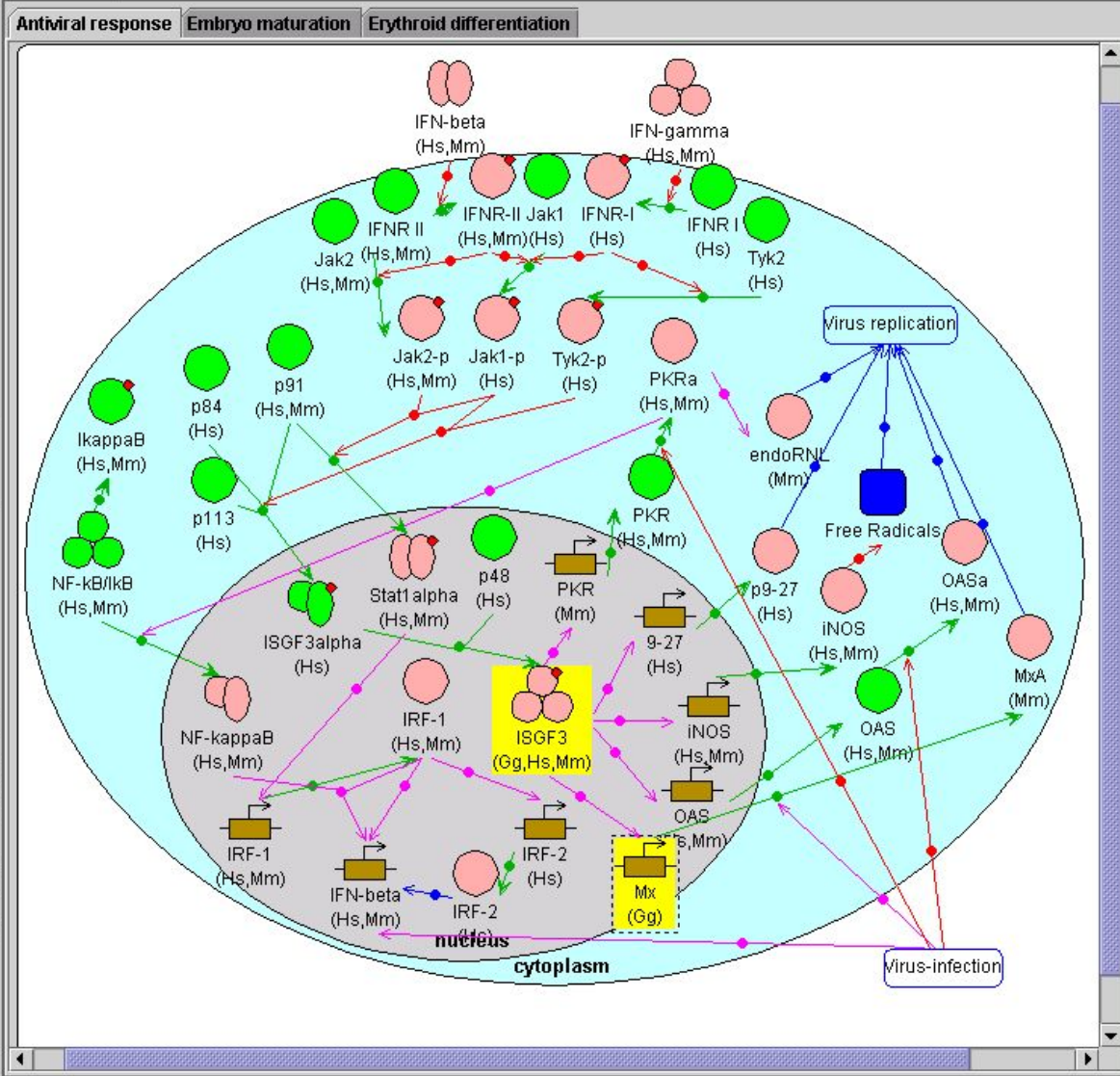


Основные классы BioUML мета-модели для моделирования динамики сложных систем





- modules
- GeneNet module
 - Data
 - cell
 - compartment
 - expert
 - gene
 - literature
 - organism
 - process
 - protein
 - relation
 - rna
 - substance
 - Diagrams
 - Antiviral response
 - Antiviral response (dynar)
 - Cholesterol
 - Embryo maturation
 - Environmental stress res
 - Erythroid differentiation
 - ethylene
 - HSP70-autoregulation
 - Leptin (organism level)
 - plant-pathogen
 - plant-pathogen general
 - redox-regulation
 - Seed reserve mobilisatio
 - Seed reserve mobilisatio
 - Seed reserve mobilisatio
 - Seed reserve mobilisatio
 - Seed reserve mobilisatio
 - seed-proof
 - Steroidogenesis (gluoco
 - Steroidogenesis (testost
 - Storage protein biosynthe
 - Storage proteins biosynt
 - tobacco



Property	Value
Diagram filter	
Filter	<input checked="" type="checkbox"/>
Species filter	
Gallus gallus	<input checked="" type="checkbox"/>
Homo sapiens	<input type="checkbox"/>
Mus musculus	<input type="checkbox"/>
Cell type filter	
Inducer filter	
Filter mode	highlight
Highlighter	yellow

Node

Title Mx

Data biouml.genenet.type.Gene@76e5d

ID GgMx

OS Gallus gallus (chicken).

SN Mx

NM Mx protein

SO Gg.fibroblast

RE IFN-alpha
IFN-beta
poly(I).poly(C)
virus infection (NDV)

DR TRRD; G001088; GgMX
TFGENE; G001088;

```
<!-- BioUML diagrams markup language (DML) v. 0.9.2 -->
```

```
<!ELEMENT dml (diagramInfo?, diagram, executableModel?)>
```

```
<!ATTLIST dml
```

```
    version CDATA "0.9.2"
```

```
    appVersion CDATA "0.7.0" >
```

```
<!ELEMENT diagramInfo>
```

```
<!ATTLIST diagramInfo value CDATA >
```

```
<!ELEMENT diagram (compartmentInfo, nodes, edges)>
```

```
<!-- "diagramType" attribute contains name of Java class -->
```

```
<!ATTLIST diagram
```

```
    diagramType CDATA #REQUIRED
```

```
>
```

```
<!ELEMENT nodes (compartment|equivalentNodeGroup|node)*>
```

```
<!ELEMENT edges (edge)*>
```

```
<!ELEMENT compartment (compartmentInfo, nodes, edges)>
```

```
<!ATTLIST compartment>
```

```
<!ELEMENT compartmentInfo (image?)>
```

```
<!--
```

```
    "kernel" attribute contains complete path for data
        element used as kernel; currently path is relative
        module/Data
```

```
    "shape" attribute possible values are:
```

```
        0-rectangle; 1-round_rectangle; 2-oval
```

```
-->
```

```
<!ATTLIST compartmentInfo
```

```
    kernel      CDATA      #REQUIRED
```

```
    x           CDATA      #REQUIRED
```

```
    y           CDATA      #REQUIRED
```

```
    width       CDATA      #REQUIRED
```

```
    height      CDATA      #REQUIRED
```

```
    title       CDATA
```

```
    comment     CDATA
```

```
    shape       CDATA      "0"
```

```
    color       CDATA      "255, 255, 255"
```

```
>
```

```
<!ELEMENT node (image?)>
<!ATTLIST node
  kernel    CDATA #REQUIRED
  title     CDATA
  comment   CDATA
  x         CDATA
  y         CDATA
>
```

```
<!ELEMENT edge>
<!ATTLIST edge
  kernel    CDATA #REQUIRED
  in        CDATA #REQUIRED
  out       CDATA #REQUIRED
  title     CDATA
  comment   CDATA
  inPort    CDATA
  outPort   CDATA
>
```



```
<!--===== -->
<!-- Executable model -->
<!--===== -->
<!ELEMENT executableModel (constant*, variable*, equation*)>
<!ATTLIST executableModel
    class          CDATA #REQUIRED
    initialTime    CDATA #REQUIRED
    completionTime CDATA #REQUIRED
    comment        CDATA
>

<!ELEMENT constant>
<!ATTLIST constant
    name          CDATA #REQUIRED
    value         CDATA #REQUIRED
    units         CDATA
    comment       CDATA
>
```

<!ELEMENT variable>

<!-- "diagramElement" attribute - diagram element name -->

<!ATTLIST variable

diagramElement	CDATA	#REQUIRED
initialValue	CDATA	"0.0"
boundaryCondition	CDATA	"false"
showInPlot	CDATA	"true"
plotLineSpec	CDATA	"-"
units	CDATA	
comment	CDATA	

>

<!ELEMENT equation>

<!--

"diagramElement" attribute - diagram element name

"type" attribute - equation type.

Possible values are: algebraic, rate or scalar. -->

<!ATTLIST equation

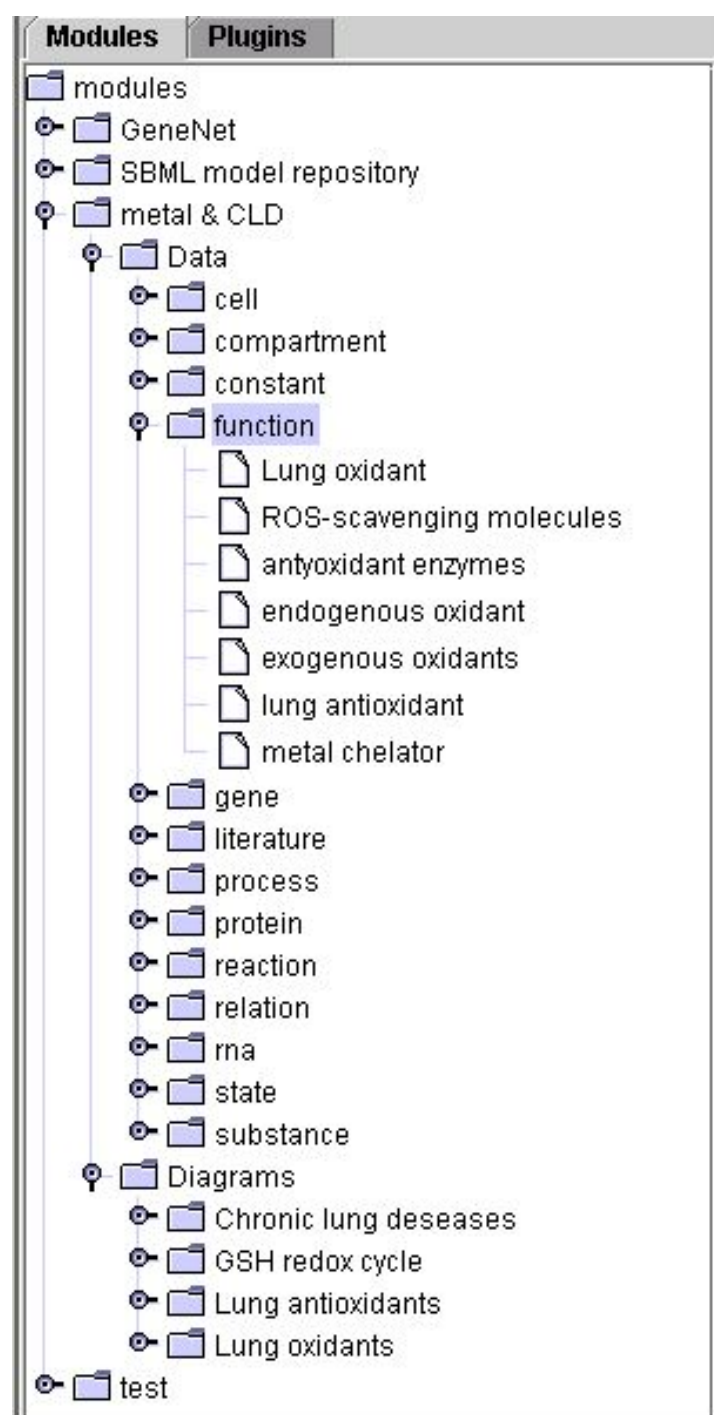
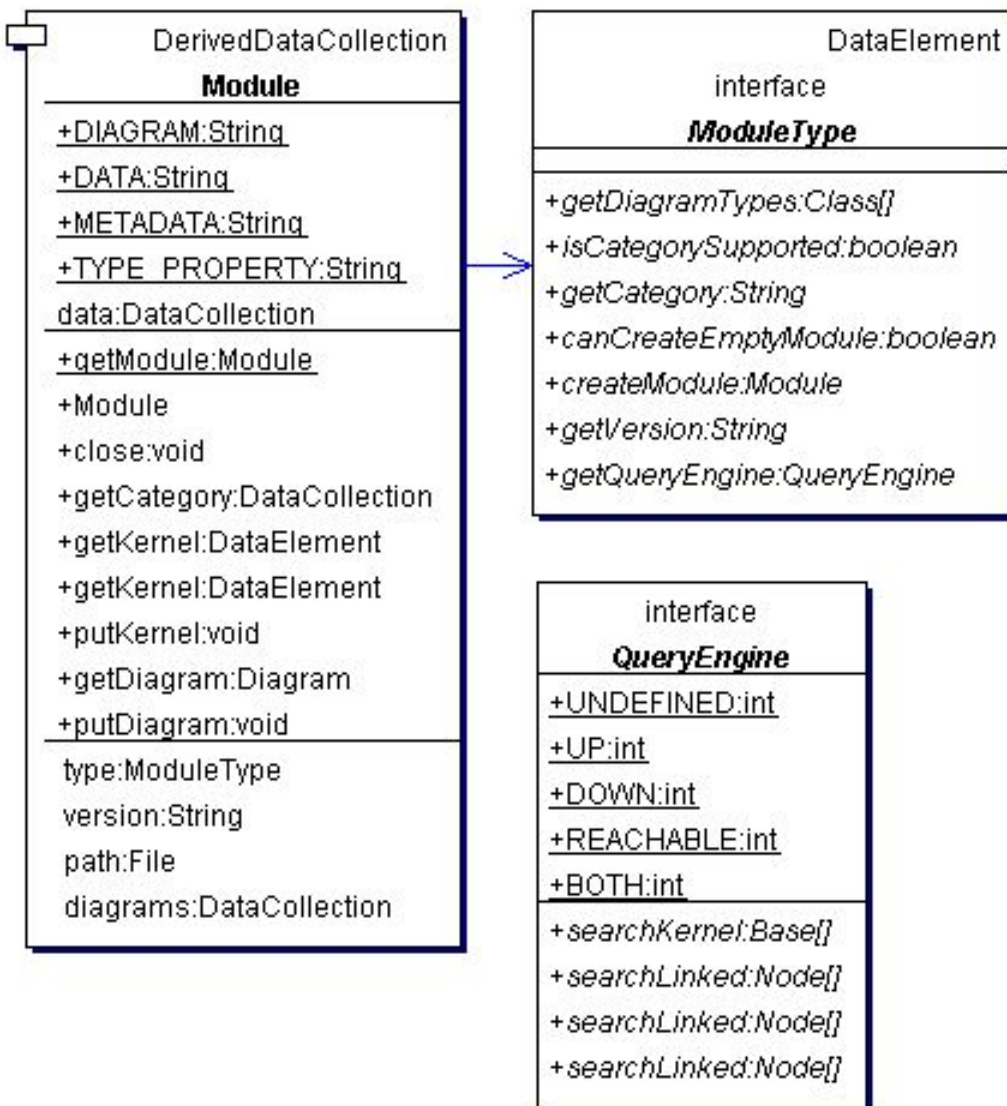
diagramElement	CDATA	#REQUIRED
variable	CDATA	#REQUIRED
formula	CDATA	#REQUIRED
type	CDATA	"rate"
units	CDATA	
comment	CDATA	

>

Концепция модуля

- Чтобы обеспечить интеграцию различных баз данных в среду BioUML, мы вводим концепцию модуля.
- Как правило, модуль создается для отдельной базы данных и определяет способ представления информации из этой базы данных в виде объектов языка Java. Модуль также может содержать специфичные для этой базы данных типы диаграмм и способы их графического отображения.

Концепция модуля



Система поиска взаимодействующих друг с другом компонентов биологических систем

SEARCH_FORM_TITLE

Search options

Property	Value
SearchOptions	
Diagram type	GeneNet diagram
Diagram name	At_seed_1
Type	Protein
Identifier	Hs:HSF1
Direction	Both
Depth	1
Layout	Layered

Start Save Cancel

Node

Title: Hs:HSF1-p
Data: DataElement[Hs:HSF1-p] class=class
 biouml.modules.genenet.type.Protein
ID: Hs:HSF1-p
OS: Homo sapiens (human).
NM: heat shock factor 1
SN: HSF1
GN: Hs:HSF1
FN: active
MM: multimer
MD: phosphorylated
SO: Hs:K562

QUERY_FORM_TITLE

	Identifier	Species	Name	Synoni...	Gene ID	Funcio...	Structure	Modifica
0	Hs:IRF-1	Homo sapi...	interferon regulatory factor -1	IRF-1	Hs:IRF-1	active	monomer	no data
1	Hs:IRF-2	Homo sapi...	interferon regulatory factor-2	IRF-2	Hs:IRF-2	active	monomer	no data
2	Hs:Jak2	Homo sapi...	Jak2 protein tyrosine kinase	Jak2		inactive	monomer	no data
3	Hs:Jak2-p	Homo sapi...	Jak2 protein tyrosine kinase	Jak2		active	monomer	phosph
4	Hs:OAS	Homo sapi...	2'-5' oligoadenylate synthetase	OAS	Hs:OAS	inactive	monomer	no data
5	Hs:OASa	Homo sapi...	2'-5' oligoadenylate synthetase	OAS	Hs:OAS	active	monomer	no data
6	Hs:PKR	Homo sapi...	dsRNA-dependent cAMP-independent protein serine/threoni...	PKR		inactive	monomer	no data
7	Hs:PKRa	Homo sapi...	dsRNA-dependent cAMP-independent protein serine/threoni...	PKR		active	monomer	no data
8	Hs:Tyk2	Homo sapi...	Tyk2 protein tyrosine kinase	Tyk2		inactive	monomer	no data
9	Hs:p113	Homo sapi...	Stat2	p113		inactive	monomer	no data
10	Hs:p48	Homo sapi...	ISGF3gamma	p48		inactive	monomer	no data
11	Hs:p84	Homo sapi...	Stat1 beta	p84		inactive	monomer	no data
12	Hs:p91	Homo sapi...	Stat1 alpha	p91		inactive	monomer	no data
13	Mm:IRF-1	Mus musc...	interferon regulatory factor -1	IRF-1	Mm:IRF-1	active	monomer	no data
14	Mm:Jak2	Mus musc...	Jak2 protein tyrosine kinase	Jak2		inactive	monomer	no data
15	Mm:Jak2-p	Mus musc...	Jak2 protein tyrosine kinase	Jak2		active	monomer	phosph
16	Mm:OAS	Mus musc...	2'-5' oligoadenylate synthetase	OAS	Mm:OAS	inactive	monomer	no data
17	Mm:OASa	Mus musc...	2'-5' oligoadenylate synthetase	OAS	Mm:OAS	active	monomer	no data
18	Mm:PKR	Mus musc...	dsRNA-dependent cAMP-independent protein serine/threoni...	PKR	Mm:PKR	inactive	monomer	no data
19	Mm:PKRa	Mus musc...	dsRNA-dependent cAMP-independent protein serine/threoni...	PKR	Mm:PKR	active	monomer	no data
20	Mm:Stat1 a...	Mus musc...	signal transducer and activator of transcription 1 alpha protein	Stat1 alpha		inactive	monomer	no data
21	Mm:iNOS	Mus musc...	nitric oxide synthase	iNOS	Mm:iNOS	active	monomer	no data

Filter **Table columns**

Property	Value
FilteringSettings	
Module	GeneNet
Type	biouml.modules.gene...
filter	
Enabled	<input checked="" type="checkbox"/>
Filters	
Source	<input type="checkbox"/>
Identifier	<input type="checkbox"/>
Synonyms	<input type="checkbox"/>
Regulation	<input checked="" type="checkbox"/> /(*IFN.*)
Date	<input type="checkbox"/>
Structure	<input checked="" type="checkbox"/> mon...
Name	<input type="checkbox"/> monomer
Gene ID	<input type="checkbox"/> homodimer
Comment	<input type="checkbox"/> heterodime
Modification	<input type="checkbox"/> multimer
	<input type="checkbox"/> unknown

Start Cancel

View **Edit**

Protein

ID Mm:OASa
OS Mus musculus (mouse).
NM 2'-5' oligoadenylate synthetase
SN OAS
GN Mm:OAS
FN active
MM monomer
MD no data
SO Mm.macrophage Mm.fibroblast Mm.spleen
Mm.liver Mm.lung Mm.thymus
RE IFN-alpha

Универсальная система поиска информации по базам данных

Модули

BioUML standard – стандартный модуль для описания и моделирования биологических систем (преимущественно на молекулярно-клеточном уровне)

SBML – Systems Biology Markup Language, level 1
[http:// www.sbml.org](http://www.sbml.org)

GeneNet - база данных по генным сетям
ИЦиГ, Новосибирск, <http://wwwmgs.bionet.nsc.ru>

KEGG/Ligand - Kyoto Encyclopedia of Genes and Genomes, база данных метаболических путей
Kyoto University, Japan, <http://www.kegg.com>

TRANSPATH - база данных по путям передачи сигнала в клетке
Biobase GmbH, Germany.

SBML – Systems Biology Markup Language, level 2
[http:// www.sbml.org](http://www.sbml.org)

CellML – Cell Markup Language
<http://www.cellml.org>

GO – Gene Ontology
<http://wwwmgs.bionet.nsc.ru>

UMLS – Unified Medical Language System
<http://www.nlm.nih.gov/research/umls/>

BioPax – Biological Pathways Exchange
<http://www.biopax.org>



BioUML - framework for systems biology

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Welcome to BioUML world

What is BioUML?

BioUML is Java framework for systems biology. It spans the comprehensive range of capabilities including access to databases with experimental data, tools for formalized description of biological systems structure and functioning, as well as tools for their visualization and simulations.

Currently BioUML framework consists from following parts:

- Meta model - provides an abstract layer to present structure of any biological system as a clustered graph.
- Viewer - a universal viewer to visualize graphs of biological systems structure as diagrams.
- Editor - universal diagram editor.
- Search engine - provides searching of components with the specified properties in biological pathway databases. The search result can be presented as graph and further edited by a user using BioUML editor.
- Modeler - allows a user to model/simulate dynamics of biological systems using block diagrams.
- Standard diagram and data types - an attempt to standardize data types and graphic notations for biological pathways.
- Database modules - provides incorporation of different databases biological pathways

Version 0.7

BioUML workbench version 0.7.1 was released.

[More...](#)

BioUML forum

The forum aims to co-ordinate a community effort towards of development of BioUML and its application for modelling of biological systems. Here you can ask your questions as well as post your comments and suggestions. [More...](#)

Have questions?

If you have any questions please contact us at info@Biosoft.Ru