# MGSmodelsDB – a new database of mathematical models of Escherichia coli cell subsystems


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## Summary:


MGSmodelsDB is a new web-accessible repository containing mathematical models of biomolecular systems. The current version of the database includes models of enzymatic reactions and gene expression regulatory processes of *de novo* nucleotide metabolism and respiration in *Escherichia coli*. The database contains 82 elementary models, each of which represents an enzymatic reaction or regulatory process rate function. Model parameters were obtained from published data or fitted to the available experimental data. MGSmodelsDB enables users to search, select and automatically generate more complex models in SBML and other formats from a subset of elementary models.

**Availability:** MGSmodelsDB is a freely accessible for academic use at http://modelsgroup.bionet.nsc.ru/MGSmodelsDB/


## 1. Introduction

Living systems have a complex hierarchical organization that allows them to be considered as a set of dynamically interacting subsystems. In this conceptual framework, the development of mathematical models of a virtual cell [Tomita *et al.*, 1997; Reed and Palsson, 2003; Covert *et al.*, 2008] can be performed as a successive description of increasingly complex cellular subsystems by combination of their more simple (elementary) components. Enzymatic reactions are elementary components of metabolic pathways (Fig. 1). In the gene regulatory networks these reactions are the processes regulating the efficiency of gene expression at the levels of initiation and termination of transcription, translation, etc.

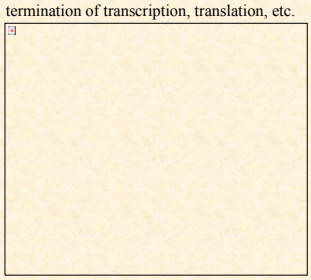

Fig. 1. Elementary models for enzymatic reactions (elementary components of metabolic pathways )

The MGSmodelsDB database's elementary models of enzymatic reactions and gene expression regulatory processes presented at the poster enables to model *de novo* nucleotide biosynthesis, aerobic/anaerobic respiration and nitrate/nitrite utilization in *Escherichia coli*. These pathways provide building blocks to simulate other, more integral molecular networks. Each elementary model represents a rational function of many variables that describes the rate of the process of interest. These variables represent concentrations of metabolites, genes, RNAs, proteins or their intermediate complexes. Parameters of mathematical models were taken from published data or fitted to the available experimental data.

The database is a freely accessible online resource for storing, viewing and retrieving curated mathematical models. The current version contains 82 elementary models, some of which have been previously published in [Khlebodarova *et al.*, 2006; Nedosekina, 2006; Ratushny and Nedosekina, 2006; Oshchepkova-Nedosekina and Likhoshvai, 2007; Likhoshvai *et al.*, 2010]. In contrast to existing internet-accessible databases of mathematical models [Sivakumaran *et al.*, 2003; Lloyd *et al.*, 2004; Olivier and Snoep, 2004; Hines *et al.*, 2004; Le Novere *et al.*, 2006; Rojas *et al.*, 2007], MGSmodelsDB can automatically generate more complex models from a subset of elementary models and save them in SBML [Hucka *et al.*, 2003] and other formats [Fadeev *et al.*, 2006; Kazantsev *et al.*, 2008].

## 2. Implementation

MGSmodelsDB has been developed using a three-tier architecture (Fig. 2):

(1) the Vaadin toolkit [http://vaadin.com] was used for GUI design and development;

(2) the EJB technology was used for the logic implementation;

(3) the model storing was implemented by Oracle DBMS.

The structure of MGSmodelsDB was arranged in a hierarchical manner (Fig. 3):

- The top level of MGSmodelsDB is a structural model of elementary processes (subsystems).
- The next level is a mathematical model of a particular subsystem.
- The lowest level is a set of parameters for the individual mathematical model.

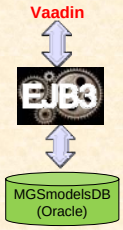


Fig. 2. The three tired architecture of the MGSmodelsDB

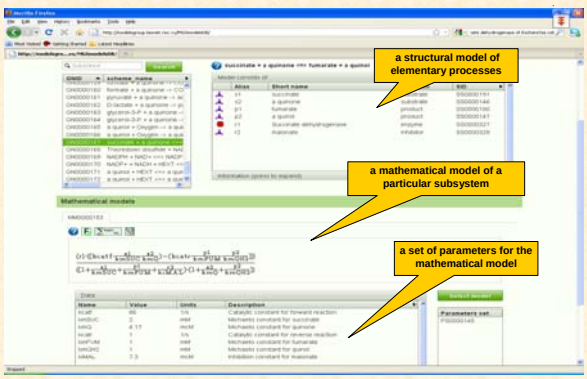


Fig. 3. MGSmodelsDB – a new database of mathematical models of biomolecular systems

The structural model is represented by a scheme of the elementary subsystems written in the gene network terms [Ananko *et al.*, 2005]. Structural models in MGSmodelsDB can be searched for by name or a part of the name of their components (metabolites, genes, RNAs or proteins). As a result of the search the system generates a list of structural models, the components of which have a match in at least one synonym. When the user selects a structural model from the resulting list, a window opens containing lists of substrates, products, regulators of the elementary subsystems with relevant links to other database as well as a set of mathematical models. Rate reaction functions are visualized as mathematical formulas.

Each model has an information field with the model description and links to relevant publications as well as a list of parameter sets in the section describing the mathematical model. A several sets of parameter values can be stored for the individual model in the database. The certain set of parameters can be selected by clicking the «select model» button which in turn allows the user to transfer mathematical model in the section «selected models».

The user creates a list of elementary models by the scheme described above. After completion of the selection procedure the user can reconstruct a mathematical model from elementary models by selecting the appropriate format and clicking the «generate» button (Fig. 4). Models are automatically assembled by the formation of global rates of component concentration (model variable) changes. The global rate represents a sum of the rates of the model variable changes in the selected elementary models:

$$S_1:\frac{dX_1}{dt}=V_1(Y_i,K_1)\quad S_2:\frac{dX_2}{dt}=V_2(Y_2,K_2)\quad \ldots\quad S_n:\frac{dX_n}{dt}=V_n(Y_n,K_n)$$

$$M:\begin{cases}\dfrac{dX}{dt}=V(Y,K), & V(Y,K)=\sum_{i=1}^{n}V_i(Y_i,K_i),\\ X=\cup X_i, Y=\cup Y_i, K=\cup K_i.\end{cases}$$

Integration by the elementary processes velocity summarize rule

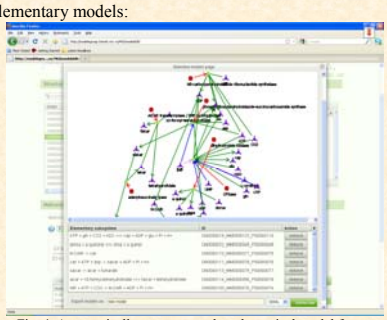

Fig. 4. Automatically reconstructed mathematical model from elementary models

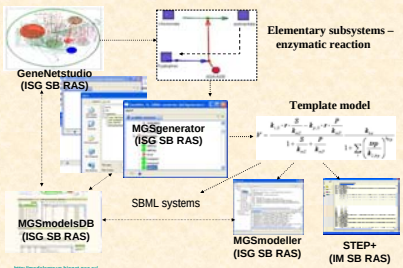


Fig. 5. The computer technology of automatical reconstruction of complex mathematical models from elementary models

## 3. Future directions

Further development of MGSmodelsDB will continue in two directions: (1) expanding the list of elementary models, (2) improving the database architecture. In the near future we plan to develop a new version of the database which will allow the user to store custom combinations of elementary models. These custom combinations can subsequently be used as building blocks for yet more complex models. We encourage the scientific community to add their own developed and published models to MGSmodelsDB.

## 4. Acknowledgments


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