# MOLECULAR SYSTEMS MODELING DATA WORKFLOW
## The IC&G Approach

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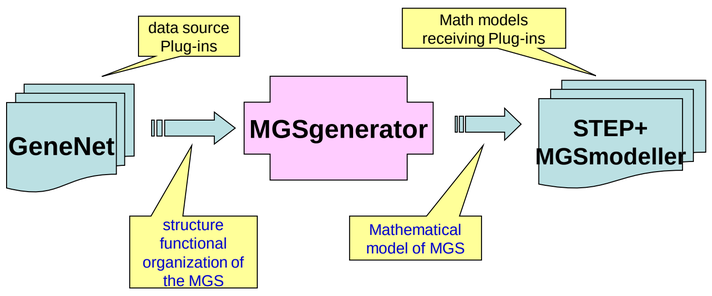
**Motivation**:
Progress in molecular biotechnology has fueled an explosion in the development of data bases that contain the structure functional organization of the molecular genetic systems (MGS). Technician progress gives us ability to make calculations of the wide and complex mathematical models of MGS. Now we need a bridge between them. In an effort to make the bridge we have developed set of software tools: MGSgenerator and MGSmodeller. Our goal is creating an uninterrupted data flow during the MGS modeling process. MGSgenerator is the tool for generation of the mathematical models on basis of reconstructed gene networks. MGSmodeller is the computer system that intended for reconstruction, calculation and analysis of the mathematical models of molecular genetic systems.

## MGSgenerator

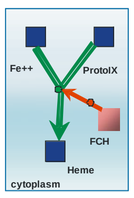



MGSgenerator system is the Java application. It has the plug-in based architecture.

The system supports following types of plug-ins. First of all is the data source modules and the second is the data export modules. Thus, this tool can be extended for conversion from different systems such as KEGG data base and for generation models in different modeling systems such as Mathematica.

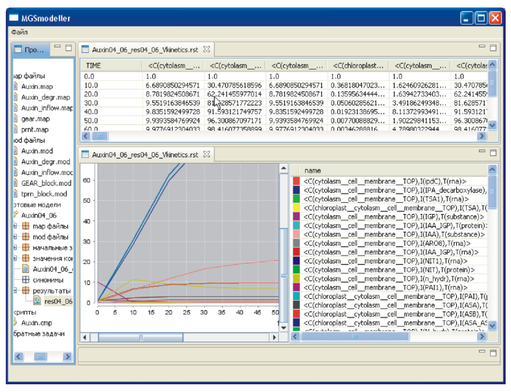
Today we have modules that support data extraction from GeneNet system and modules that allow us to convert output mathematical models to the STEP+ and MGSmodeller systems.

The reaction rate is described on basis of Hill functions, that allow to represent different types of the molecular-genetic regulation. It's computer system could be used for generation mathematical models only for correct described subset of patterns that could be representing in gene networks. Anyway it might be networks where are complex processes that couldn't be described by pre-set rules. In this case user can manually sets the necessary reaction rate equations.




$$V = \frac{k_0 \cdot x \cdot \frac{S_1}{k_1} \cdot \frac{S_2}{k_2}}{\left(1+\frac{S_1}{k_3}\right)\cdot\left(1+\frac{S_2}{k_4}\right)}$$

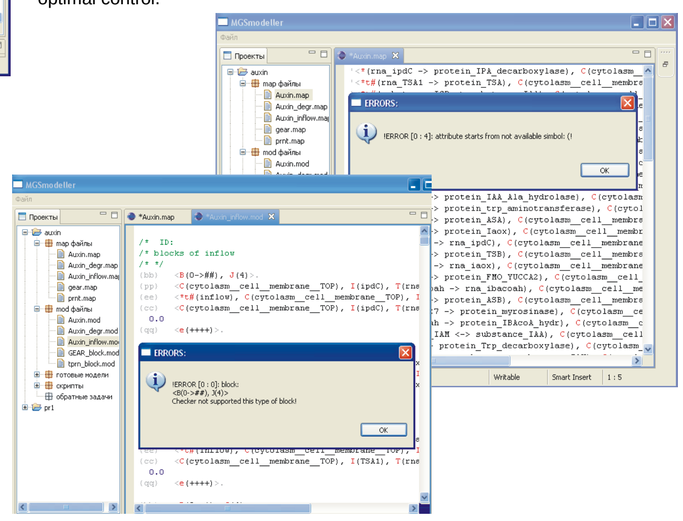
## MGSmodeller




User interface of the MGSmodeller allows to hierarchically represent data, edit them and to clearly represent the calculation results and to perform analysis of molecular genetic models.
MGSmodeller has a functional text editor that supports syntax and semantic analyses of SiBML format structures.

MGSmodeller is a computer system that provide functionality to create and calculate models using original standard SiBML. The SiBML standart uses for specification mathematical models of molecular genetic networks. SiBML based on the generalized chemical kinetic method [1] and taking into account the structure of their genetic and compartmental levels.

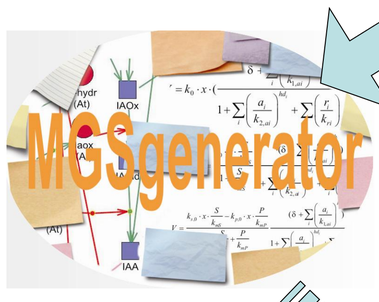
MGSmodeller system includes:
1) tools for model reconstruction with arbitrary structure of the molecular genetic systems taking into account positional relationship and orientation genes in genomes, polyallel genes, matrix principles of the passing such fundamental processes as replication, transcription and translation, and miltiocompartmental structure of studying systems
2) tools for dynamic calculation, solving of inverse problems and problems of optimal control.




## MGS in Action: A Sample Session

Here is an example of using the MGS tools to create and to simulate model. As source model we have chosen the model of auxin metabolism in a shoots of *Arabidopsis thaliana L* [2]. To create the mathematica model we have to make iterative step process (we'll make a first round).

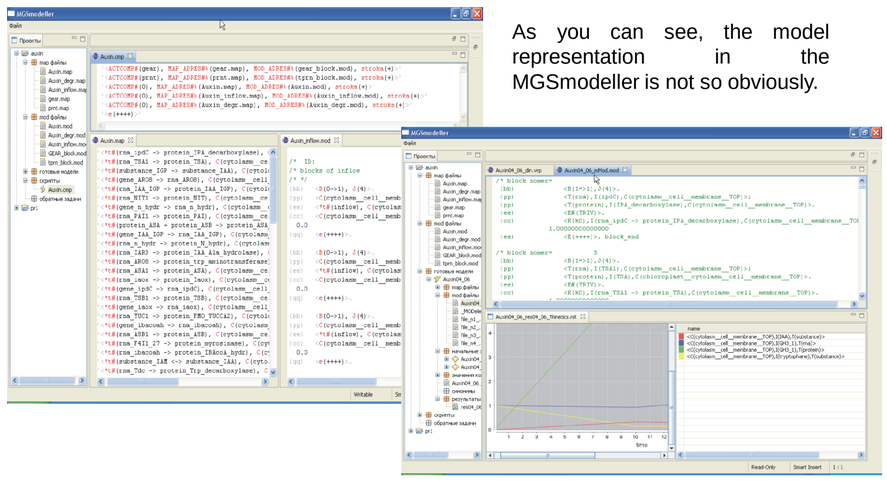
First we need to reconstruct the structure functional model of system under discussion or take the ready one from data store. For that purpose we use the GeneNet system (http://wwwmgs.bionet.nsc.ru/mgs/gnw/genenet). The next step is to modify gene network to take under consideration only processes that we need to model (remove ones or/and add ones)



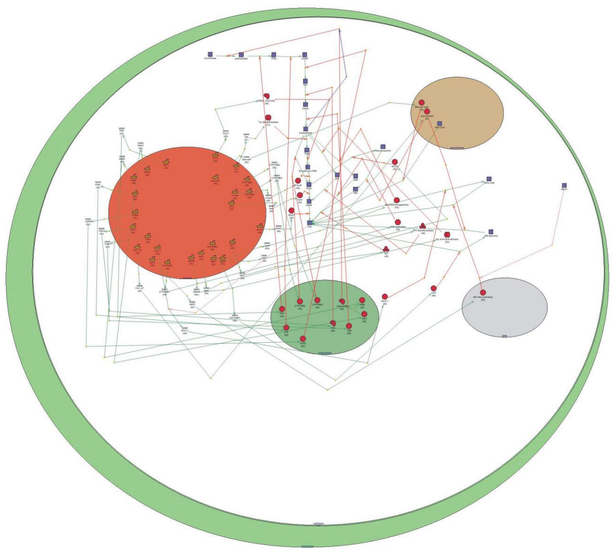

The second step is to make mathematical model of the system. For that purpose we use the MGSgenerator system. Using the MGSgenerator system we decrease probability of errors appearance and time remaining on the task.

Now we have mathematical model of our gene network. The model consists from 98 reactions and has 90 variables and 446 parameters.

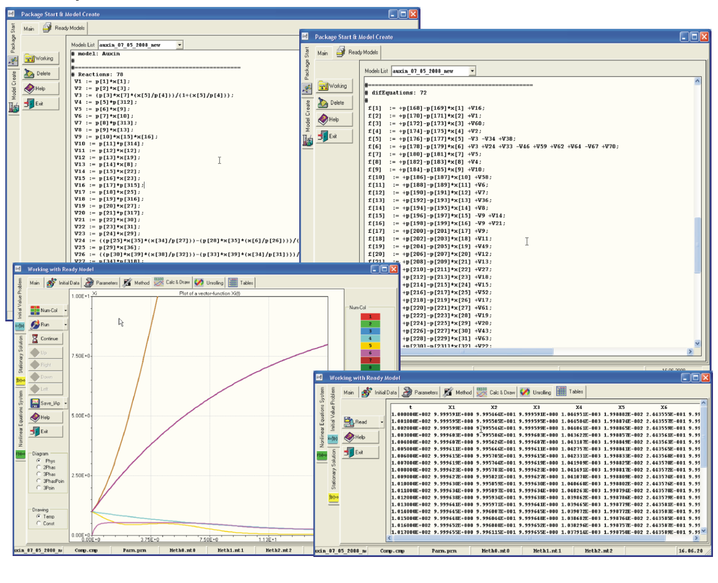
Next step is to export the model in other systems to solve direct tasks. On that moment we can export the model both the STEP+ system and the MGSmodeller.



As you can see, the model representation in the MGSmodeller is not so obviously.

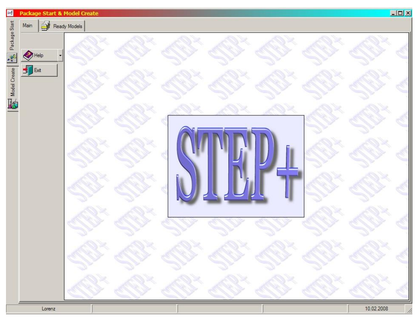


The model representation in the STEP+ system is more traditional for such systems.




## STEP+

Software "Step+" is oriented on the complex studying of the autonomous equations set, their stationary solutions and stability of the stationary solutions in dependence on parameters. Also the computer system is useful for decision of the unlinear systems in a general view.




## CONCLUSIONS

The software tool MGSgenerator could be and is used to generate math models of gene network patterns subset. Today we have a few plug-in modules that allow us to convert format XML of the GeneNet computer system into SiBML format of the MGSmodeller. The gene network that we used for MGSgenerator testing didn't allow us to describe for less then 20% of molecular-genetic processes by the mathematical models, but after gene network annotations modification we converted all processes in this gene network to the SiBML.
The original format of SiBML models description, algorithms and the MGSmodeller system are developed for generation, reconstruction, edition and calculation of molecular genetic networks models. This system was used for reconstruction the auxin metabolism mathematical model.

References:
1.V.A. Likhoshvai et al. (2001). Generalized chemokinetic method for gene network simulation, *Mol. Biol.*, **35:**1072-1079.
2. I.R. Akberdin et al, Mathematical model of auxin metabolism in shoots of arabidopsis thaliana L// *Proceedings of the Sixth International Conference on bioinformatics of genome regulation and structure (BGRS'2008)*

All information relatively MGS group is available on the web-site: http://modelsgroup.bionet.nsc.ru