

# Aggregation Connector: A Tool for Building Large Molecular Network Models from Components

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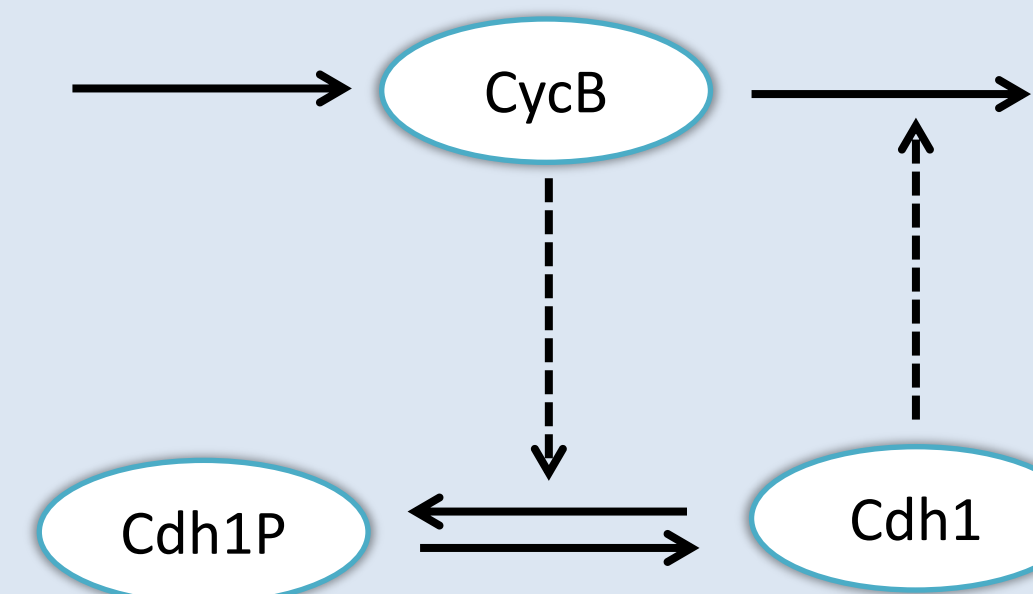
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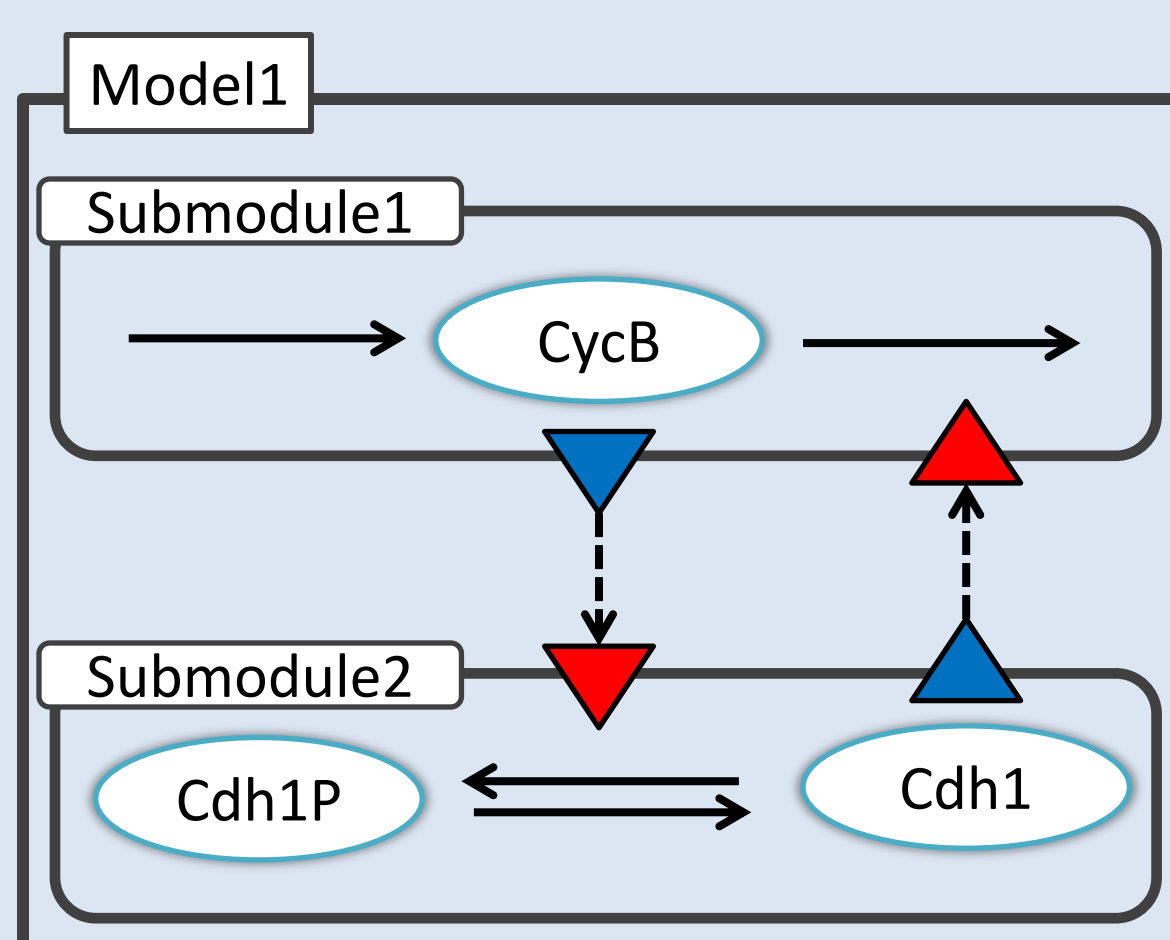
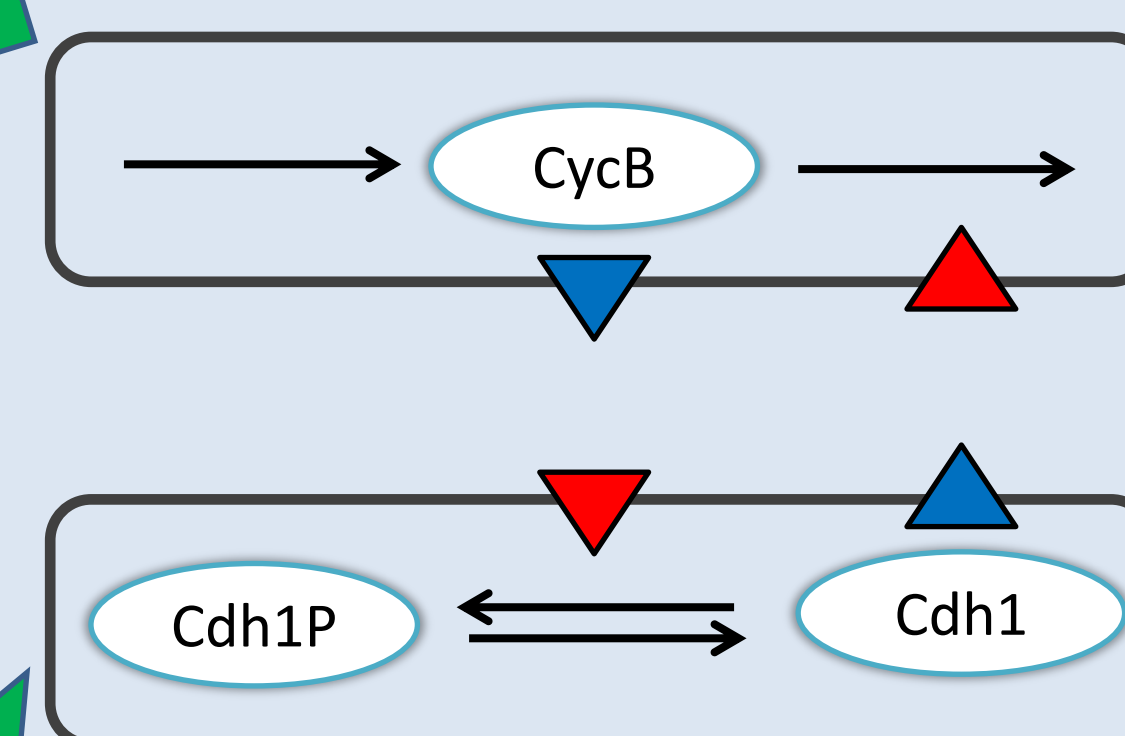
## Synopsis

The ever-growing size and complexity of molecular network models makes them difficult to construct and understand. Our approach to modeling is to build large models by combining together smaller models, making them easier to comprehend. At the base, the smaller models (called modules) are defined by small collections of reactions. Modules connect together to form larger models through clearly defined interfaces called ports<sup>[1]</sup>. We present the Aggregation Connector, a software tool that supports large-scale molecular network modeling.

## The Process

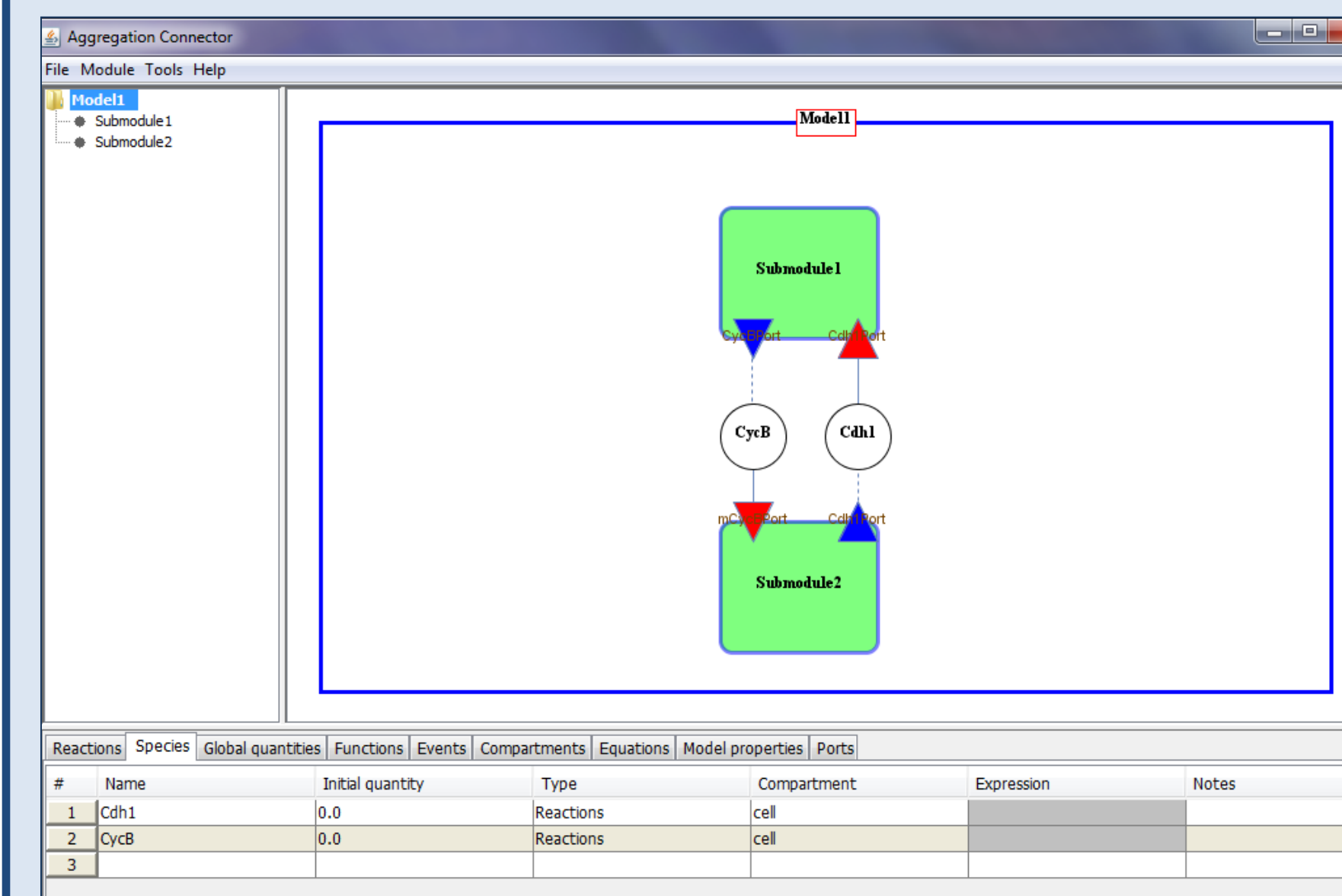


*Modularization:* group reactions together as a single module with a defined set of inputs and outputs



*Aggregation:* connect modules together (using ports) to create a larger model

## Interface



### TreeView

Displays the hierarchical structure of the model and submodules.

### DrawingBoard

Displays the graphical representation of the model and submodules.

### ModelBuilder

Displays the reactions, species, etc. of the model.

ModelBuilder for Submodule1

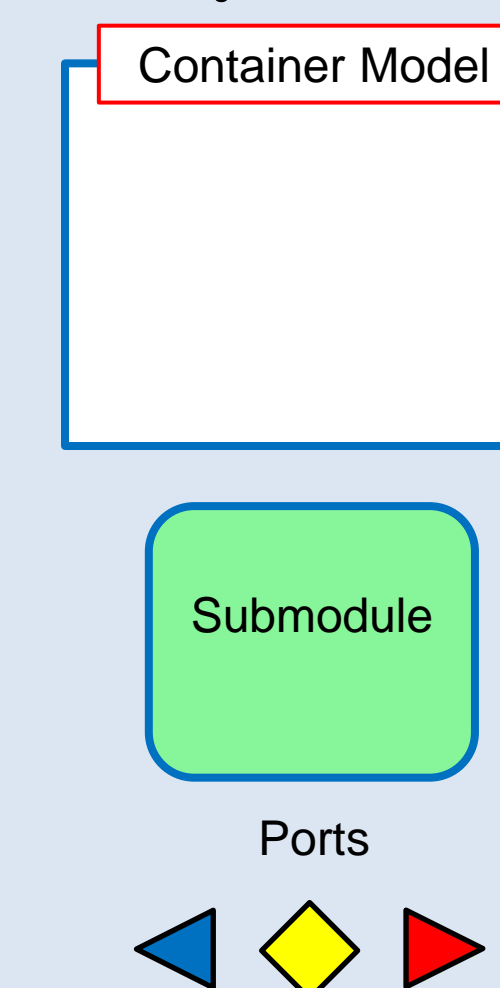
#	Name (opt)	Reaction	Kinetic Type	Kinetic Law	Notes
1		CycB: F	User Defined	syn(0,0,1,F)	
2		CycB -> Cdh1	User Defined	deg(0,0,0,1,Cdh1,CycB)	
3					

ModelBuilder for Submodule2

#	Name (opt)	Reaction	Kinetic Type	Kinetic Law	Notes
1		Cdh1P -> Cdh1	User Defined	MM(0,0,0,0,0,1,1,1,1,1)	
2		Cdh1P -> Cdc14	User Defined	MM(0,0,0,0,0,1,1,1,1,1)	
3					

## Model Components

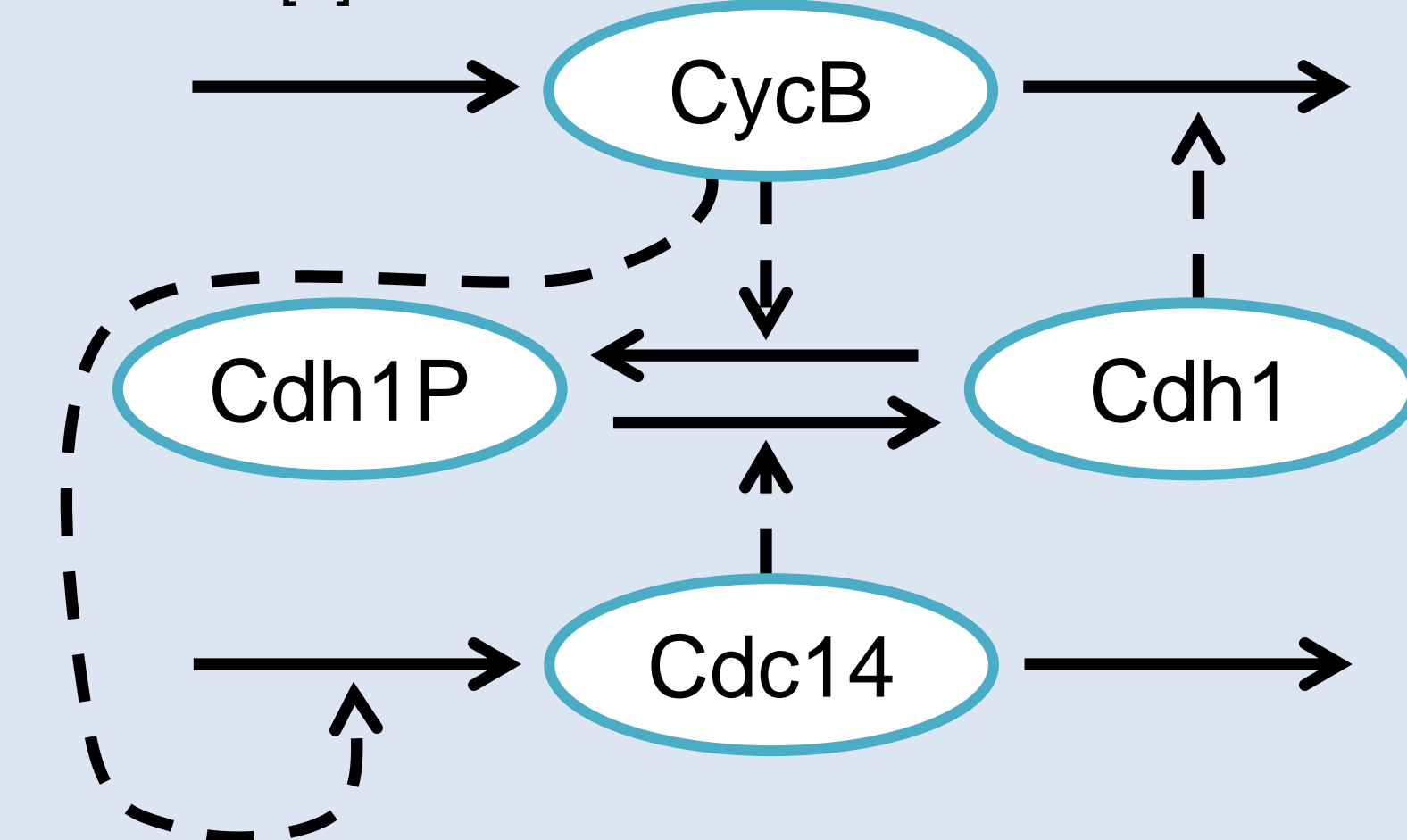


## Functionality

- Construct large models by connecting smaller modules together
- Create a module template and import it multiple times
- Complete models can be saved and later imported as submodules
- Import models in Systems Biology Markup Language (SBML) format
- Export models in SBML format, using the new SBML Hierarchical Model Composition and Layout packages
- Once exported, the SBML files can be imported into COPASI for further analysis<sup>[2]</sup>

## Cell Cycle Model

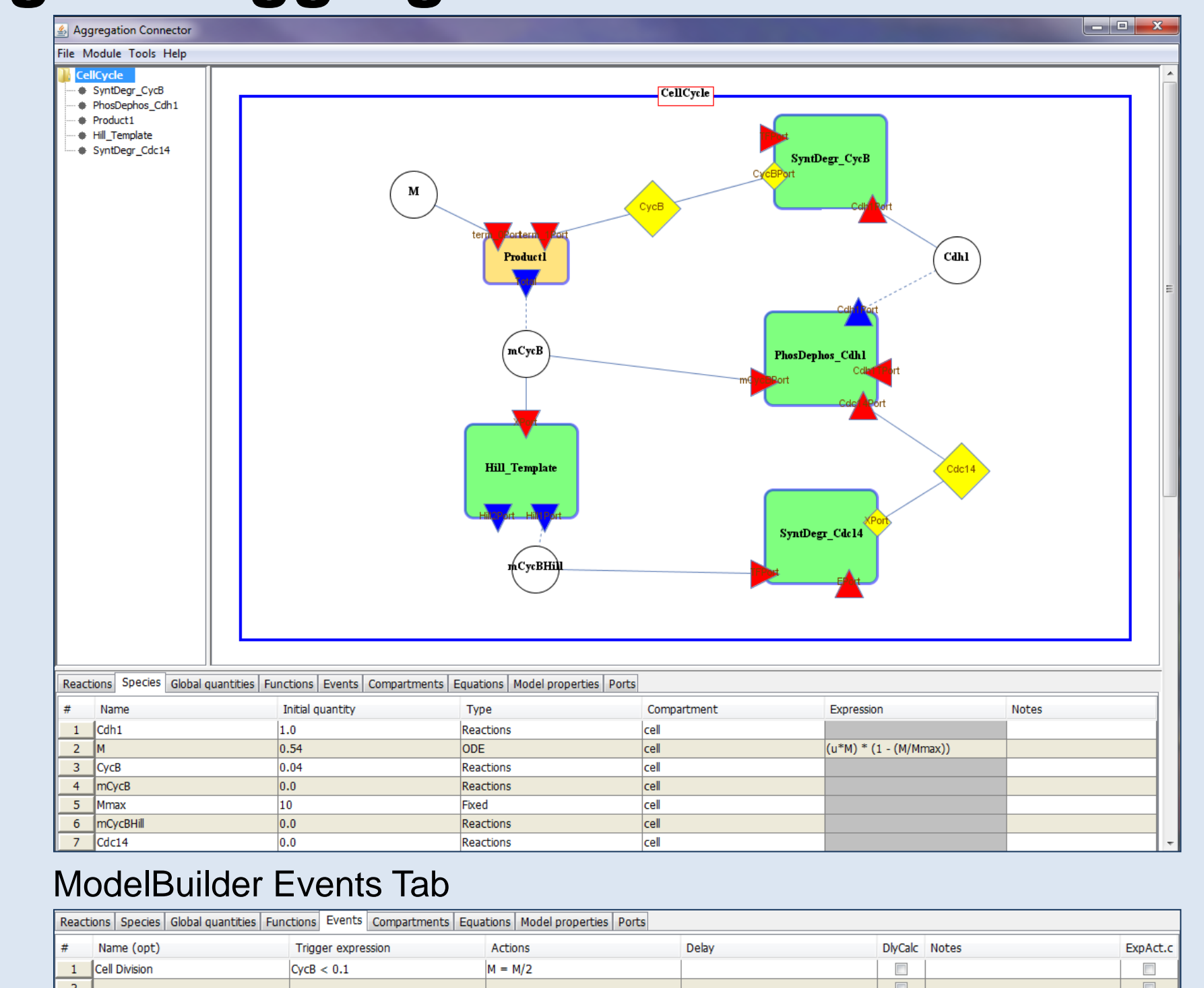
Original Model <sup>[3]</sup>



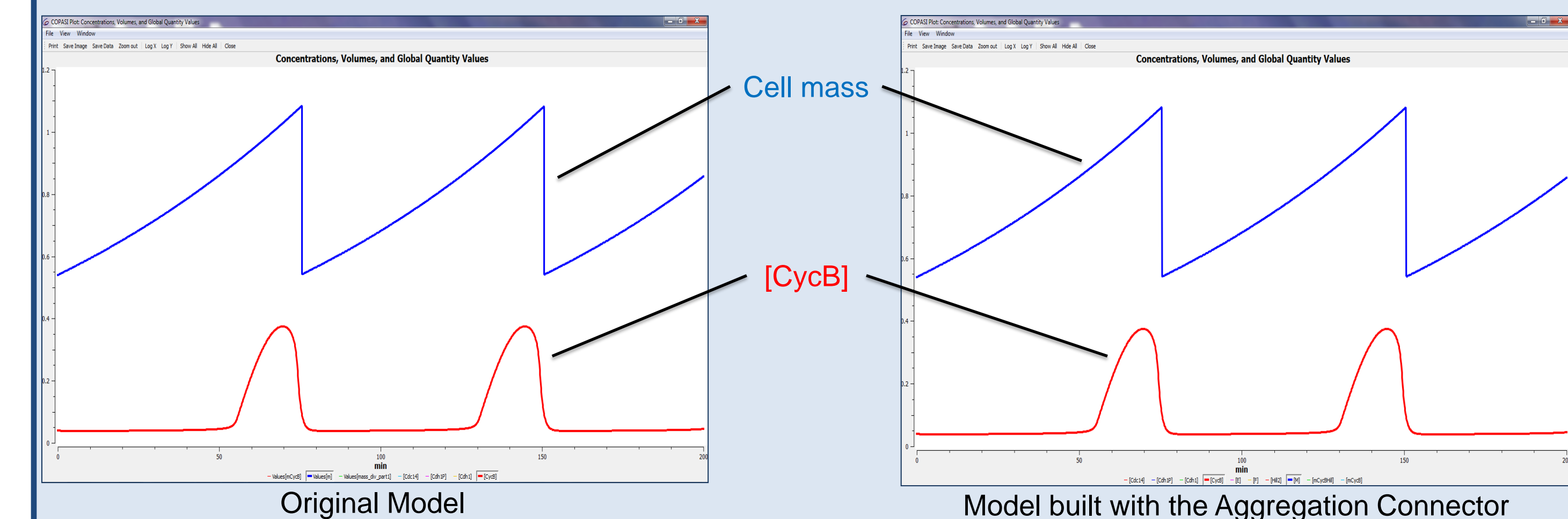
## Model created using the Aggregation Connector

Submodule Components

1. Synthesis and Degradation of CycB
2. Synthesis and Degradation of Cdc14
3. Hill function
4. Phosphorylation and Dephosphorylation of Cdh1



## COPASI simulation results



## References

- [1] R. Randhawa, C. Shaffer, and J. Tyson. (2008) Model Composition for Macromolecular Regulatory Networks. IEEE/ACM Trans. Comput. Biol. Bioinform., 99
- [2] Hoops S., Sahle S., Gauges R., Lee C., Pahle J., Simus N., Singhal M., Xu L., Mendes P. and Kummer U. (2006). COPASI: a Complex Pathway Simulator. *Bioinformatics* 22, 3067-74.
- [3] Fall, Christopher P., Eric S. Marland, John M. Wagner, and John J. Tyson. "Cell Cycle Controls." *Computational Cell Biology*. New York: Springer, 2002. 261-84.

## For More Information:

<http://www.copasi.org/softwareProjects>