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

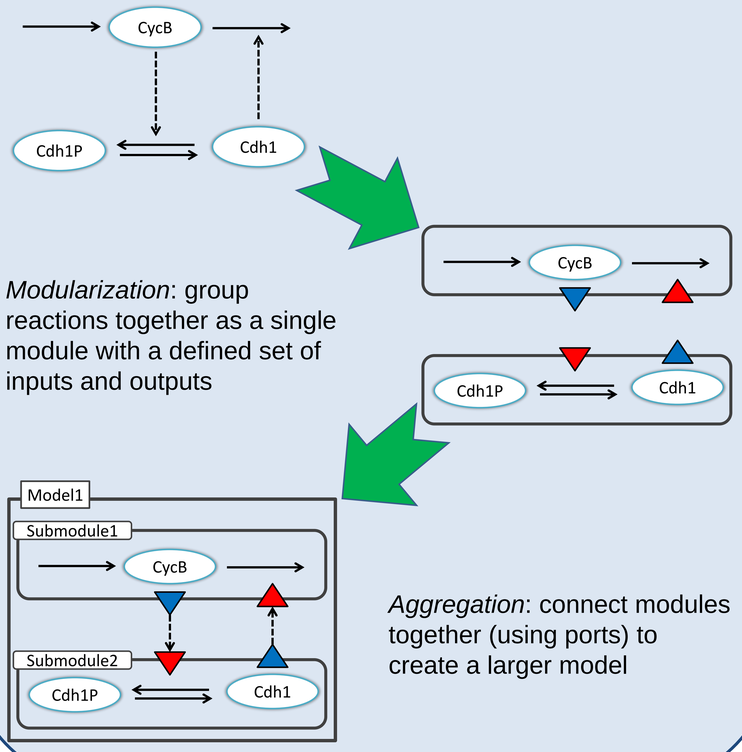
Thomas C. Jones Jr[1], Clifford A. Shaffer[1], Alida Palmisano[2], Stefan Hoops[3], Layne T. Watson[1], and John J. Tyson[2]

[1]Department of Computer Science, Virginia Tech, Blacksburg, VA
[2]Department of Biological Sciences, Virginia Tech, Blacksburg, VA
[3]Virginia Bioinformatics Institute, Virginia Tech, Blacksburg, VA
{tjones21, shaffer, alida.palmisano, shoops, ltw, tyson}@vt.edu

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 modules through clearly defined interfaces called ports[1]. We present the Aggregation Connector, a software tool that supports large-scale molecular network modeling.

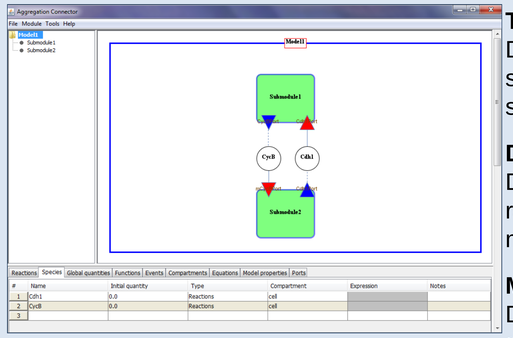
The Process



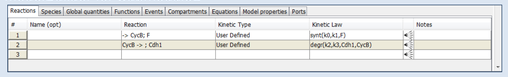
Modularization: group reactions together as a single module with a defined set of inputs and outputs

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

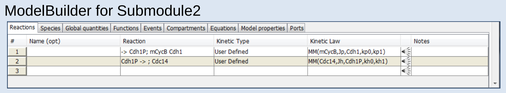
Interface



ModelBuilder for Submodule1



ModelBuilder for Submodule2

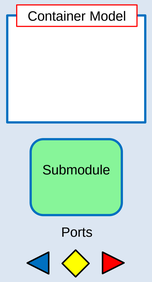


TreeView
Displays the hierarchical structure of the model and submodules.

DrawingBoard
Displays the graphical representation of the model and submodules.

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

Model Components

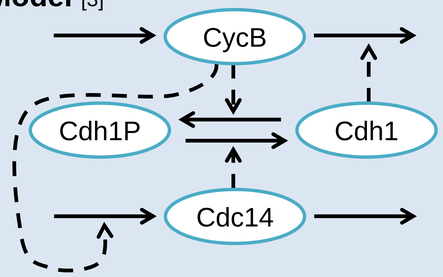


Functionality

- 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[2]

Cell Cycle Model

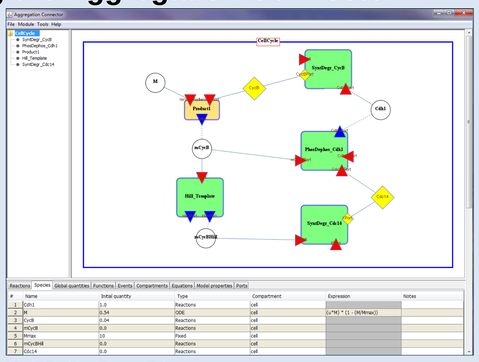
Original Model [3]



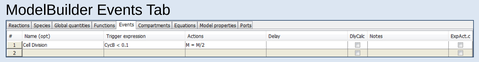
Model created using the Aggregation Connector

Submodule Components

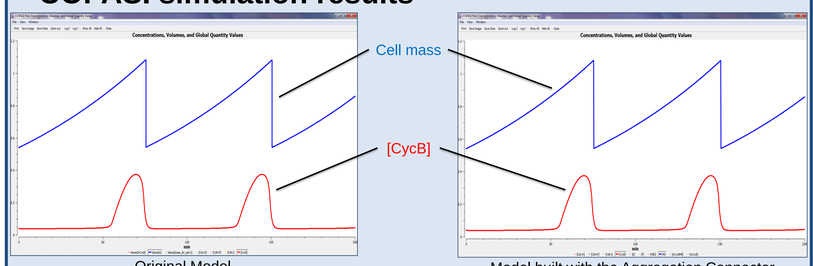
1. Synthesis and Degradation of CycB
2. Synthesis and Degradation of Cdc14
3. Hill function
4. Phosphorylation and Dephosphorylation of Cdh1



ModelBuilder Events Tab



COPASI simulation results



Original Model

Model built with the Aggregation Connector

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

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