Visualization Plugin for Optflux: tools for the creation of metabolic layouts and analysis of flux distributions

Authors: Paulo Vilaca[1,2], Alberto Noronha[2],Isabel Rocha[2], Miguel Rocha[2]

1- SilicoLife, Ltd, Portugal; 2- Centre of Biological Engineering, University of Minho, Portugal

The reconstruction of genome scale metabolic models is one of the major challenges of Systems Biology. These models are used to better understand the organisms' metabolic functions and predict their behavior in the form of flux distributions. Their increasing availability and use for the integrated analysis with high-throughput data has exacerbated the need for tools to visualize large scale models/networks. This problem was addressed with graph-drawing software such as Cytoscape, which allows the visualization of arbitrary graphs. However, the output from these platforms is visually distinct from the more traditional and empirically based metabolic layouts.

In this work, we present a new plugin for the OptFlux[1] framework, an open-source and modular software to support *in silico* Metabolic Engineering. The main goals of this novel plugin are to allow the creation, edition and visualization of metabolic layouts and to provide a user-friendly way to analyze results generated by other tools in OptFlux, such as phenotype simulation and strain optimization results. To represent metabolic layouts, the software uses a directed bipartite graph, where nodes are reactions and metabolites. Metabolites can be marked as a currency metabolite, a feature used to represent cofactors or other secondary metabolites. Reactions represent interactions between two sets of metabolites (products and reactants).

The plugin is able to read metabolic layouts from several file formats, including specialized formats, such as CellDesigner SBML variant, KEGG -ML or BIGG maps, and generic representations, such as SBGN-ML or XGMML (a format that is supported, for instance, by Cytoscape). Users can also create their own layouts using a set of reactions from a pre-loaded model. The framework uses a force directed layout[2] strategy to calculate the best position of each node and allows the user to fix, replicate or merge nodes to simplify the visualization.

An important feature is the ability to overlap results from other OptFlux plug-ins over the metabolic layout. An example is the overlap of flux distributions, where the thickness of the reaction edges are changed according to the flux values, while the genetic transformations (e.g. deletions, over/under expression) are also highlighted, with the relevant nodes changed in color and shape. Users are also able to compare flux distributions.

[1] M. Rocha, P. Maia, R. Mendes, J.P. Pinto, E.C. Ferreira, J. Nielsen, K.R. Patil, I. Rocha. Natural computation meta-heuristics for the *in silico* optimization of microbial strains. BMC Bioinformatics, 9, 2008.

[2] Thomas M. J. Fruchterman, Edward M. R. Graph drawing by force-directed placement. Software: Practice and Experience, 11, 1991.