Cupe - The CUBIC Pathway Editor

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Cupe(CUBIC Pathway Editor) is a graphical editor for the automatic or interactive generation and display of metabolic networks. Cupe combines the user guidance by its graphical user interface (GUI) with the ability of automatic graph drawing and the possibility for manual interaction. Furthermore, it provides a programming interface for analysis, simulation and cross linking of reactions.

One of the outstanding features of Cupe is its automatic layout mechanism which is provided by utilising the well-known AGD library. The adaptation and development of layout algorithms for the requirements of metabolic networks is an interdisciplinary cooperation between the Department of Computer Science, Cologne University, the Chair of Algorithm Engineering, Dortmund University, and the Cologne University Bioinformatics Center.

More information about Cupe can be found at www.cupe.uni-koeln.de.

1 Metabolic Networks

A *metabolic network* is a connected set of reactions. Each reaction follows in principle a pattern like: $A + B \rightleftharpoons C + D$. A *path* is a connected set of reactions leading from a substrate to a product. In Cupe, a metabolic network is represented as a bipartite graph $G = (M, R, E)$, where M is the set of metabolites, R is the set of enzymes, and E is the set of edges. Furthermore, there are some special properties in metabolic
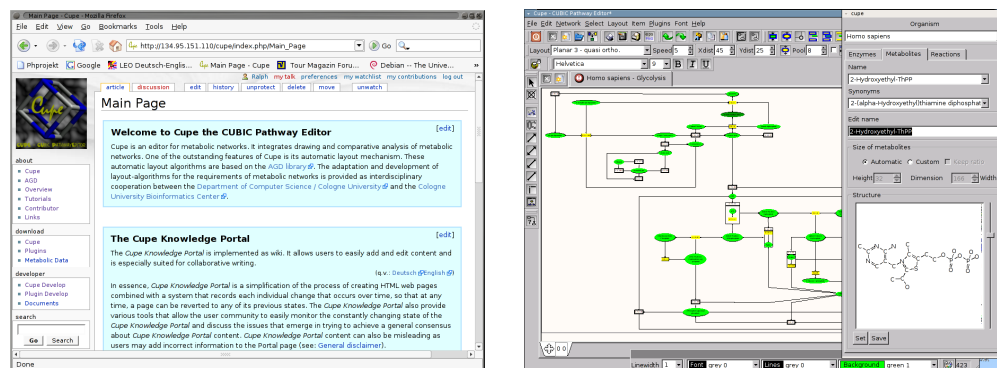

Fig. 1. Cupe' homepage and main window.

networks, e.g., not all paths in a reaction network are reasonable or coexistent metabolic paths (atom-mapping) and *side-metabolites* could carry a disproportionately high node degree.

2   Automatic Graph Layout

In the current version of Cupe, automatic graph layout is provided by the AGD library. The next version will replace AGD with AGD's successor OGDF (*Open Graph Drawing Framework*). Besides all the standard layout algorithms already provided by AGD, Cupe has some special layout capabilities.

Extended usage of automatic graph layout. Cupe is able to group parts of a metabolic network according to the biological question in focus. The resulting clusters can be recursive and laid out partially autonomous. Moreover, expanding and collapsing clusters is supported. Metabolites can be shown pooled and/or networked at the same time. These features are an important tool for reducing the complexity of large metabolic graphs; it becomes possible to work with a mental map preserving low level version of the diagram without dealing with high abstraction levels.

Adapted layout algorithms. A biologist is used to some standardised representations of reaction systems, e.g., reaction cycles should be drawn as cycles or incoming and outgoing edges of enzyme-nodes should be separated. It is also desired to achieve a similar layout for similar paths. The adaption of layout algorithms to these special needs are conducted as independent projects. Some of them are already successfully completed and their results will be integrated into Cupe with the transition to OGDF.

3   Extensibility

Cupe is a complete tool set for generating and analysing all kinds of metabolic reaction networks. Therefore, Cupe can be utilised for almost all kinds of questions and approaches of analysis on metabolic networks. However, it was not the goal of the Cupe project to implement all of these methods. Instead, Cupe is equipped with an easy-to-use plugin interface. Plugins are able to access all modules (data, layout, drawing, analysis). Moreover, it is possible to add, save and reread custom-defined data types and information, without corrupting the file format or making the file format dependent on a particular plugin. At the moment, there are already three plugins contributed by users of Cupe.

The Cupe Knowledge Portal. The further development of academic software is often constrained by the expert-knowledge of the initial developer. Once the initiator of such a project is gone, the barriers for getting acquainted with the project become so high, that the further development might disrupt. To avoid such a dilemma, Cupe's development is organised via a Wiki-network called the *Cupe Knowledge Portal*. The whole knowledge-transfer about plugins, modules, and documentation is distributed via this web site.