BRIME: A tool for visualization of metabolic models

Timo Lühr*, Maurice Scheer*, Melanie Busch*, Michael Rother, Ida Schomburg and Dietmar Schomburg
*) These authors contributed equally to this work
Technische Universität Braunschweig, Department of Bioinformatics and Biochemistry, Langer Kamp 19 B, 38106 Braunschweig, Germany
t.luehr@tu-bs.de, m.scheer@tu-bs.de, melanie.busch@tu-bs.de

Building a network model containing all biochemical reactions of an organism's metabolism has become a frequent task in systems biology. An overview of the reconstructed network and its biochemical dependencies is helpful for metabolic modeling to avoid gaps and implausible reactions.
To facilitate this process, we created an online tool for the visualization of metabolic networks and its fluxes displayed on a reference map. This manually edited and verified map contains more than 1,500 biochemical reactions based on the enzyme information system BRENDA [Sch11]. Matching the reactions of the reference map to those from the KEGG [Kan10] and MetaCyc [Cas10] database was performed, yielding in about 70% correlation.
To display a model in the context of the interactive map, it can be uploaded on the web interface of BRIME (BRaunschweig Interactive Metabolism Explorer) and matched automatically to the map. Additionally, it is possible to search for enzymes, substances, biochemical reactions, whole pathways or organisms in the reference network. Those items can be used for customizing the display of the map manually, for example by adding to an uploaded metabolic model. Therefore a search field for finding single reactants, enzymes or pathways was introduced. A live search proposes constituents from the reference map containing the already typed part of the word. Furthermore, the equation of a biochemical reaction or parts of it can be searched. These reactions can be added to a search list allowing a combined search of all demanded items.
The resulting matches are displayed in a dynamic navigation tree and can be highlighted in the reference map. For a better overview, values calculated in metabolome experiments can be depicted and visualized by fading out all network components except those of interest. A menu is given to adjust search and display settings and to provide a download of the map in picture format.
To evaluate the findings, an intuitive navigation is supported by arrow buttons as well as drag and drop mode comparable to interactive street maps. By pointing the cursor on a special node in the map, a window is opened, providing a brief description of the corresponding enzyme or substance and a link to related database entries. Therefore, BRIME can be used as a graphical starting point to more detailed information in the databases BRENDA, KEGG and MetaCyc.
In summary BRIME allows the user to map an existing metabolic model in order to visualize or review the collected data. Starting from this overview, it will be much easier to find limits of the model and erase them with the aid of the given links to further information.

References

[Sch11] Scheer M., Grote A., Chang A., Schomburg I., Munaretto C., Rother M., Söhngen C., Stelzer M., Thiele J., Schomburg D. : BRENDA, the enzyme information system in 2011 . Nucleic Acids Res., 39(Database issue): D670-D676 (2011)

[Cas10] Caspi R., Altman T., Dale J.M., Dreher K., Fulcher C.A., Gilham F., Kaipa P., Karthikeyan A.S., Kothari A., Krummenacker M., Latendresse M., Mueller L.A., Paley S., Popescu L., Pujar A., Shearer A.G., Zhang P., Karp P.D.: The MetaCyc database of metabolic pathways and enzymes and the BioCyc collection of pathway/genome databases. Nucleic Acids Res., 38(Database issue): D473-D479 (2010)

[Kan10] Kanehisa M., Goto S., Furumichi M., Tanabe M., Hirakawa M.: KEGG for representation and analysis of molecular networks involving diseases and drugs. Nucleic Acids Res. 38(Database issue): D355-D360 (2010)