

Comparison of atom mapping algorithms for metabolic reactions

German Preciat¹, Hulda S. Haraldsdóttir^{1*} (hulda.haraldsdottir@uni.lu), and Ronan M. T. Fleming¹

¹Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg

<http://stanford.edu/group/SOL/multiscale/>

Project Goals: We aim to represent metabolic reactions at atomic resolution by saturating metabolic databases with structural formulas for metabolites and atom mappings for reactions. Atom level representations of metabolites and reactions extend the range of applications for metabolic network reconstructions to include, for example, estimation of thermodynamic parameters [1], identification of conserved moieties [2], and stable isotope assisted metabolic flux analysis [3].

Metabolic reactions conserve mass and elements. Each instance of a reaction must therefore map every substrate atom to a specific product atom of the same element. Realizable atom mappings are determined by organic chemistry and reaction mechanisms. Atom mapping data for metabolic reactions open the door to a growing list of applications [3, 4, 5, 2] that are not available with data at the level of reaction stoichiometry. Until recently, acquiring atom mapping data for genome-scale metabolic network reconstructions was a labour intensive prospect. However, a number of algorithms to predict atom mappings have now become available. Here, we compare four recently published algorithms on criteria including accuracy, speed, and availability. The algorithms are DREAM [6], Pathway Tools [7], ICMAP [8] and CLCA [9]. Accuracy was determined by comparison to a set of manually curated atom mappings. We discuss common issues including hydrogen atom mapping and molecular symmetry. We conclude with an effective strategy to increase the coverage of high quality atom mapping data in the metabolic databases.

References

- [1] Noor E, Haraldsdóttir HS, Milo R, Fleming RMT (2013) Consistent Estimation of Gibbs Energy Using Component Contributions. *PLoS Comput Biol* 9: e1003098.
- [2] Haraldsdóttir HS, Fleming RMT (2015) Identification of conserved moieties in metabolic networks by graph theoretical analysis of atom transition networks. Submitted .
- [3] Wiechert W (2001) 13c Metabolic Flux Analysis. *Metabolic Engineering* 3: 195–206.
- [4] Kotera M, Okuno Y, Hattori M, Goto S, Kanehisa M (2004) Computational Assignment of the EC Numbers for Genomic-Scale Analysis of Enzymatic Reactions. *Journal of the American Chemical Society* 126: 16487–16498.
- [5] Pey J, Planes FJ, Beasley JE (2014) Refining carbon flux paths using atomic trace data. *Bioinformatics* 30: 975–980.
- [6] First EL, Gounaris CE, Floudas CA (2012) Stereochemically Consistent Reaction Mapping and Identification of Multiple Reaction Mechanisms through Integer Linear Optimization. *Journal of Chemical Information and Modeling* 52: 84–92.
- [7] Latendresse M, Malerich JP, Travers M, Karp PD (2012) Accurate Atom-Mapping Computation for Biochemical Reactions. *Journal of Chemical Information and Modeling* 52: 2970–2982.
- [8] Kraut H, Eiblmaier J, Grethe G, Löw P, Matuszczyk H, et al. (2013) Algorithm for reaction classification. *Journal of Chemical Information and Modeling* 53: 2884–2895.
- [9] Kumar A, Maranas CD (2014) CLCA: Maximum Common Molecular Substructure Queries within the MetRxn Database. *Journal of Chemical Information and Modeling* 54: 3417–3438.

This work was supported by the U.S. Department of Energy, Offices of Advanced Scientific Computing Research and the Biological and Environmental Research as part of the Scientific Discovery Through Advanced Computing program, grant #DE-SC0010429.