175. Integrating atom mapping information within MetRxn: Application to metabolic flux elucidation through MFA

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Project Goals: This project aims to organi e and disseminate standardi ed metabolite and reaction information to improve metabolic modeling by accurately describing reaction stoichiometry, directionality, atom mapping from reactants to products, and gene to protein to reaction relations. Developed standardi ation algorithms automatically curate information to remove incompatibilities in content representation, fix stoichiometric errors such as elemental or charge imbalances and resolve incomplete atomistic details.

MetRxn is a standardized non-redundant searchable collection of published metabolic models and databases from a wide variety of organisms. The standardization procedure follows a workflow that starts by matching metabolite entries using lexicographic and phonetic techniques, and structure comparison using atomistic details. The reactions are first charge and mass balanced and subsequently atom/bond mapping resolution algorithms are applied. For each reaction, metabolite stoichiometry, atom transition and metabolite compartment information is stored. The reaction and metabolite information is downloadable in SBML 3.0 and in a tabular format. The current MetRxn update includes recently published metabolic data for a total of 112 metabolic models and 8 metabolic databases. The number of distinct reactions that have been mapped is greater than 20,000 and MetRxn contains tools that allow users to download atom mapping data for each reaction.

As part of our ongoing effort we have enhanced the MetRxn knowledgebase with additional information such as reaction transition information and reaction standard free energies. In accordance with our data integration goal, we have integrated the ncbi taxonomy database, uniprot gene id's and ncbi gene id's within MetRxn. We developed a customized algorithm for quickly generating unique molecular graphs and detecting symmetries for all metabolites in the database. This is used to create atom transition information between reactants and products for all reactions contained in MetRxn. This information is leveraged for the construction of genome- scale size mapping models to support metabolic flux elucidation using C13 labeled substrates through MFA. Algorithmic details and the impact of migrating to genome-scale models on flux elucidation fidelity are discussed. The current release, MetRxn 2.0 (http://www.metrxn.che.psu.edu/) makes available information on metabolites, reactions, enzymes and reaction atom transitions required by metabolic flux elucidation tools such as Metran, OpenFlux, 13CFlux2 and FiatFlux.

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