GAP-FILLING WITH THE ATLAS OF BIOCHEMISTRY TO RESOLVE METABOLIC GAPS IN *E. coli*

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ABSTRACT

Advances in medicine and biotechnology rely on the further understanding of biological processes. Despite the technological advances and increasing available types and amounts of omics data, significant biochemical knowledge gaps remain uncharacterized. We necessitate methods that enable systematically analysing the growing sets of data and identifying the knowledge gaps. Several approaches [1][2] have been developed during the past decades to identify missing metabolic annotations in genome-scale models (GEMs), which are biochemical databases for an organism. However, these approaches suggest missing metabolic reactions within a limited set of already characterized metabolic capabilities.

In this study, we propose a workflow to identify, classify and characterize missing metabolic capabilities in GEMs using the ATLAS of Biochemistry [3]. The ATLAS of Biochemistry, which involves more than 130,000 possible enzymatic reactions between known biological compounds, represents the upper bound of missing biochemistry and is hence a guide to fill the gaps. We apply our gap-filling approach to the latest genome-scale model of *Escherichia coli* (iML1515) [4] and develop a database of top suggested biochemistry that can indicate its missing metabolic capabilities. Interestingly, some gaps cannot be filled with the ATLAS of Biochemistry and represent biochemical bottlenecks for further analysis. Overall, our approach will be a reference and valuable tool for the reconstruction and refinement of metabolic networks, and our results will accelerate experimental studies toward fully annotated genomes.

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