Standardization and Comparison of the Biomass Objective Functions of Manually Curated Genome-scale Metabolic Models

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The biomass objective function (BOF) is an abstractive equation used in genome-scale constraint-based modelling (GS-CBM) to predict growth phenotypes. The BOF represents all the growth requirements upon cell division, which stoichiometric representation is ideally based on experimental measurements for cells growing in log phase (1). For growth rate calculations it is sufficient to know the macromolecular content of the cell, its detailed composition (amino acids, nucleotides and fatty acids.) and energetic costs of growth (2). However, to examine network essentiality another level of detail is required, which includes cofactors and ions and the analysis of which are the minimally essential biomass components (2) often called the core biomass (3, 4). There is no defined strategy in the literature for choosing which components are to be parts of a detailed BOF and the core BOF. In order to obtain a universal core prokaryotic BOF, we integrated BOFs of 71 genome-scale manually curated prokaryotic models, the ModelSEED framework for biomass composition (5) and data from the literature. We used a semi-automatic process to standardize the nomenclature of metabolites in the 71 BOFs, as there is still not a norm for the terminology of metabolites in GS- CBM. We found that the clustering of these 71 models based on their BOFs fails to represent the phylogenetic relationship of the modelled prokaryotes. No cofactor was present in all the BOFs analysed, including the important redox cofactors nicotinamide adenine dinucleotide (NAD) or NAD-Phosphate. Both the ModelSEED framework and other literature indicate some cofactors and many ions as universally essential. We conclude that not only the redox cofactors but also others as coenzyme A, flavins and thiamin might need to be added to the BOFs for improving future essentiality studies. We present a proposal of a set of cofactors for a universal core prokaryotic BOF.

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