Insights on Metabolic Features of Bacillus subtilis Based on Multistrain Genome-Scale Metabolic Modeling

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Summary

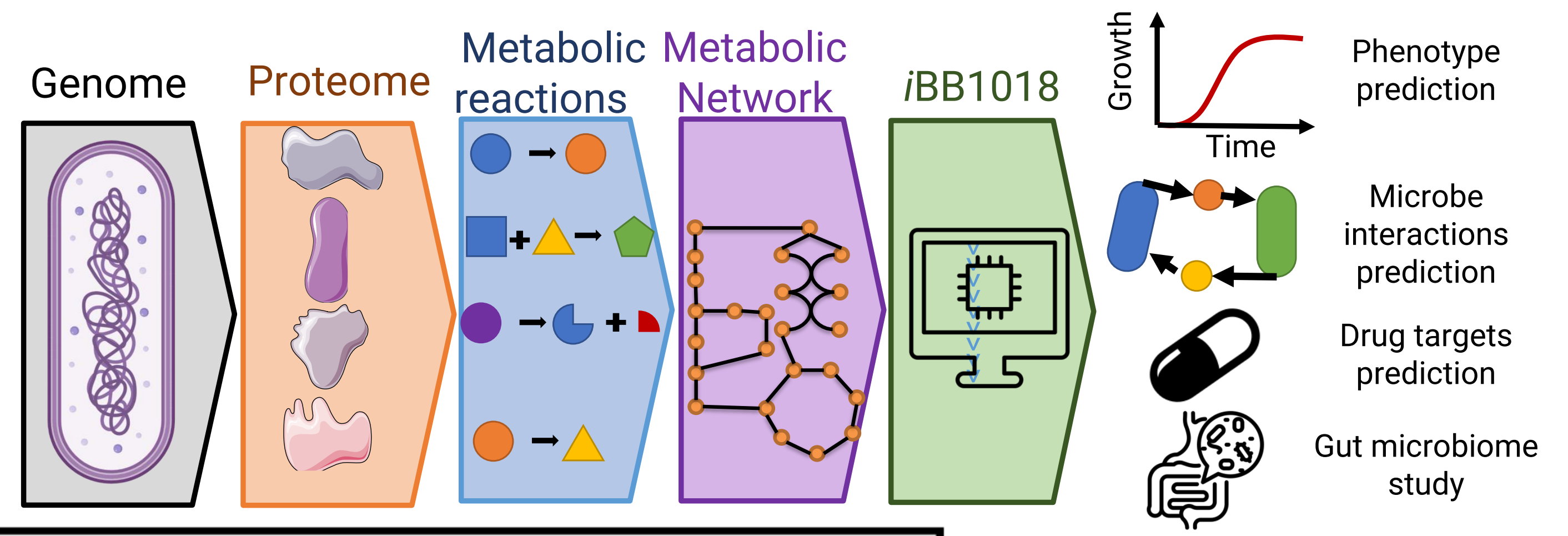
Bacillus subtilis is an effective workhorse for the production of many industrial products. The high interest aroused by *B. subtilis* has guided a large metabolic modeling effort of this species. Genome-scale metabolic models (GEMs) are powerful tools for predicting the metabolic capabilities of a given organism. However, high-quality GEMs are required in order to provide accurate predictions. In this work, we construct a high-quality, mostly manually curated GEM for *B. subtilis* (*i*BB1018). The constructed model was further used as a tool for the construction of the panphenome of *B. subtilis* as a species, by means of multistrain genome-scale reconstruction. The panphenome space was defined in the context of 183 GEMs representative of 183 *B. subtilis* strains and the array of carbon sources sustaining growth. Our analysis highlights the large metabolic versatility of the species and the important role of the accessory metabolism as a driver of the panphenome, at a species level.

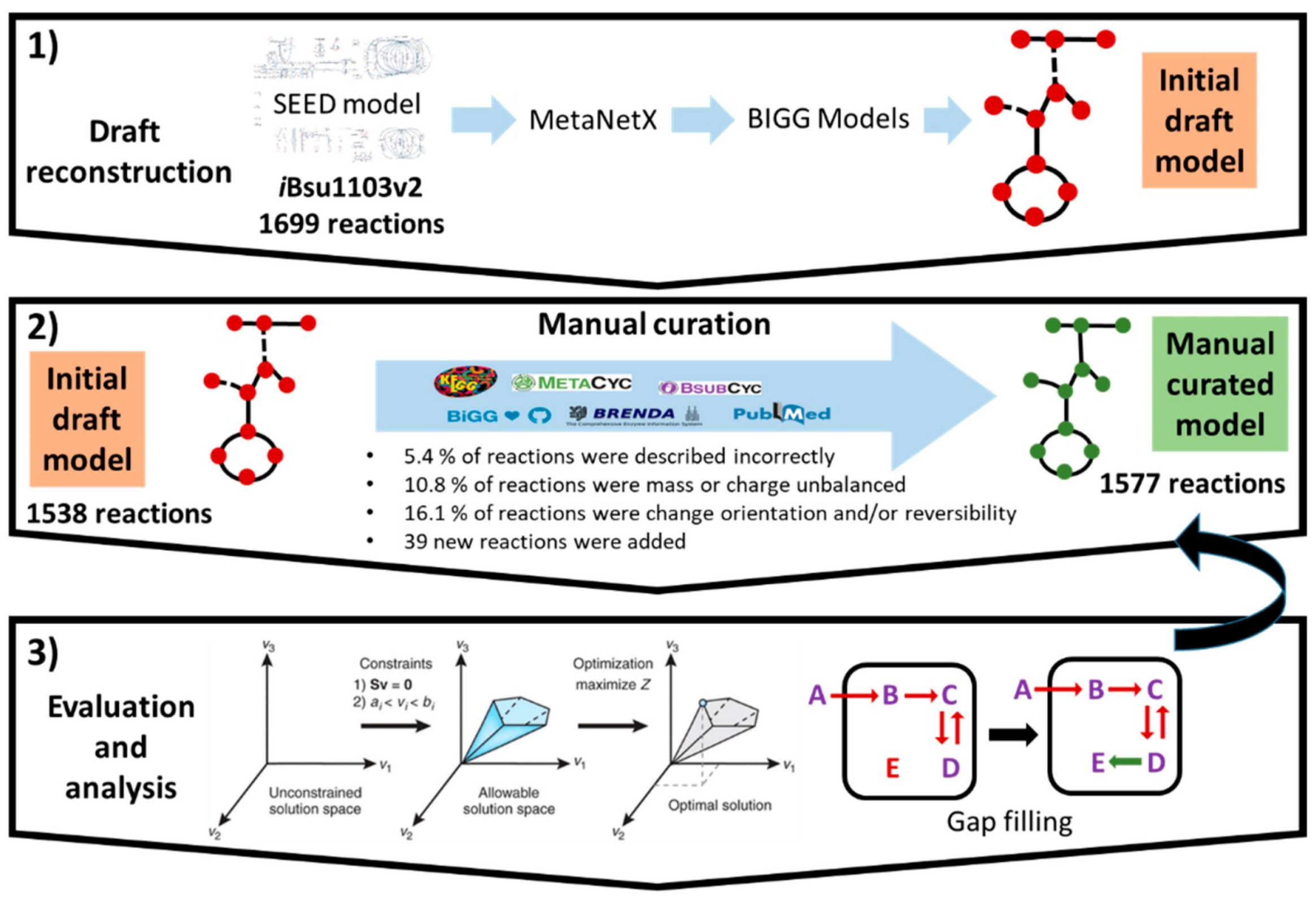
Research

REFERENCE *B. subtilis sp. 168* GEM

Computational description of gene-protein-reaction associations for entire metabolic genes in *B. subtilis* 168

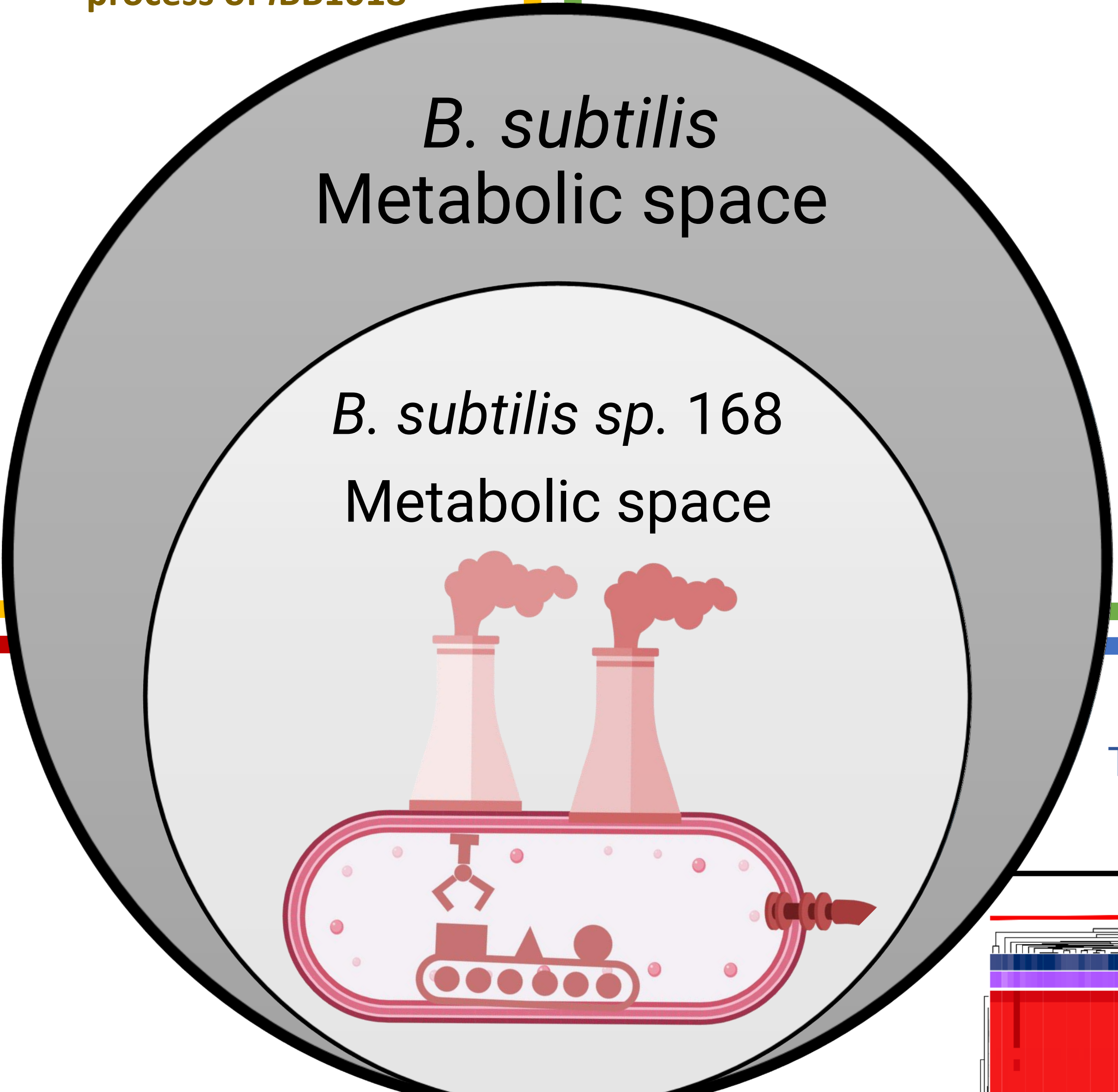
Workflow for GEM reconstruction and examples of application >





- 5.4 % of reactions were described incorrectly
- 10.8 % of reactions were mass or charge unbalanced
- 16.1 % of reactions were change orientation and/or reversibility
- 39 new reactions were added

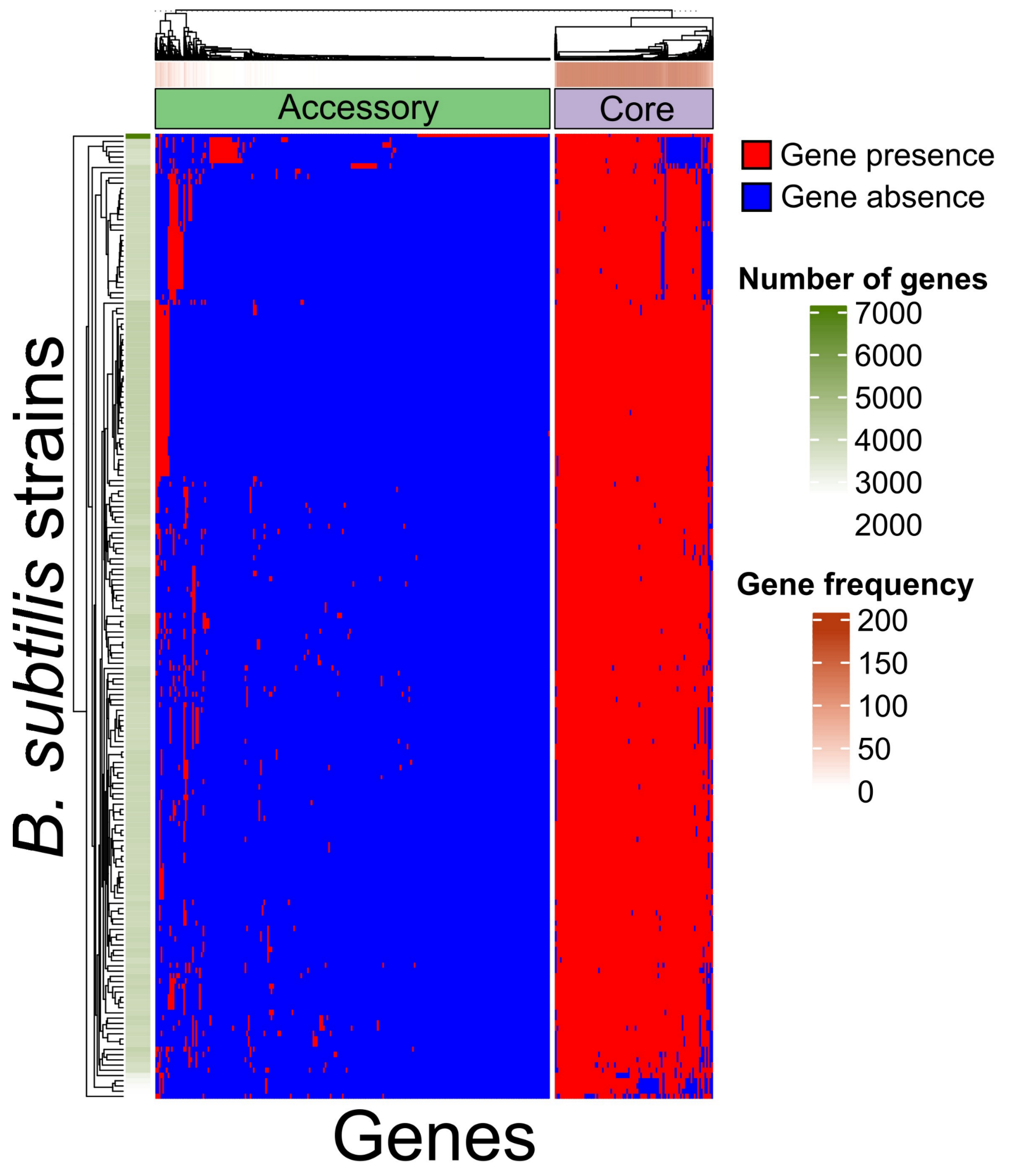
< Exhaustive reconstruction process of *i*BB1018



PANGENOME

Entire set of genes from all strains within *B. subtilis* clade

Heatmap of B. subtilis pangenome. The pangenome of 184 *B. subtilis* strains was addressed by performing a homology analysis in order to identify orthologous genes among the analyzed strains. The strains are represented on the columns and the genes are represented on the rows. The color represents the presence (red) or absence (blue) of gene in the correspondence strains. The upper line diagram represents the frequency of the presence of the genes in the total number of strains. We defined the core pangenome as that including those genes present in a high percentage of strains (>95%), while the accessory pangenome was defined as that representing unique or shared functions by a reduced group of strains

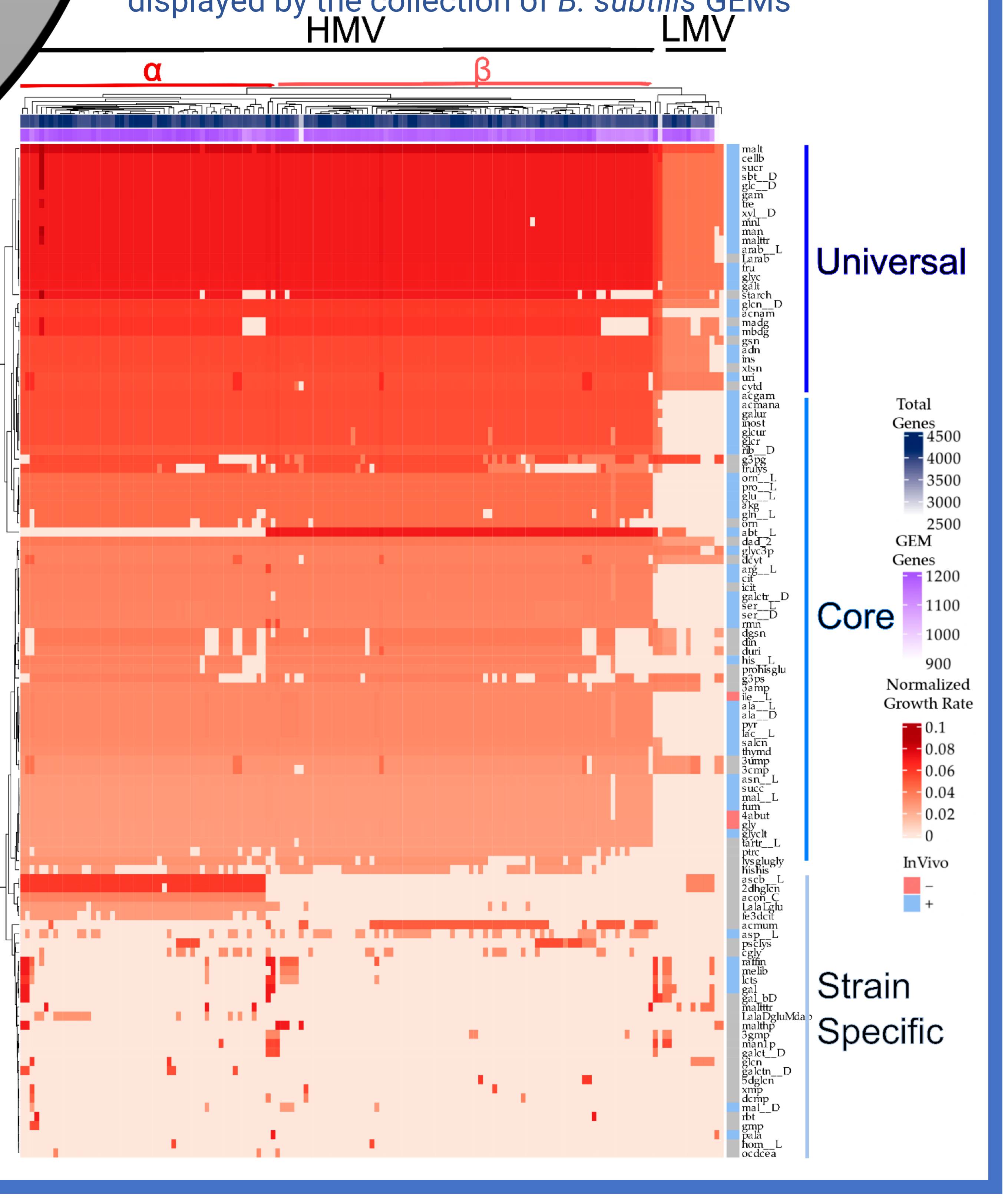


RESULTS

PANPHENOME

The set of all the in silico metabolic phenotypes displayed by the collection of *B. subtilis* GEMs

Heatmap with the panphenome growth rates across multiple carbon sources. The top color bars indicate the total number of genes per genome (blue) and the total genes included in the GEMs (purple). The right bar indicates if the carbon source was tested in Biolog with *B. subtilis* 168 and the growth result in vivo. The α and β symbols represent HMV subgroups. The universal class contains carbon sources with more than 90% of the strains with growth, the core class contains between 30% and 90%, and the strain-specific class contains less than 30%.



The most **complete** *B. subtilis* sp 168 GEM (*i*BB1018)	**28** new potential carbon sources	**183** GEMs of *B. subtilis* strains	New putative **accessory metabolism** detection

Publication

Blázquez, B., San León, D., Rojas, A., Tortajada, M., & Nogales, J. (2023). New Insights on Metabolic Features of Bacillus subtilis Based on Multistrain Genome-Scale Metabolic Modeling. *International Journal of Molecular Sciences*, *24*(8), 7091.

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