

## Methane utilization in *Methylobacterium alcaliphilum* 20Z<sup>R</sup>: new routes of C<sub>1</sub>-metabolism

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**Motivation and Aim:** Biological methane utilization is one of the main sink of the greenhouse gas in nature and it represents an attractive platform for production of fuels and value-added chemicals. A number of methanotrophic bacteria have been isolated, but only a few of them, including *Methylobacterium alcaliphilum* 20Z<sup>R</sup> (20Z<sup>R</sup>), have been established as promising and efficient catalysts for industrial applications. Robust growth, complete and expert-annotated genomic information, and a large set of genetic tools make 20Z<sup>R</sup> one of the best systems for understanding and exploiting biological methane oxidation.

**Methods and Algorithms:** We applied a set of systems-level approaches for comprehensive investigation of the methane utilization network in 20Z<sup>R</sup>. A genome-scale metabolic model of 20Z<sup>R</sup> was constructed and refined using enzymatic, metabolic, proteomics, and gene expression data collected under different environmental conditions.

**Results:** The model simulations demonstrated that a significant portion of consumed methane, a quarter of consumed carbon, is used for non-growth-associated energy maintenance. Developed genome-scale model has highlighted the dynamic behavior of methane oxidation machinery and indicated the necessity of an additional constraint on the O<sub>2</sub> consumption rate to correctly reproduce experimentally observed parameters (growth rate and corresponding yields).

**Conclusion:** The flux balance analysis of the model combined with global, non-targeted metabolomic profiling and enzymatic assays highlighted the importance of the substitution of ATP-linked steps with PPI-dependent reactions and supported the presence of a carbon shunt from acetyl-CoA to the pentose-phosphate pathway and highly branched TCA cycle [1].

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### References

1. Akberdin I.R. et al. (2018) Methane utilization in *Methylobacterium alcaliphilum* 20Z<sup>R</sup>: a systems approach. Scientific reports. 8(1):2512.