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► To cite this version:

Juliette Audemard, Sébastien Halary, Gabriel Markov, Jeanne Got, Anne Siegel, et al.. Metagenome-scale metabolic modelling for the characterization of cross-feeding interactions in Microcystis-associated microbial communities, in the context of freshwater cyanobacterial blooms. JOBIM 2024 - Journées Ouvertes en Biologie, Informatique et Mathématiques, Jun 2024, Toulouse, France. pp.1-1, 2024. hal-04654522

HAL Id: hal-04654522

<https://inria.hal.science/hal-04654522v1>

Submitted on 19 Jul 2024

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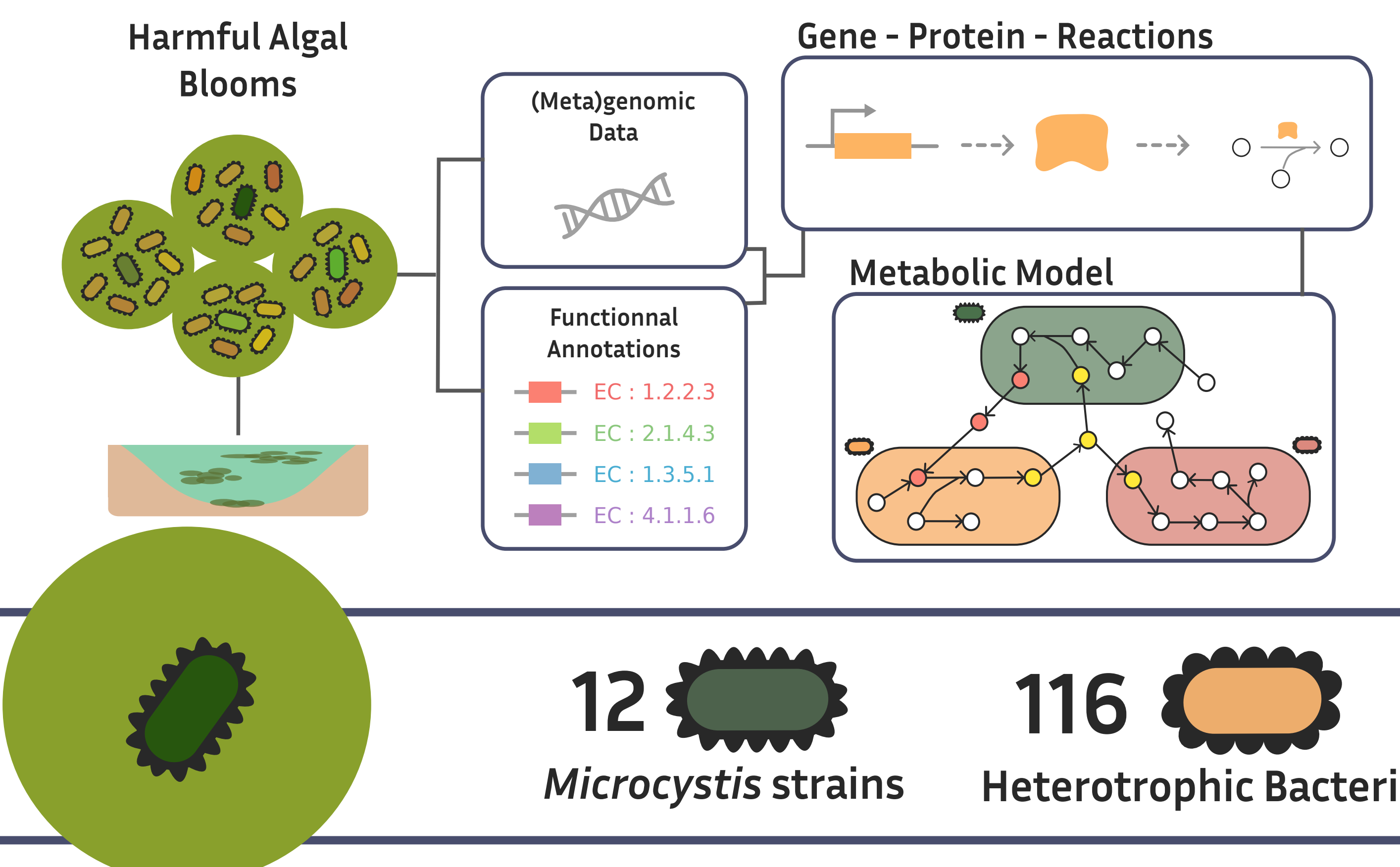


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Metagenome-scale metabolic modelling for the characterization of cross-feeding interactions in *Microcystis*-associated microbial communities, in the context of freshwater cyanobacterial blooms

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Introduction

Fueled by eutrophication and global warming, harmful algal blooms are an international concern, being both a sanitary and an economic burden [1]. At its center, one phylum: *Cyanobacteria*. *Microcystis* is one of the most pervasive genus of freshwater bloom-forming and toxin producing cyanobacteria. The complex cooperative interactions with its surrounding heterotrophic bacterial community favour bloom's development, but the global process behind them remains unknown [2]. We built and analysed 12 communities of Genome-Scale Metabolic Networks (GSMNs) from a bloom, and explored them using mechanistic metabolic modelling.

Objectives

- Reproduce accurate Genome-Scale Metabolic Networks of *Microcystis* and their communities
- Integrate a key toxin biosynthesis pathway in their GSMNs, currently absent from metabolic reactions databases
- Characterize similarity and dissimilarity between *Microcystis* and its community
- Identify key metabolites produced by *Microcystis* through cooperation with its community

12 *Microcystis* strains, 116 Heterotrophic Bacteria, 128 Genome-Scale Metabolic Networks

Heterotrophic bacterial taxa surrounding *Microcystis* in blooms

- Caulobacteraceae*
- Pseudomonaceae*
- Nocardiaceae*
- Acetobacteraceae*
- Beijerinckiaceae*
- Sphaerotilaceae*
- Burkholderiales*



Microcystin-LR Biosynthesis

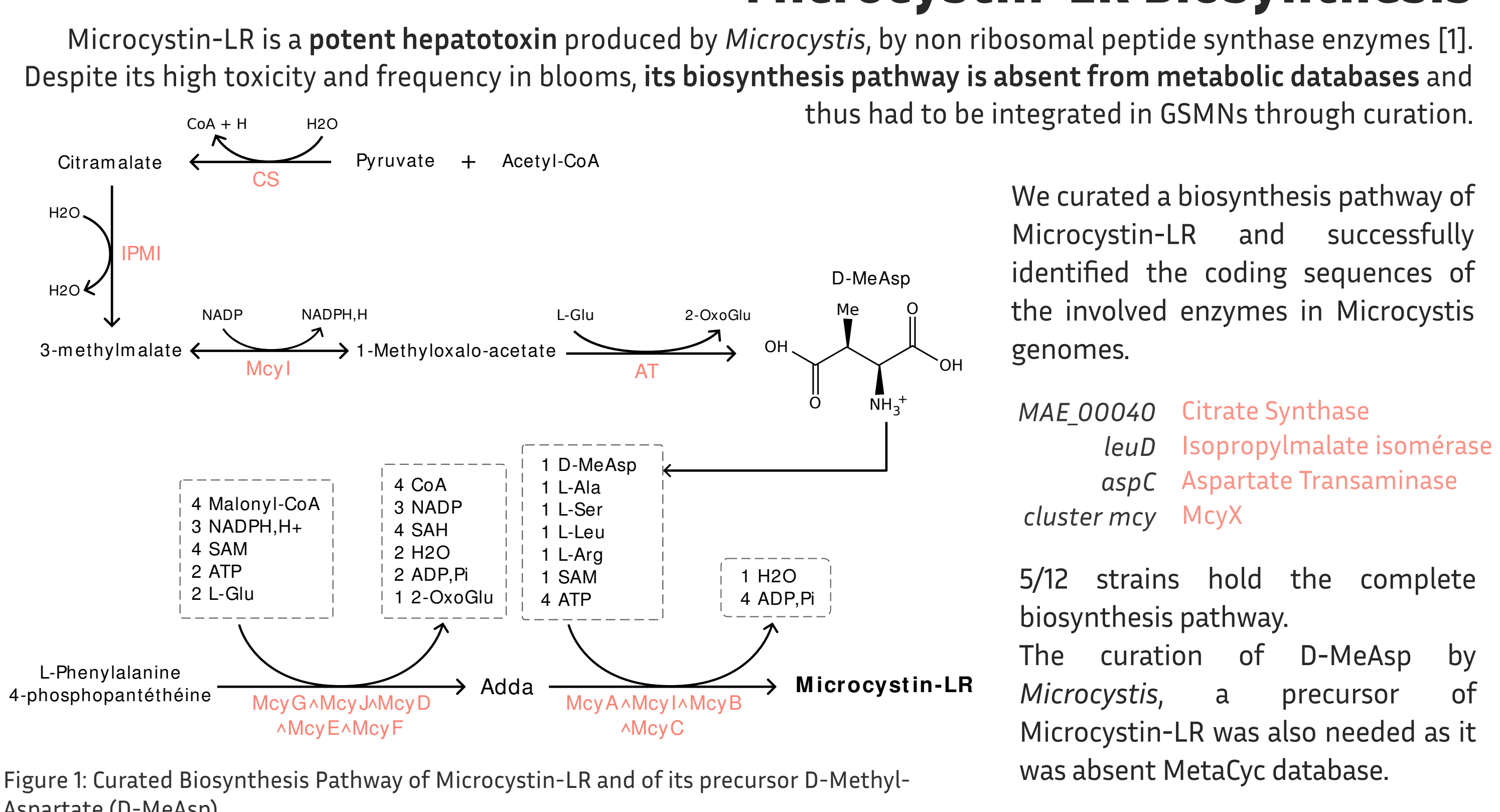


Figure 1: Curated Biosynthesis Pathway of Microcystin-LR and of its precursor D-Methyl-Aspartate (D-MeAsp)

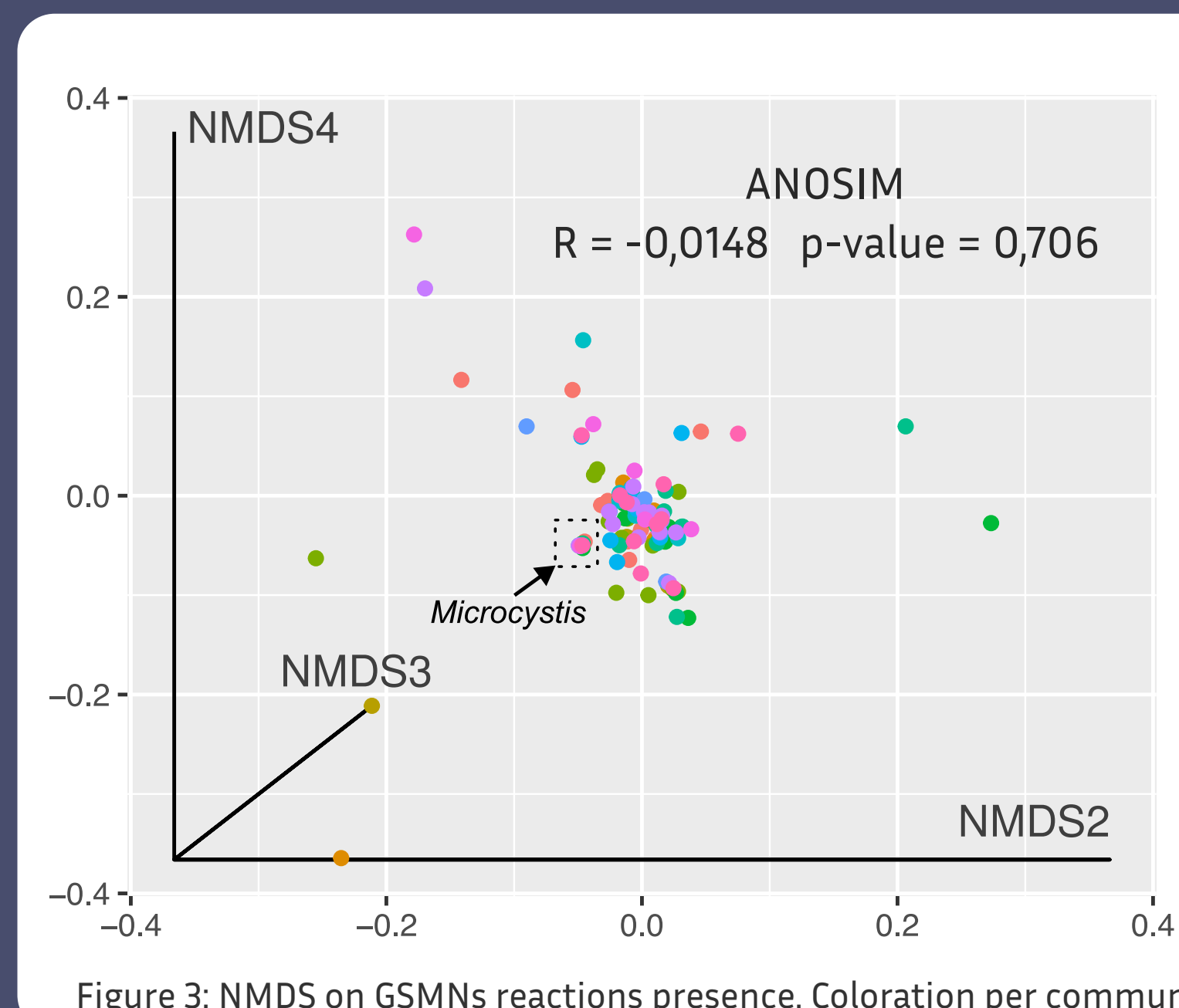


Figure 3: NMDS on GSMNs reactions presence. Coloration per community

Community comparison

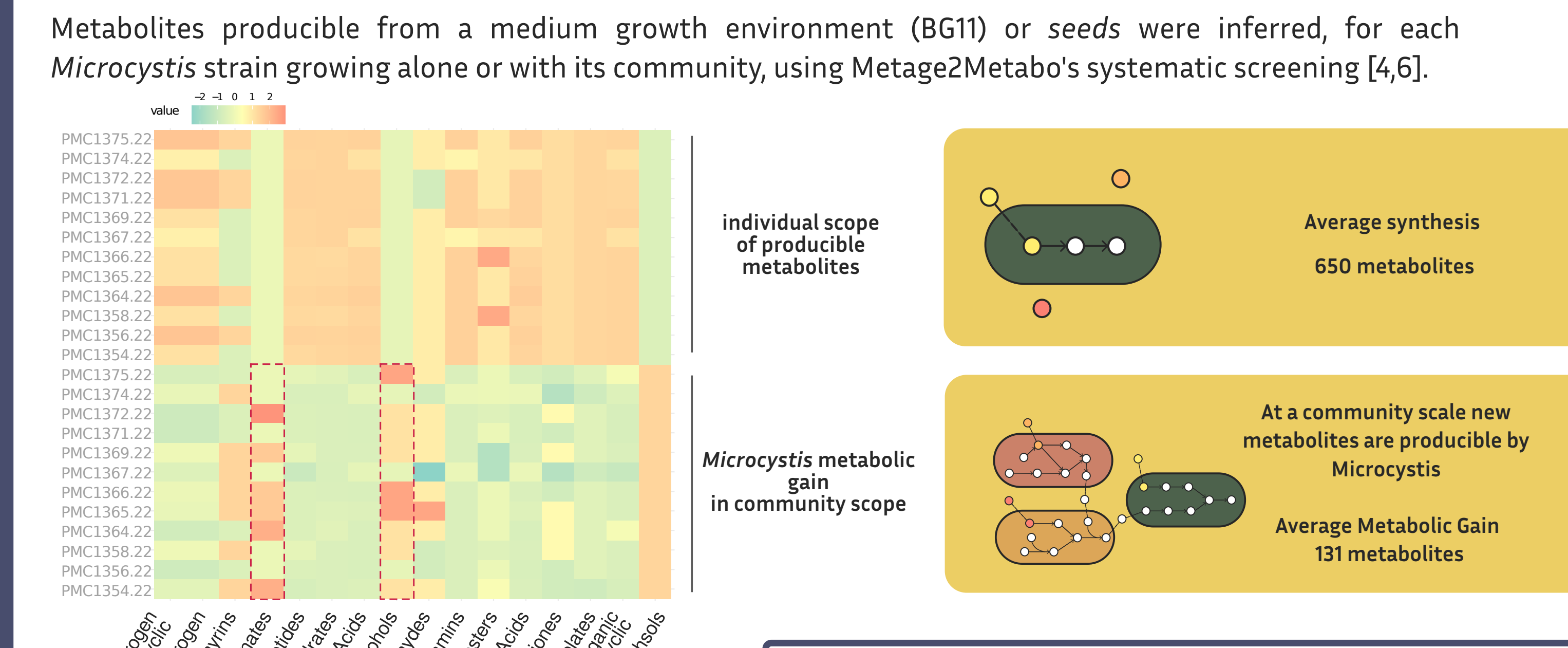
Between 5 and 16 Metagenomes-Assembled Genomes were reconstructed for each *Microcystis* strain

Metabolism similarity Across Communities

- Microcystis*-centered microbial communities from a same bloom are not significantly different
- Dissimilarity within community is higher than across communities

Microbial community of a same bloom are shaped by similar overall metabolic functions, by gathering diverse bacterias around a *Microcystis* strain

Added value of heterotrophic bacterial community for metabolite synthesis by *Microcystis*

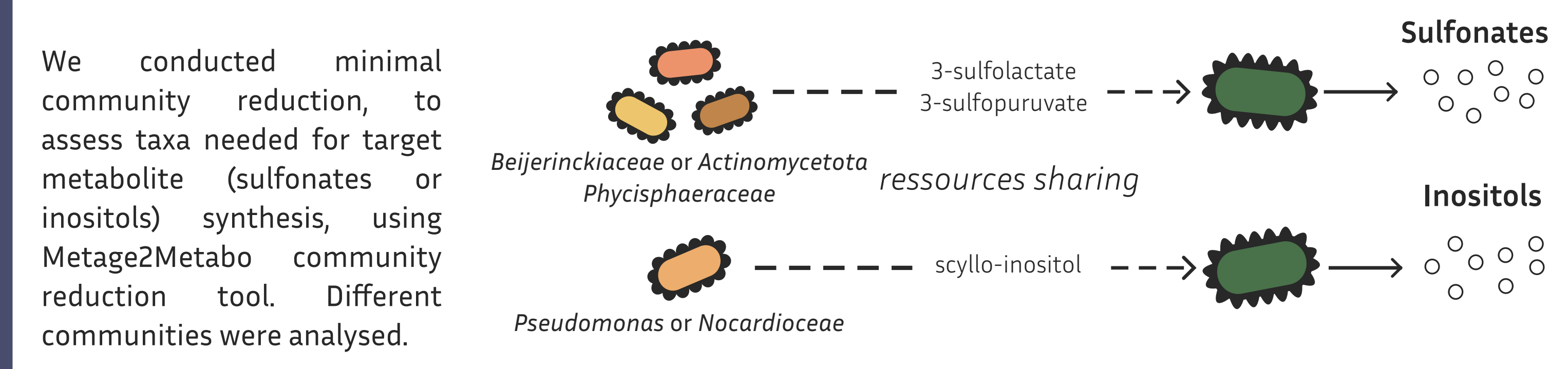


Key Metabolites categories reachable by cooperation

Inositols Community give scyllo-inositol to *Microcystis*. Its degradation benefits *Microcystis* osmotic regulation [7]

Sulfonates Production of odorous compounds and sulfur integration [8,9]

Bacteria cooperating with *Microcystis* for key metabolites



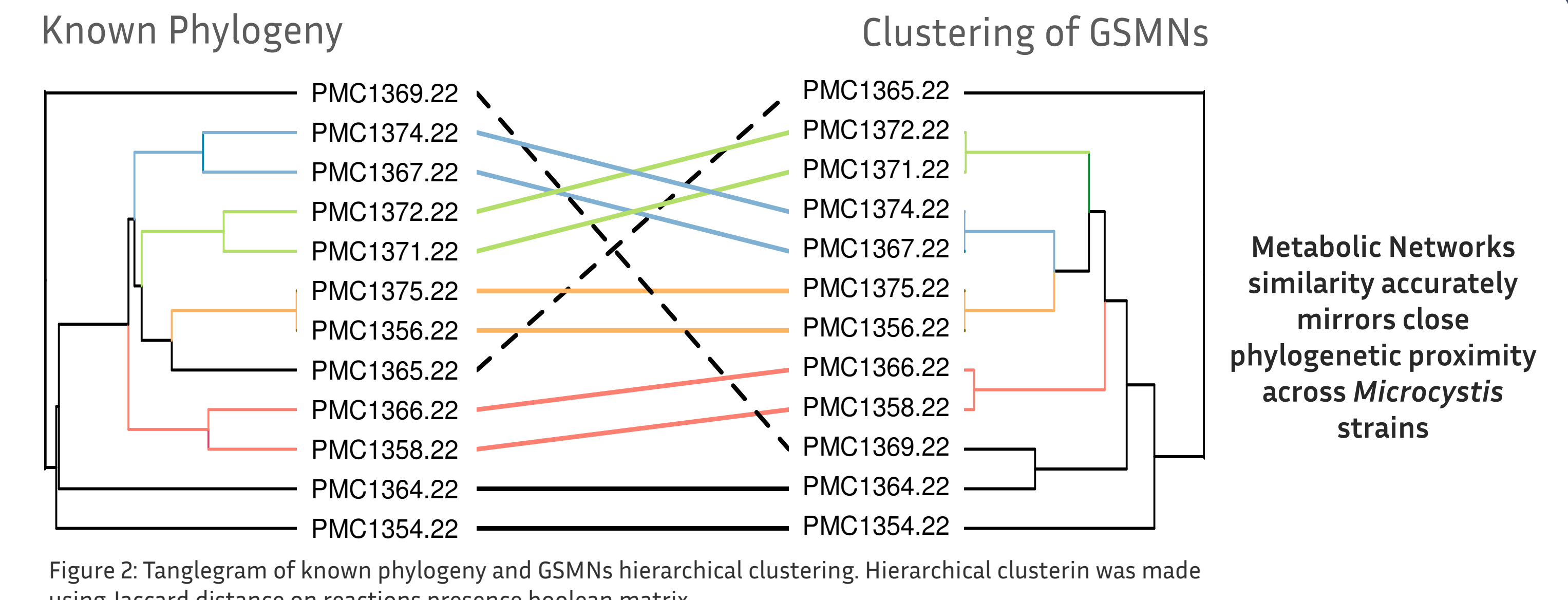
Automatic GSMNs Reconstruction

PathwayTools mpwt, MetaCyc, Metabolic Pathway Genome Database [5]

PathwayTools is a gene to reactions software for metabolic network reconstruction [3]. The process is automatized with the mpwt package [4].

Microcystis	Complete metabolic pathway	Reactions		Genes	Metabolites
		amount	with genes association (%)		
PMc1366.22	340	1776	68.1	4483	1882
PMc1367.22	329	1772	68.0	4729	1903
PMc1354.22	342	1845	67.3	4600	1968
PMc1371.22	343	1783	67.9	4859	1891
PMc1364.22	342	1793	68.5	4623	1911
PMc1372.22	343	1782	67.9	4856	1890
PMc1374.22	329	1772	68.0	4764	1903
PMc1369.22	333	1787	68.7	4956	1913
PMc1375.22	344	1788	67.7	4815	1906
PMc1356.22	344	1788	67.7	4811	1906
PMc1365.22	339	1791	68.5	4226	1897
PMc1358.22	340	1779	68.2	4460	1884

Phylogeny proximity and Metabolism proximity



Conclusion

We curated a Microcystin-LR toxin biosynthesis pathway in a collection of 12 *Microcystis* GSMNs. Out of the 12, 5 hold the full pathway. Our reconstructions of GSMNs are consistent with the phylogeny of *Microcystis*, which suggests accurate reconstruction of its metabolism. We assessed the metabolic functions carried by the heterotrophic community of *Microcystis* and identified categories of metabolites that are only producible through cooperation with the community and are expected to benefit the metabolism of *Microcystis*. For those categories, we identified essential taxa enabling target molecules synthesis by *Microcystis*.

Perspectives

We expect new (meta)genomic data from long-read sequencing, which may better capture the genomes of the heterotrophic community and its complementarity with *Microcystis*. Parallel to this work, metabolomic analysis on those same communities are conducted and results will furtherly be integrated into our analysis.

Funding

COMIC Project
 Metaprogramme
 HOLOFLUX

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