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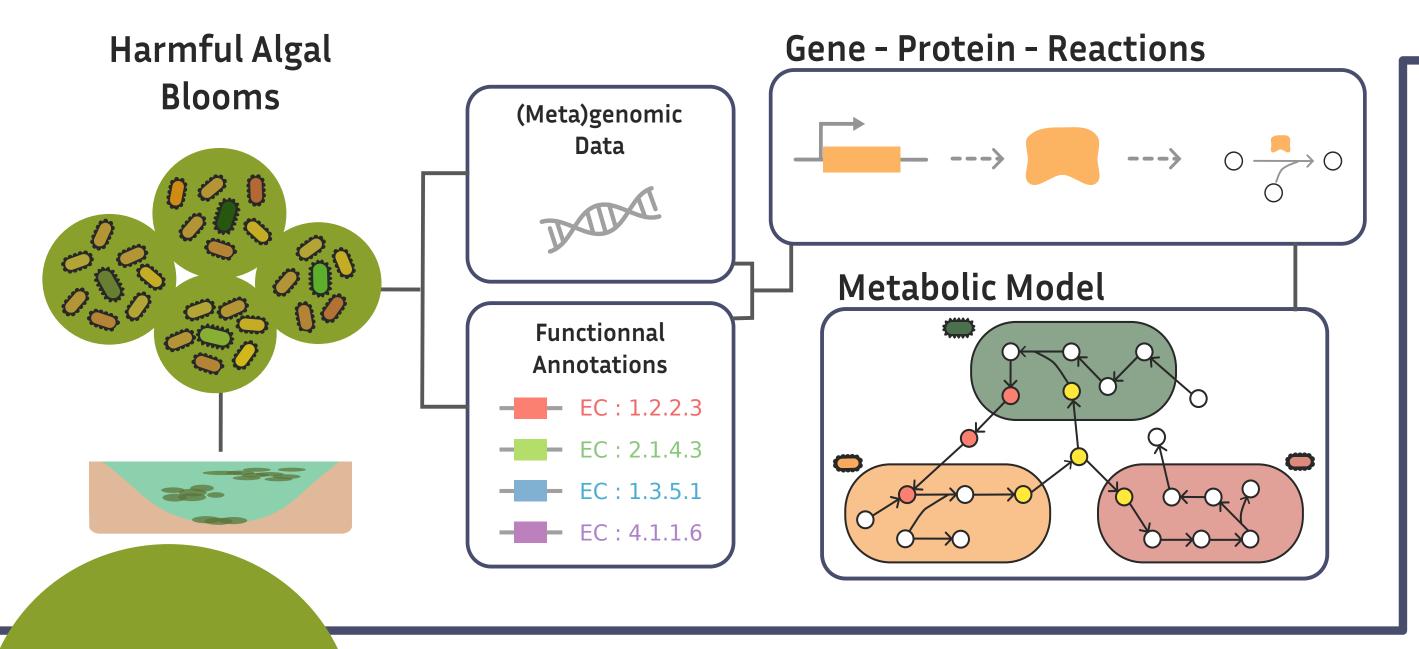
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# Metagenome-scale metabolic modelling for the characterization of cross-feeding interactions in *Microcystis*-associated microbial communities, in the context of freshwater cyanobacterial blooms

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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 metabolism 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.

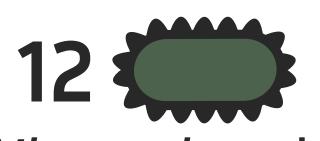
Reproduce accurate Genome-Scale Metabolic Networks of Microcystis and their communities

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

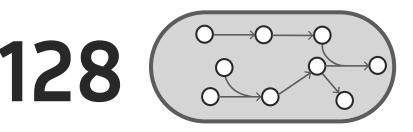
cooperation with it's community



*Microcystis* strains

16

Heterotrophic Bacteria



Genome-Scale Metabolic Networks

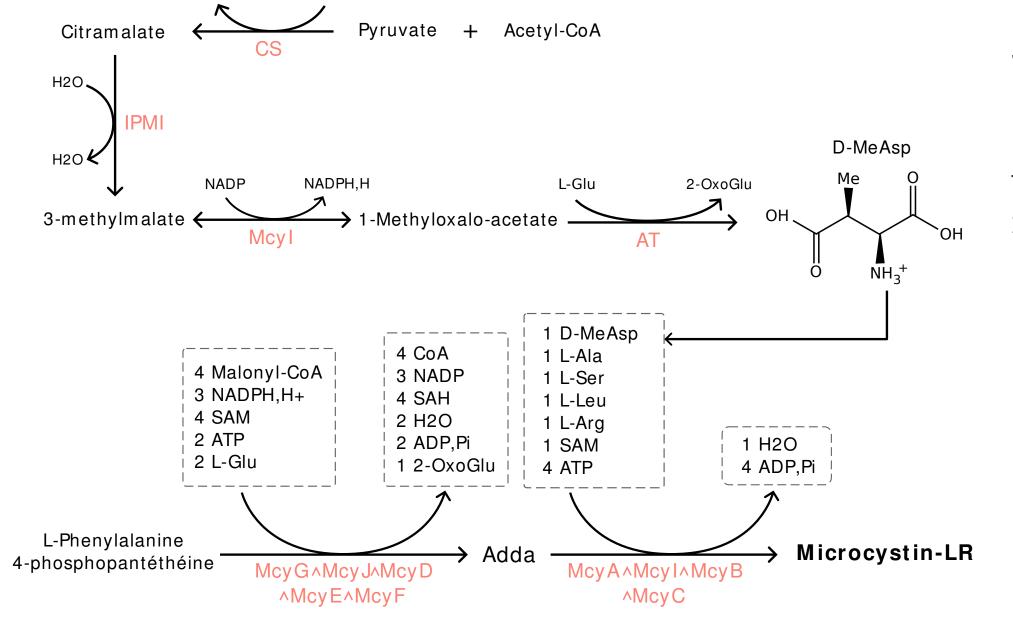
Heterotrophic bacterial taxa surrounding *Microcystis* in blooms

Caulobacteraceae Pseudomonaceae Nocardioceae Acetobacteraceae Beijerinckiaceae Sphaerotilaceae Burkholderiales



# Microcystin-LR Biosynthesis

Microcystin-LR is a potent hepatotoxin produced by Microcystis, by non ribosomal peptide synthase enzymes [1]. Despite its high toxicity and frequency in blooms, its biosynthesis pathway is absent from metabolic databases and thus had to be integrated in GSMNs through curation.



We curated a biosynthesis pathway of Microcystin-LR and successfully identified the coding sequences of the involved enzymes in Microcystis genomes.

MAE\_00040 Citrate Synthase Isopropylmalate isomérase Aspartate Transaminase cluster mcy McyX

biosynthesis pathway. The curation of D-MeAsp by Microcystis, precursor Microcystin-LR was also needed as it was absent MetaCyc database.

5/12 strains hold the complete

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

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Figure	e 3: NMDS on (	GSMNs ro	eactions	presenc	e. Colora	ation pe	r comm	unit

## **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 significally 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

#### Metabolites **Microcystis** with gene.s metabolic pathway amount association (%) 1776 4483 1882 PMC1366.22 329 1772 68.0 4729 1903 PMC1367.22 1968 342 67.3 4600 PMC1354.22 1845 1891 4859 343 67.9 PMC1371.22 1783 4623 342 1793 68.5 1911 PMC1364.22 1890 PMC1372.22 343 1782 67.9 4856 329 1903 PMC1374.22 68.0 4764 333 1787 68.7 4956 1913 PMC1369.22 344 1788 67.7 1906 PMC1375.22 344 67.7 4811 1906 PMC1356.22 1897 4226 PMC1365.22 1791 340 1779 68.2 4460 PMC1358.22

# **Automatic GSMNs** Reconstruction



mpwt

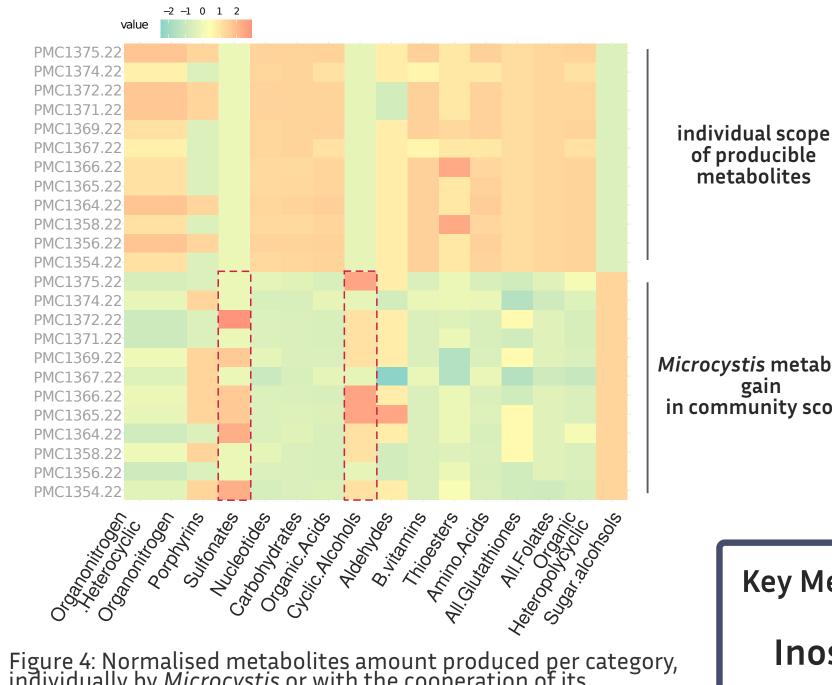


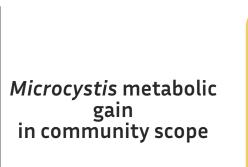
PathwayTools is a gene to reactions software for metabolic network reconstruction [3] process automatised with

Metabolic Pathway Genome Database [5]

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

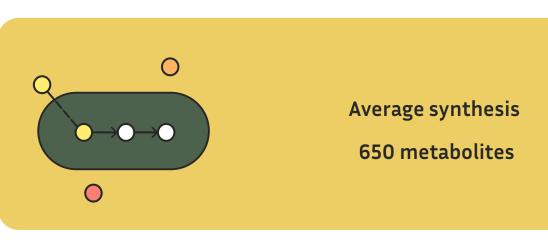
Metabolites producible from a medium growth environment (BG11) or seeds were inferred, for each Microcystis strain growing alone or with its community, using Metage2Metabo's systematic screening [4,6].





of producible

metabolites



At a community scale new metabolites are producible by Microcystis Average Metabolic Gain 131 metabolites

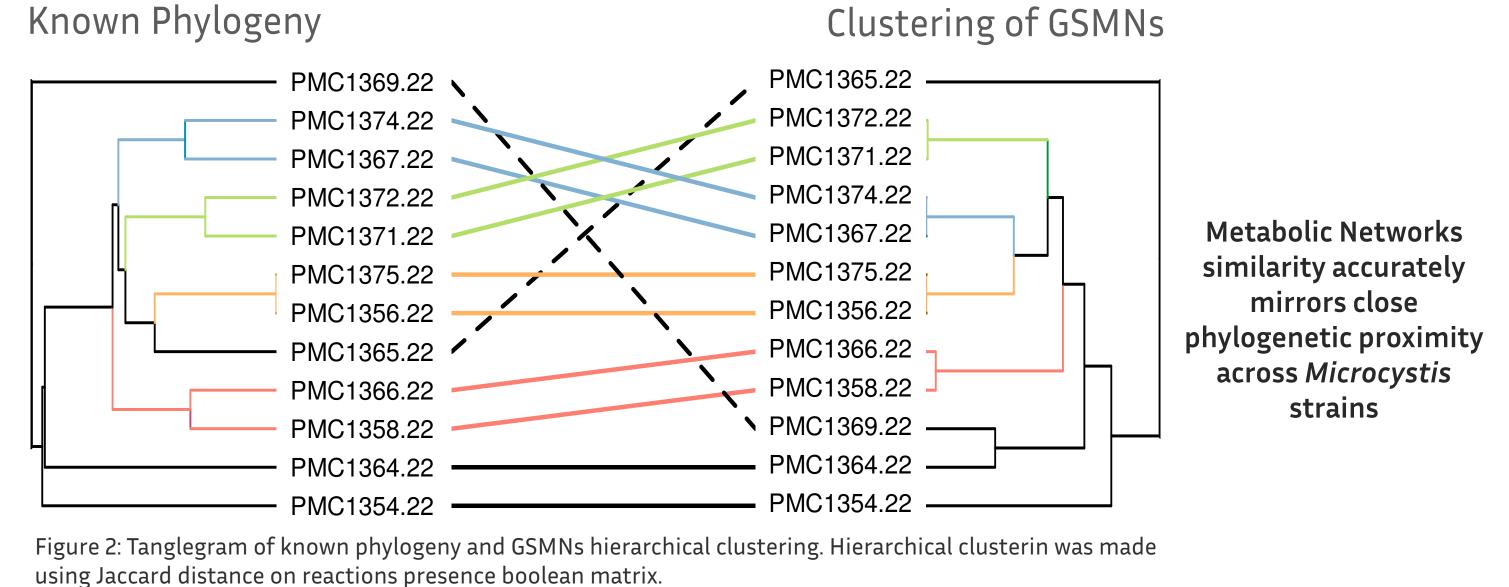
Figure 4: Normalised metabolites amount produced per category, individually by *Microcystis* or with the cooperation of its

Key Metabolites categories reachable by cooperation Community give scyllo-inostol to Microcystis. Its degradation benefits Microcystis osmotic Inositols regulation [7]

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

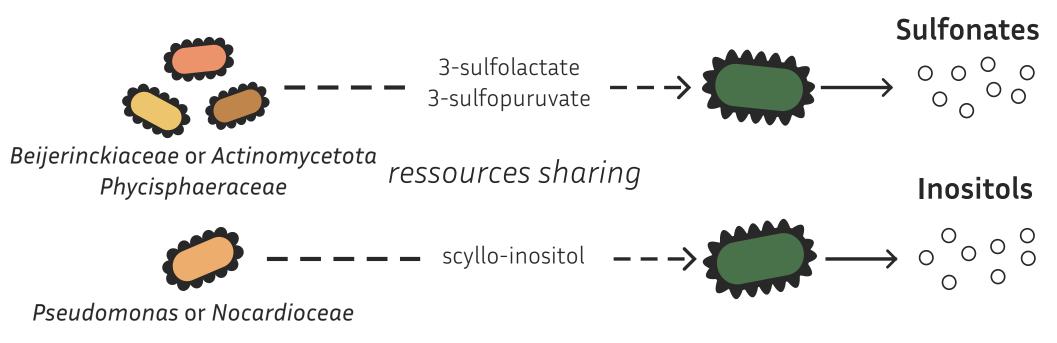
# Phylogeny proximity and Metabolism proximity Clustering of GSMNs

mpwt package [4].



# **Bacteria cooperating with** Microcystis for key metabolites

conducted minimal reduction, to assess taxa needed for target metabolite (sulfonates Metage2Metabo Different tool. communities were analysed.



## 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 heterophic 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** 

[1] Ibelings et al. 'Cyanobacterial blooms. Ecology, prevention, mitigation and control: Editorial to a CYANOCOST Special Issue', Aquat Ecol, 2016. [2] Louati, et al. 'The phyto-bacterioplankton couple in a shallow freshwater ecosystem: Who leads the dance?', Harmful Algae, 2023. [3] Karp, et al. 'The Pathway Tools software', Bioinformatics, 2022. [4] Belcour, et al. 'Metage2Metabo, microbiota-scale metabolic complementarity for the identification of key species', eLife, 2020.

[5] Caspi et al., 'The MetaCyc database of metabolic pathways and enzymes and the BioCyc collection of Pathway/Genome Databases', Nucleic Acids

Research, 2014. [6] Frioux, et al. 'Scalable and exhaustive screening of metabolic functions carried out by microbial consortia', Bioinformatics, 2018.

[9] Giordano et al. 'Nitrogen and sulfur assimilation in plants and algae', Aquatic Botany, 2014.

[7] Wang, et al. 'The inositol monophosphatase all2917 (IMPA1) is involved in osmotic adaptation in anabaena sp. PCC7120' Environmental Microbiology Reports, 2012. [8] Zhang, et al. 'Characterization of typical taste and odor compounds formed by Microcystis aeruginosa', Journal of Environmental Sciences, 2013.











