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Juliette Audemard, Sébastien Halary, Gabriel Markov, Jeanne Got, Anne Siegel, et al.. Metagenomescale metabolic modelling for the characterization of cross-feeding interactions in Microcystisassociated 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 Jul2024

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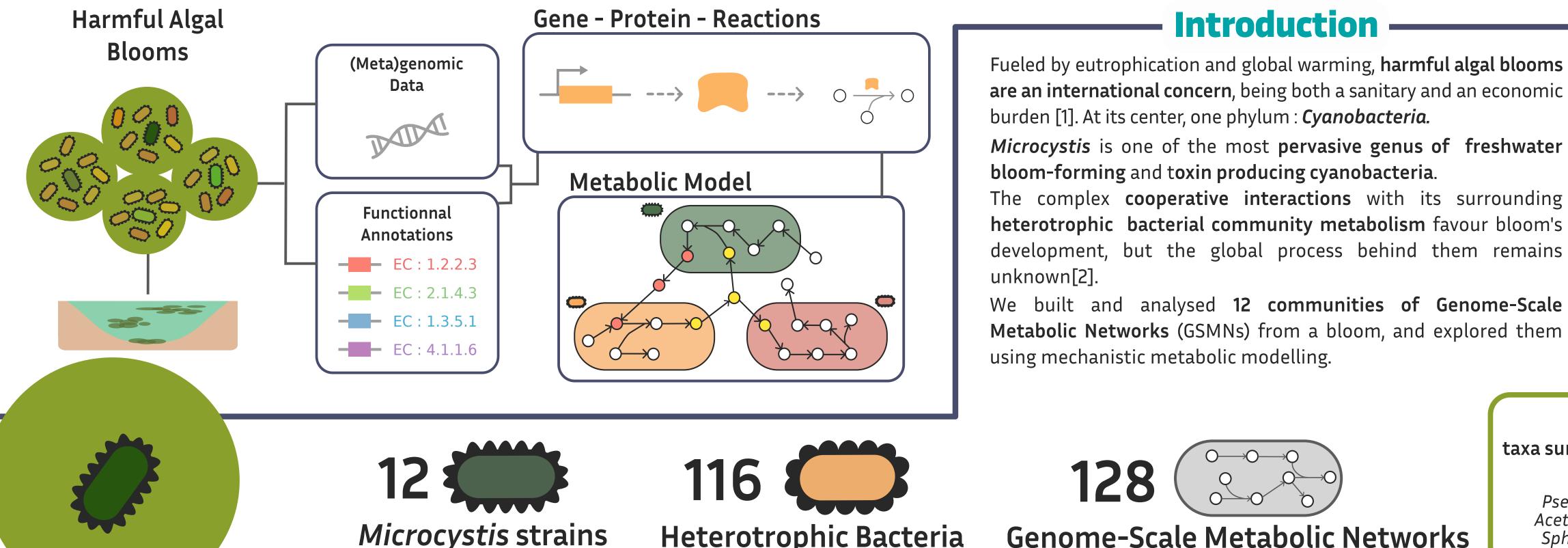


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# Metagenome-scale metabolic modelling for the characterization of cross-feeding interactions in *Microcystis*-associated microbial communities, in the context of freshwater cyanobacterial blooms

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**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 it's community



Heterotrophic bacterial

taxa surrounding *Microcystis* in blooms

Caulobacteraceae Pseudomonaceae Nocardioceae Acetobacteraceae Beijerinckiaceae Sphaerotilaceae Burkholderiales

Genome-Scale Metabolic Networks

0.4 -

0.2 -

0.0

-0.2 -

-0.4 -

-0.4

Heterotrophic Bacteria

NMDS4

Microcvstis

0.0

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

NMDS3

-0.2

**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

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

NMDS2

0.2

ANOSIM

R = -0,0148 p-value = 0,706

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].

# **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.

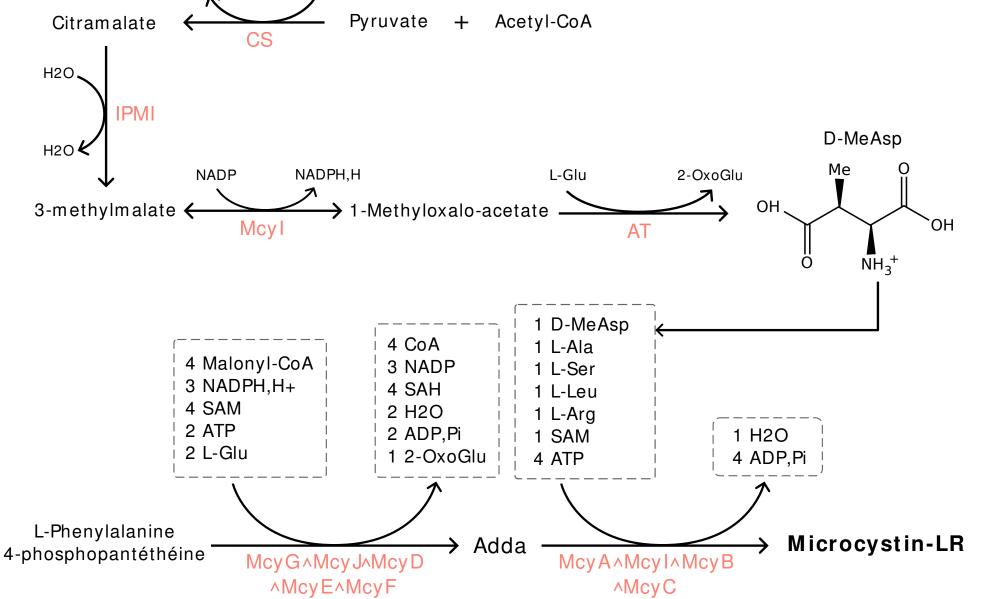


Figure 1: Curated Biosynthesis Pathway of Microcystin-LR and of its precursor D-Methyl-Aspartate (D-MeAsp)

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

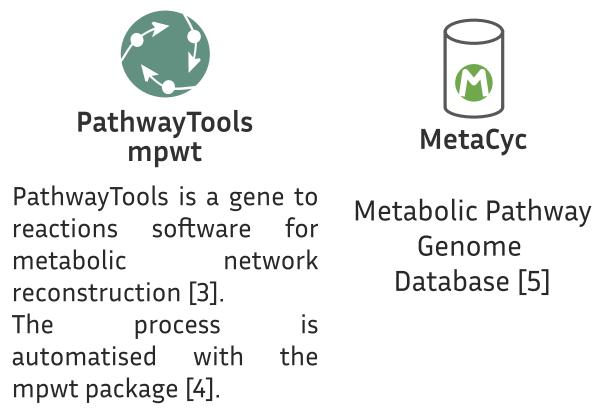
MAE 00040 Citrate Synthase Isopropylmalate isomérase leuD Aspartate Transaminase aspC cluster mcy McyX

5/12 strains hold the complete biosynthesis pathway.

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

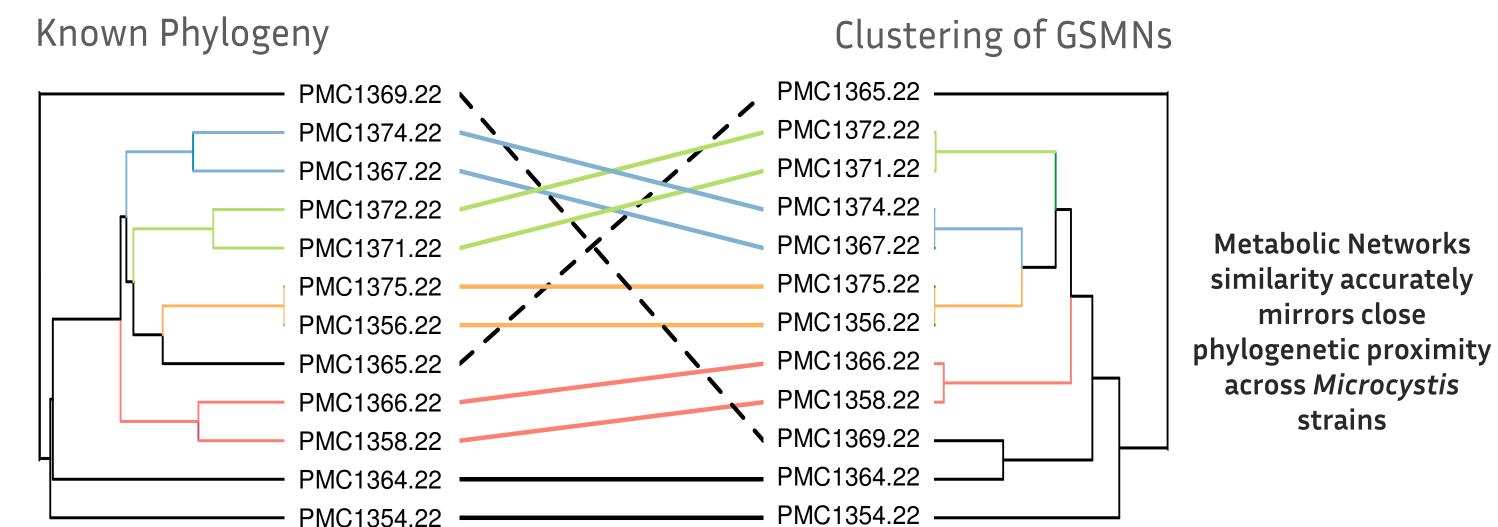
Microcystis	Complete metabolic pathway	Reactions			
		amount	with gene.s association (%)	Genes	Metabolites
PMC1366.22	340	1776	68.1	4483	1882
PMC1367.22	329	1772	68.0	4729	1903
PMC1354.22	342	1845	67.3	4600	1968
PMC1371.22	343	1783	67.9	4859	1891
PMC1364.22	342	1793	68.5	4623	1911
PMC1372.22	343	1782	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

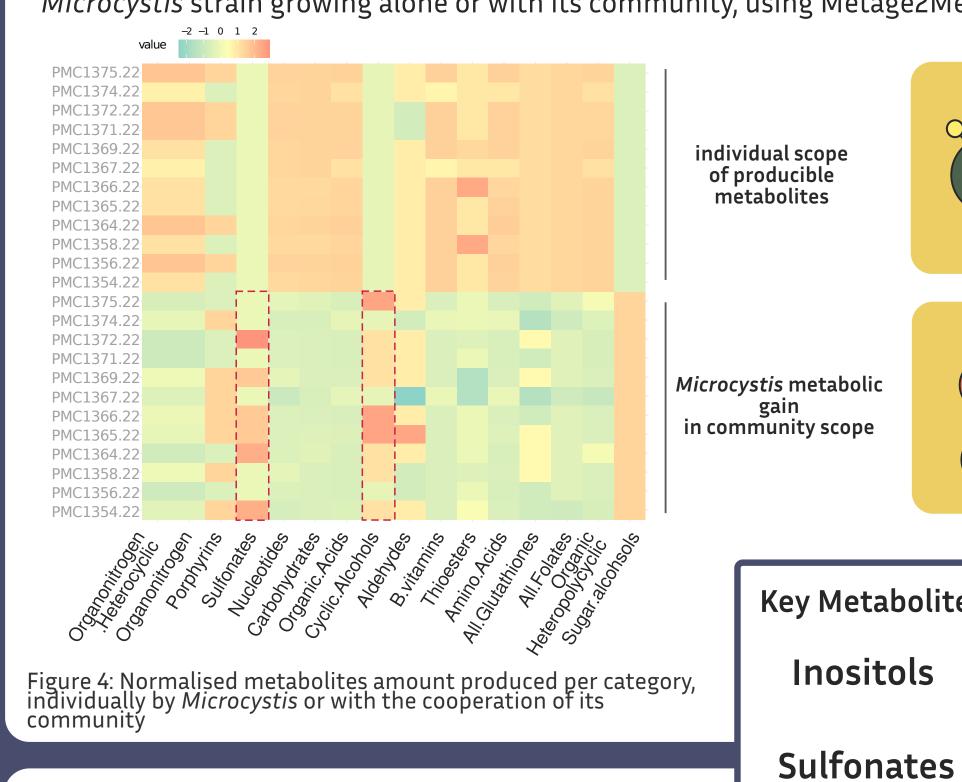




## Phylogeny proximity and Metabolism proximity

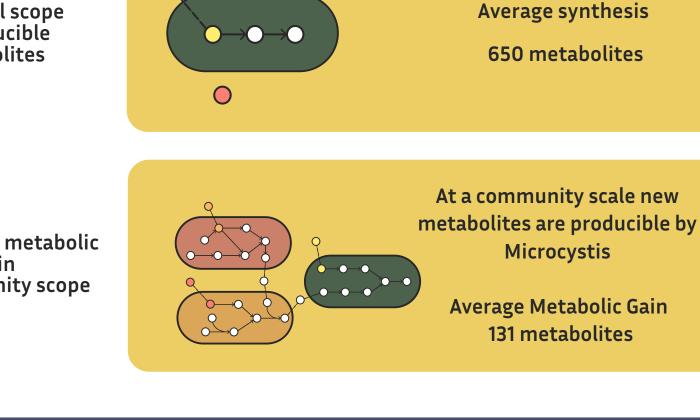
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# **Bacteria cooperating with** Microcystis for key metabolites

We conducted minimal reduction, to community assess taxa needed for target metabolite (sulfonates or inositols) synthesis, using Metage2Metabo community Different reduction tool.



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

Microcystis

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

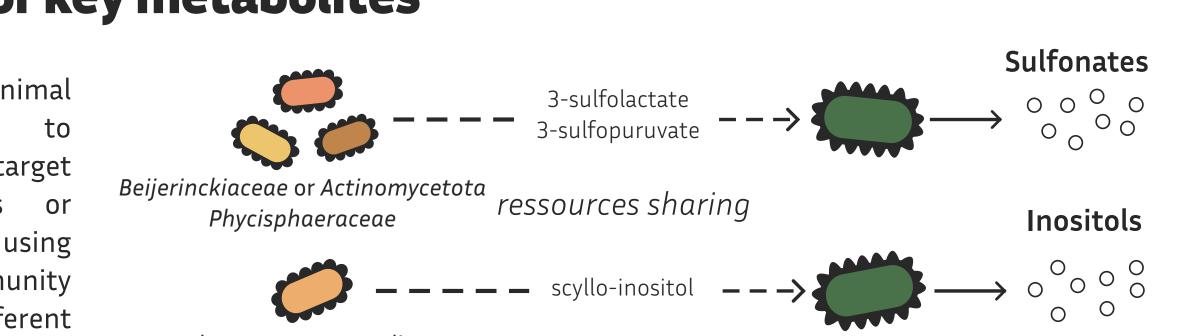


Figure 2: Tanglegram of known phylogeny and GSMNs hierarchical clustering. Hierarchical clusterin was made using Jaccard distance on reactions presence boolean matrix.

## 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.

## communities were analysed.

## Pseudomonas or Nocardioceae

## 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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