



iNAP2.0: Harnessing metabolic complementarity in microbial network analysis

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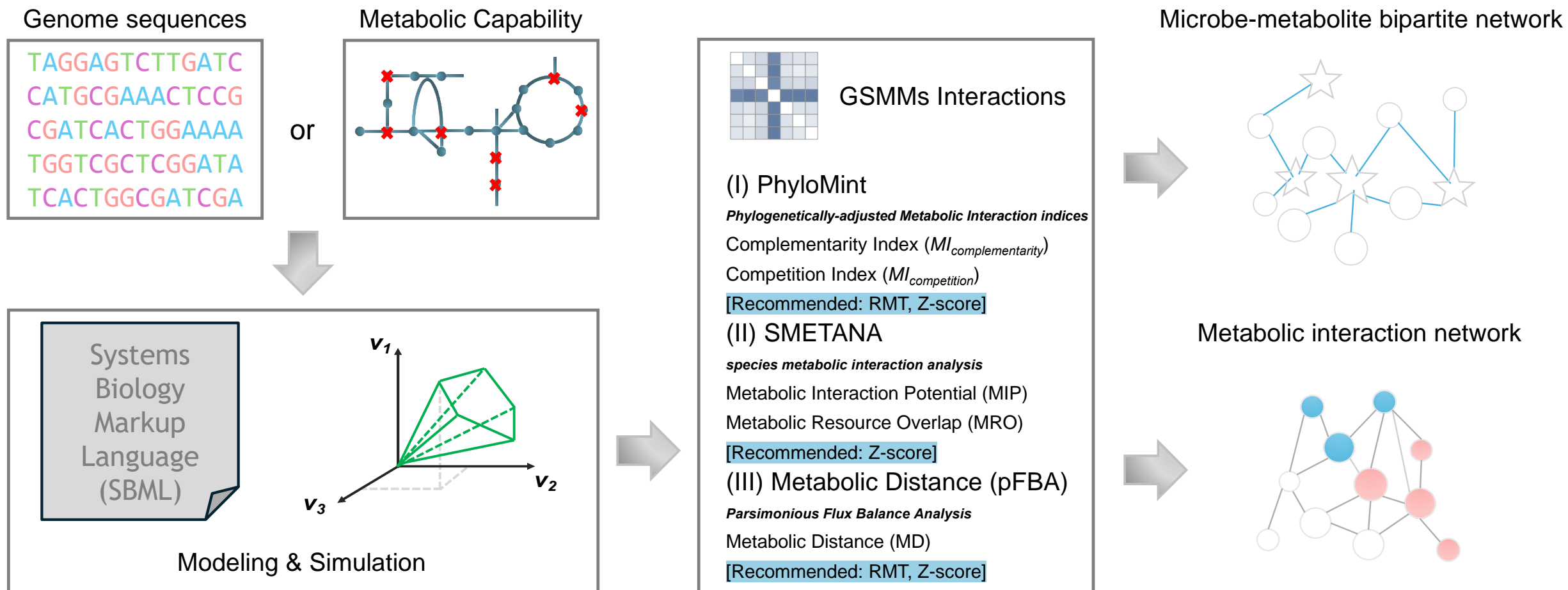


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<https://doi.org/10.1002/imt2.235>



Introduction



An overview of the schematic design and implemented tools of metabolic interaction network analysis of iNAP 2.0. Users can start from genome or protein sequence to reconstruct genome-scale metabolic models and proceed to multiple analyses.

<https://inap.denglab.org.cn/>



Highlights

METABOLIC MODELINGS (TESTING)

Build metabolic models

Find interactions between models

Construct metabolic network

Analyze metabolic network

1. The updated integrated network analysis pipeline (iNAP 2.0) is an advanced platform that facilitates the calculation of various metabolic complementarity and competition indices, including the PhyloMint index, SMETANA, and metabolic distance, as well as the construction and analysis of metabolic interaction networks.
2. Innovatively, iNAP 2.0 uses the random matrix theory (RMT) approach to determine the threshold for metabolic interaction networks.
3. PhyloMint PTM in iNAP 2.0 allows users to view potentially transferable metabolites between microbial interactions and integrate them as network nodes to construct a microbe-metabolite bipartite network alongside the microbial interaction network.

Visualize PTM network Microbe-Metabolite network visualization (Galaxy Version Beta 1.0) ☆ Favorite ▾ Options

PhyloMint PTMs Result (.txt)

96: RMT chi square result of example.txt

Execute

Metabolic Modeling Network function: Get Potentially Transferable Metabolites (PTMs)

[bigg_models_metabolites.txt] Download from http://bigg.ucsd.edu/data_access. It provided the namespace of all bigg collected metabolite ids.

[get_PTMs.py] Modified on the base of <https://github.com/mgtools/PhyloMint/blob/master/lib/BuildGraphNetX.py> because our results are also from this tool.



iNAP2.0 Section I: Prepare genome-scale metabolic models

Build metabolic models

Prokka (Testing) Rapid prokaryotic genome annotation

CarveMe (Testing) Genome-scale metabolic model reconstruction

CarveMe (Gap-filling)(Testing) Genome-scale metabolic model reconstruction (Gap-filling)

Step 1 : Prokka

Step 2 : CarveMe

Step 3 : Gap filling - CarveMe

CarveMe (Gap-filling)(Testing) Genome-scale metabolic model reconstruction (Gap-filling)
(Galaxy Version CarveMe Release 1.5.2)

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▼ Options

Prokka Predicted Protein Sequences (Zipped, .zip)

53: Prokka_faa.zip

Source of Media Compositions Library

CarveMe's pre-built library of media compositions ▼

Growth Medium for Gap-filling

LB

CarveMe provides with a very small pre-built library of media compositions. You can specify multiple media names by separate them with comma, e.g. LB,M9.

✓ Execute

CarveMe Release 1.5.2

CarveMe is a python-based tool for genome-scale metabolic model reconstruction.

About self-provided media library

CarveMe currently supports 5 pre-built libraries of media compositions:

- **LB** (Lysogeny broth)
- **LB-O2** (Lysogeny broth, anaerobic)
- **M9** (Minimal M9 medium)
- **M9-O2** (Minimal M9 medium, anaerobic)
- **M9-glyc** (Minimal M9 medium, glycerol as carbon source)

iNAP2.0 Section II: Infer pairwise interactions of GSMMs

PHYLOMINT
PhyloMint Pathway-based and phylogenetically adjusted quantification of competition and cooperation between microbial species
PhyloMint PTM Find Potentially Transferable Metabolites
Create PhyloMint Matrix (Competition and Complementarity) Create PhyloMint matrix

SMETANA
Create Community List Create input file for SMETANA
SMETANA Global SMETANA (Global Mode)
Iterative SMETANA Global SMETANA (Global Mode, iterative)
SMETANA Detailed SMETANA (Detailed Mode)
Iterative SMETANA Detailed SMETANA (Detailed Mode, iterative)
Create SMETANA Matrix Convert MIP/MRO results to adjacent matrices




METABOLIC DISTANCE
Metabolic Distance Calculates metabolic dissimilarity

PhyloMint




Core function: Find PhyloMint PTM

PhyloMint PTM Find Potentially Transferable Metabolites (Galaxy Version Beta 1.0) ☆ Favorite ▼ Options


Zipped CarveMe Models (.zip)

   55: CarveMe_models.zip  

PhyloMint Result (txt)

   57: PhyloMint_result.txt  


Genome File Extension

xml (Extensible Markup Language) 

MaxCC

5

Must be equal to the value set in PhyloMint!

 Execute

Metabolic Modeling Network function: Get Potentially Transferable Metabolites (PTMs)

[bigg_models_metabolites.txt] Download from http://bigg.ucsd.edu/data_access. It provided the namespace of all bigg collected metabolite ids.

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SMETANA

Metabolic distance

iNAP2.0 Section III: Construct metabolic interaction networks

Construct metabolic network

Random Matrix Theory (cutoff) To show the cutoff using adjacent matrix

Newly added

Random Matrix Theory (cutoff, Kolmogorov-Smirnov test) RMT cutoff determination using Kolmogorov-Smirnov test

Z-Score Outlier Detection

Standard and modified Z-score for outlier detection

Construct Network Adjacent

Matrix Use RMT cutoff to generate adjacent network

Random Matrix Theory (cutoff, Kolmogorov-Smirnov test) RMT cutoff determination using Kolmogorov-Smirnov test (Galaxy Version 1.1.0)

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▼ Options

Adjacent Matrix(txt)



96: RMT chi square result of example.txt



✓ Execute

Kolmogorov-Smirnov test RMT method

Using Random Matrix Theory (RMT) with Kolmogorov-Smirnov test

Notice your distance matrix must follow the form provided below:

	Species_Apple	Species_Bravo	Species_Candy	Species_Dancing	Species_ET
Species_Apple	1	0.03862660944206009	0.29545454545454547	0.2553191489361702	0.2696629213483146
Species_Bravo	0.03862660944206009	1	0.2839506172839506	0.25	0.25301204819277107
Species_Candy	0.29545454545454547	0.2839506172839506	1	0.05660377358490566	0.04716981132075472
Species_Dancing	0.2553191489361702	0.25	0.05660377358490566	1	0.038834951456310676
Species_ET	0.2696629213483146	0.25301204819277107	0.04716981132075472	0.038834951456310676	1

Z-Score Outlier Detection Standard and modified Z-score for outlier detection (Galaxy Version 1.0.0)

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▼ Options

Z-score outlier detection for network cutoff

Adjacent Matrix (tabular file)



96: RMT chi square result of example.txt



Standard or modified Z-score

Modified Z-score



iNAP2.0 Analyze metabolic interaction networks

Analyze metabolic network

Global Network Properties and Individual Nodes' Centrality

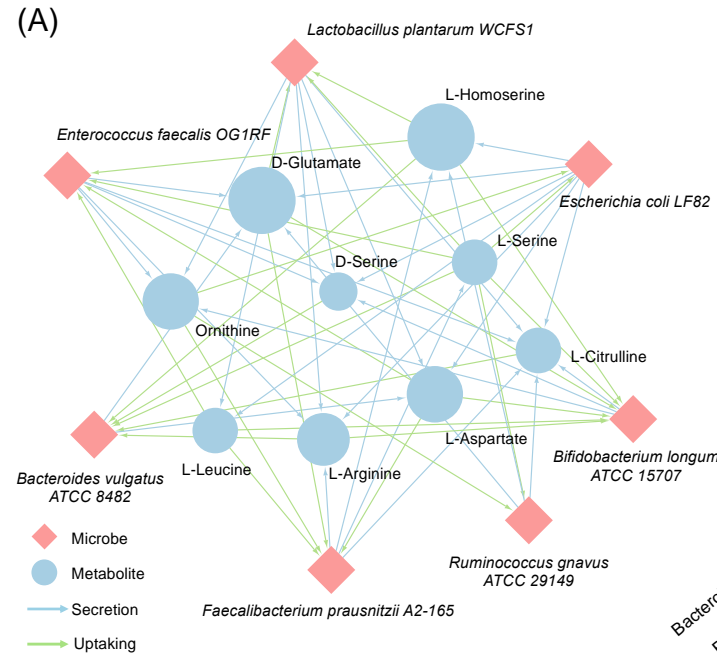
Module separation and module hubs Modularization and Z-P result for module hubs

Integrate Node Attribute Put node centrality, modularity and annotation into one table **Newly added**

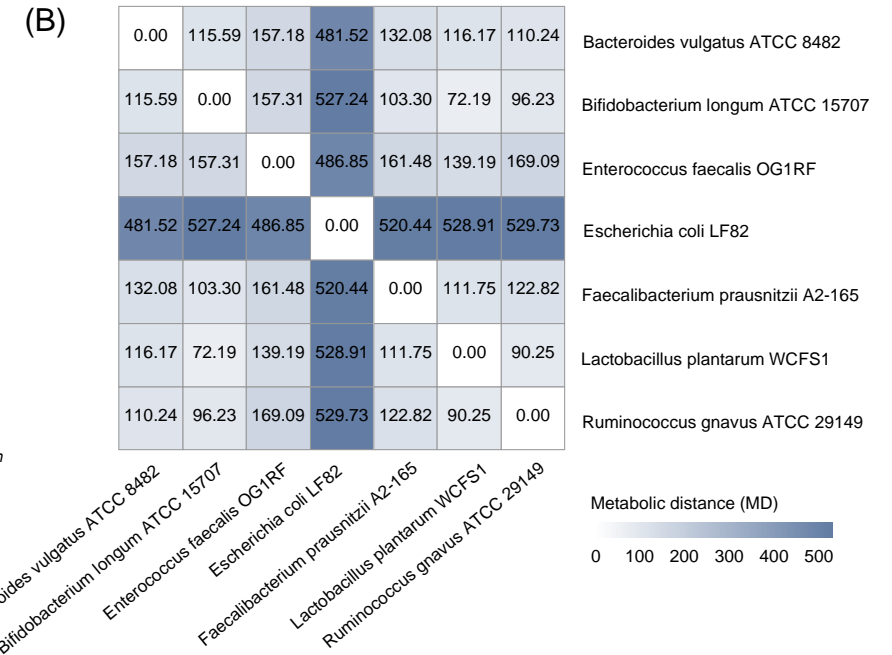
Network Intersection Find shared edges and nodes between two networks

Visualize PTM network Microbe-Metabolite network visualization

Metabolic distance heatmap
Visualize metabolic distance



Microbe-PTM metabolite bipartite network



Metabolic distance heatmap



An example of the application of iNAP2.0

nature communications



Article

<https://doi.org/10.1038/s41467-024-52532-x>

Metabolic interdependencies in thermophilic communities are revealed using co-occurrence and complementarity networks

Received: 8 March 2024

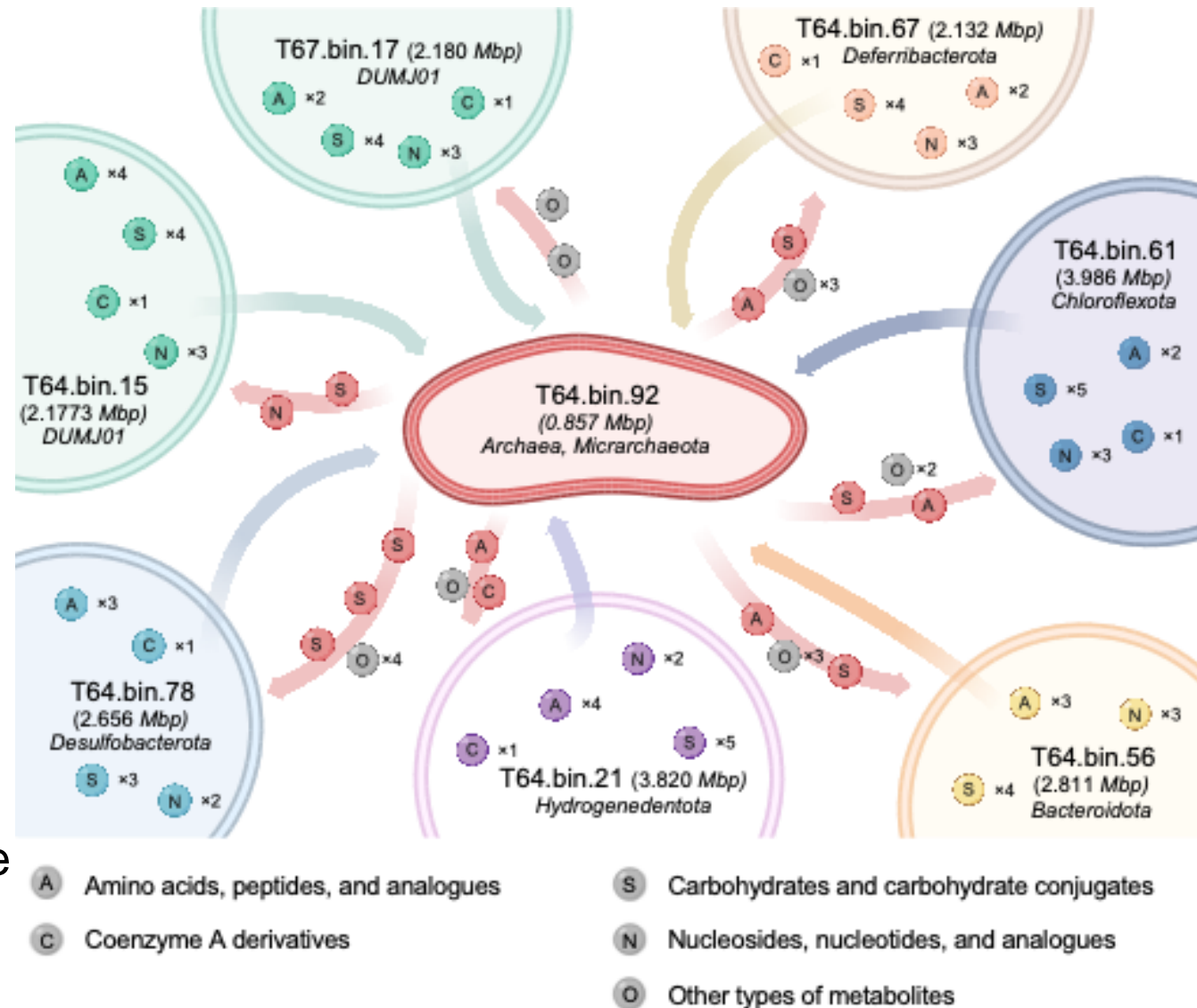
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Accepted: 9 September 2024

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The survival strategies of thermophilic bacteria in hot spring environments and changes in community network structure were analyzed by combining the microbial metabolic complementarity network with the co-occurrence network.

The relevant results were published in Nature Communications.



<https://www.nature.com/articles/s41467-024-52532-x>



Conclusion

- ❑ Here, we introduced the updated iNAP2.0, whose main function is to integrate metabolic interaction analysis based on metagenomic sequencing data into molecular ecological networks ;
- ❑ The updated iNAP2.0 has added 20 new tools, allowing users to build and analyze metabolic interaction networks ;
- ❑ the platform is open for registration, allowing users to upload data for *de novo* analysis or start analysis using intermediate data, and the platform provides corresponding demo data for researchers to learn and use ;
- ❑ **iNAP 2.0 website** : <https://inap.denglab.org.cn/>

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iMeta: Integrated meta-omics to change the understanding of the biology and environment


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