



HAL
open science

Analyzing and modelling functions carried by key species in minimal microbial communities

Chabname Ghassemi Nedjad, Clémence Frioux

► **To cite this version:**

Chabname Ghassemi Nedjad, Clémence Frioux. Analyzing and modelling functions carried by key species in minimal microbial communities. JOBIM 2022 - Journées Ouvertes en Biologie, Informatique et Mathématiques, Jul 2022, Rennes, France. hal-03910438

HAL Id: hal-03910438

<https://inria.hal.science/hal-03910438>

Submitted on 22 Dec 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Analyzing and modelling functions carried by key species in minimal microbial communities

Inria

Chabname GHASSEMI NEDJAD¹ and Clémence FRIOUX¹

¹Inria Université de Bordeaux, INRAE, 33400 Talence, France

From Genome-Scale Metabolic Network to Metabolic potentials

Hundreds of **bacteria species** colonize the **human gut**.

Interaction in microbiota: competition or **cooperation**.

Metabolic modelling:

- Genome-scale metabolic Networks (GSMNs) [1]
- Producibility modelling: network expansion [2]

Community **metabolic potential**:

- **Individual scope**.
- **Production of new metabolites** through metabolic exchanges.

→ By whom and how?

Minimal community selection:

- **Metage2Metabo (M2M)** [3] **model** the interactions.

Minimal communities for six families of compounds as targets

Community initial: 1,500 bacteria [3]

		TOTAL
Aminoacids and derivatives (5 targets)	KS	227
4 bact. per community	ES	0
120,329 communities	AS	227
Aromatic compounds (11 targets)	KS	72
5 bact. per community	ES	3
950 communities	AS	69
Carboxyacids (14 targets)	KS	59
9 bact. per community	ES	4
48,412 communities	AS	55
CoA derivatives (10 targets)	KS	174
5 bact. per community	ES	1
95,256 communities	AS	173
Lipids (28 targets)	KS	185
7 bact. per community	ES	4
58,520 communities	AS	181
Sugar derivatives (58 targets)	KS	142
11 bact. per community	ES	5
7,860,528 communities	AS	137

Key Species (KS):

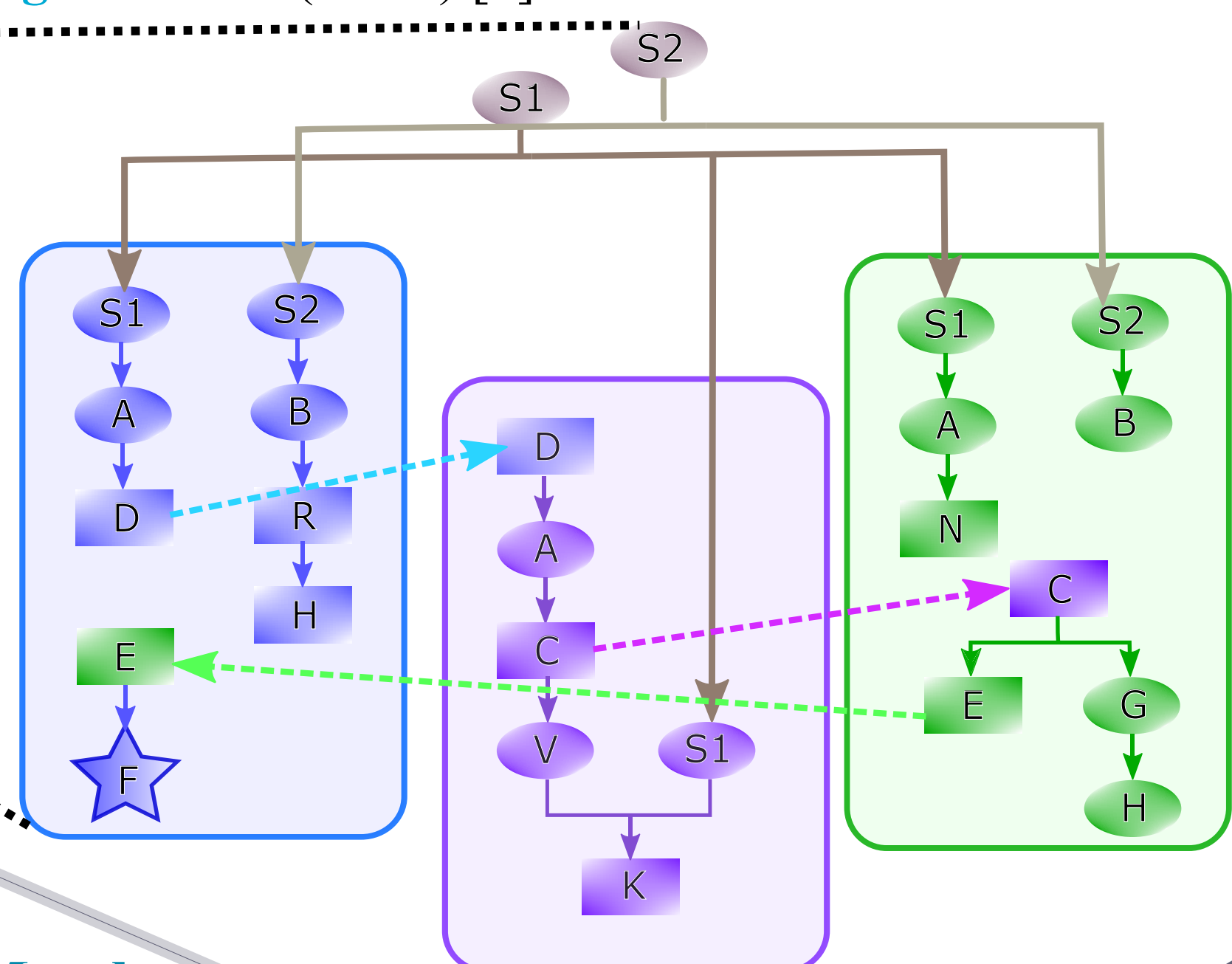
Species occurring at least in **one minimal community**

Essential Symbionts (ES):

Species occurring in **all minimal communities**

Alternative Symbionts (AS):

Species occurring in **some minimal communities**



Logic Programming

ASP

Answer Set Programming [4]

Declarative programming paradigm.

Solve **combinatorial** problems with knowledge.

Knowledge

```

bacteria("B1").
metabolite("M_S1_c", "S1", "B1").
metabolite("M_S2_c", "S2", "B1").
metabolite("M_A_c", "A", "B1").
metabolite("M_B_c", "B", "B1").
reaction("R1", "B1").
reactant("M_S1_c", "R1", "B1").
reactant("M_S2_c", "R1", "B1").
product("M_A_c", "R1", "B1").
reaction("R2", "B1").
reactant("M_A_c", "R2", "B1").
product("M_B_c", "R2", "B1").
seed("S1").
seed("S2").
    
```

Set of rules with two parts:

HEAD :- BODY
 Head is true
 if all element of body is true

Individual scope rules

```

iscope(M,S,B) :- seed(M), species(M,S,_), bacteria(B).
iscope(M,S,B) :- bacteria(B), product(M,R,B),
    reaction(R,B), metabolite(M,N,B),
    iscope(M2,N2,B) : reactant(M2,R,B).
    
```

Rules to verify hypotheses:

Unique metabolite

A metabolite produced by **all bacteria of a group**, and **not other bacteria of minimal communities**.

Unique reaction

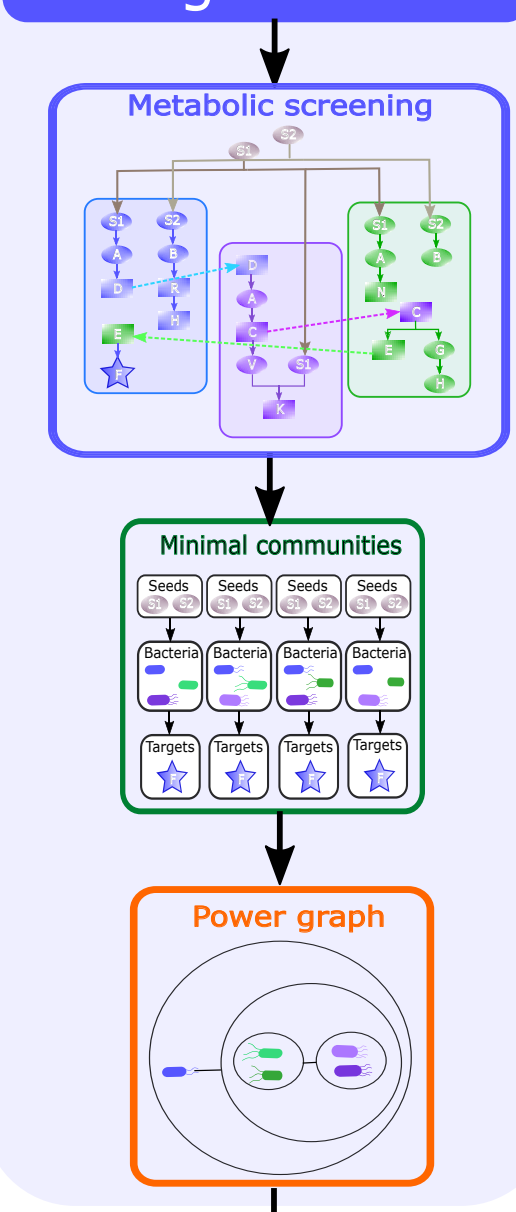
A reaction activated by **all bacteria of a group**, and **not by any other bacteria of community**.

Unique metareact

A **unique metabolite produced by unique reaction** carried by all bacteria of a group and **not by others**.

From Metage2Metabo to PowerFun

Metage2Metabo



1,520 GSMNs + Seeds (env.) + Targets

PowerFun is an extension of the M2M study.

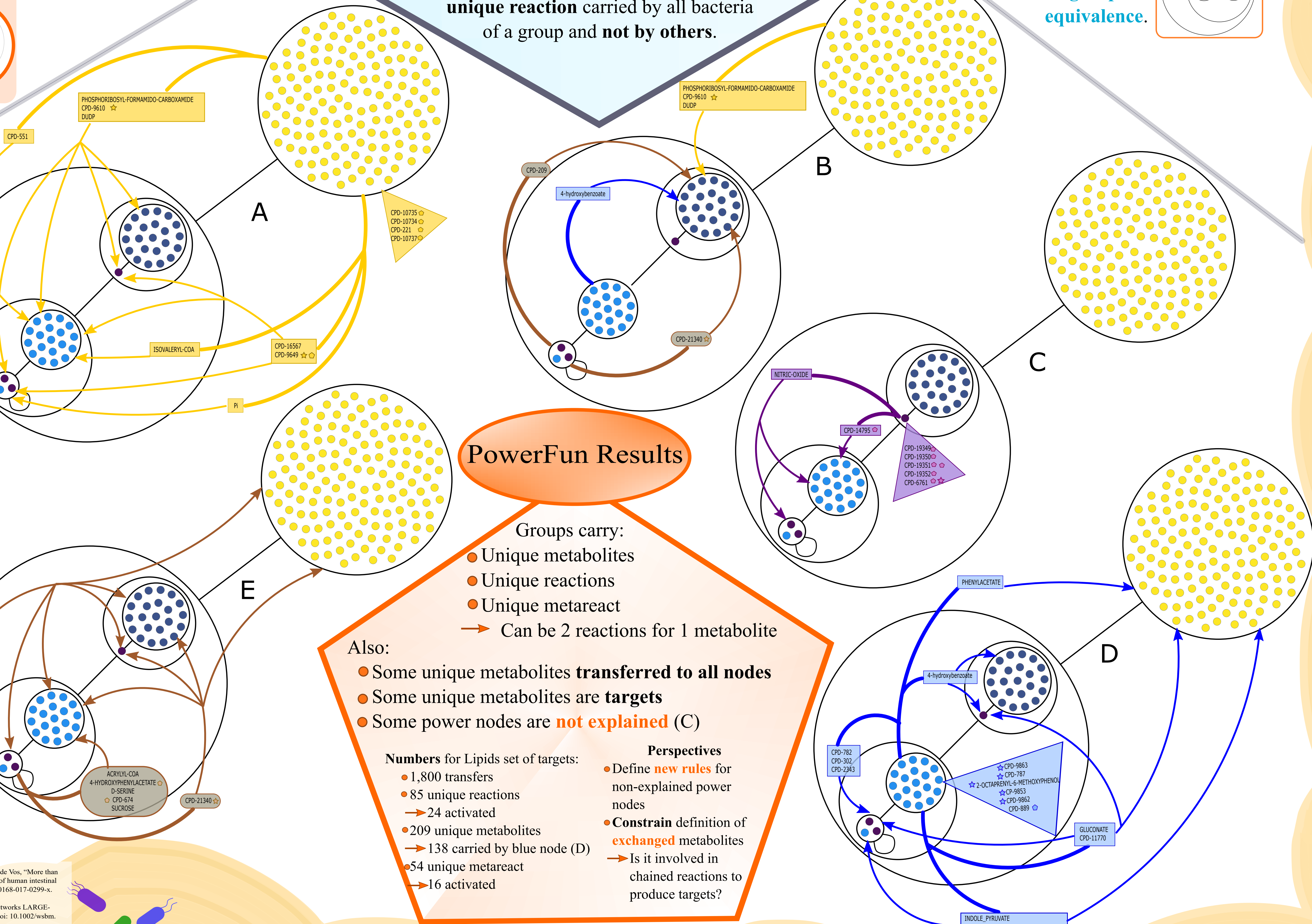
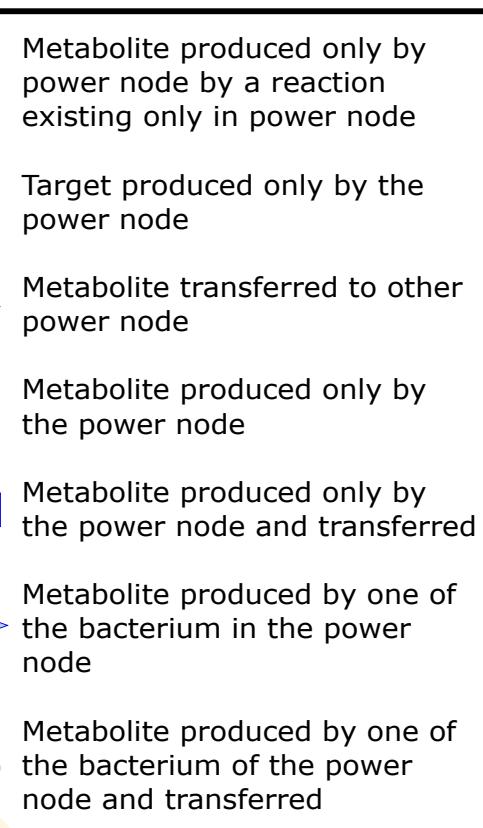
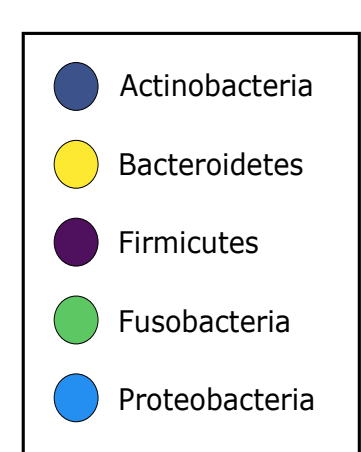
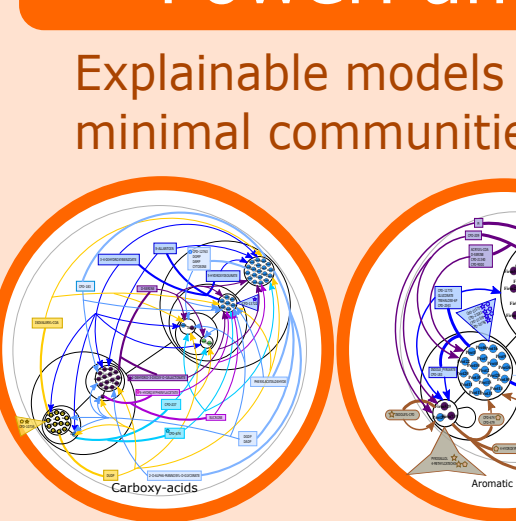
Groups of equivalence have been identified with power graphs.

Why are the bacteria gathered together? **Which functions are carried by the group?**

Hypotheses:

- **Unique metabolite produced**
- **Unique reaction activated**
- **Unique metareact**

PowerFun



PowerFun Results

Groups carry:

- Unique metabolites
- Unique reactions
- Unique metareact
- Can be 2 reactions for 1 metabolite

Also:

- Some unique metabolites **transferred to all nodes**
- Some unique metabolites are **targets**
- Some power nodes are **not explained** (C)

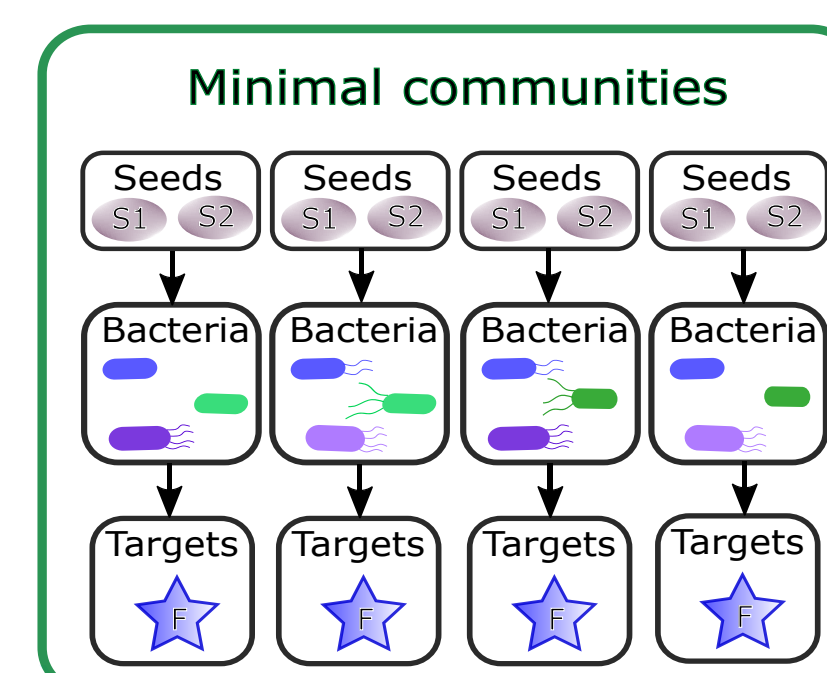
Numbers for Lipids set of targets:

- 1,800 transfers
- 85 unique reactions
- 24 activated
- 209 unique metabolites
- 138 carried by blue node (D)
- 54 unique metareact
- 16 activated

Perspectives

- Define **new rules** for non-explained power nodes
- **Constrain** definition of **exchanged metabolites**
- Is it involved in chained reactions to produce targets?

Power graph compression method

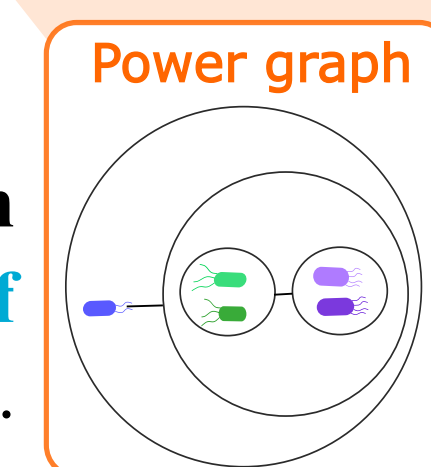
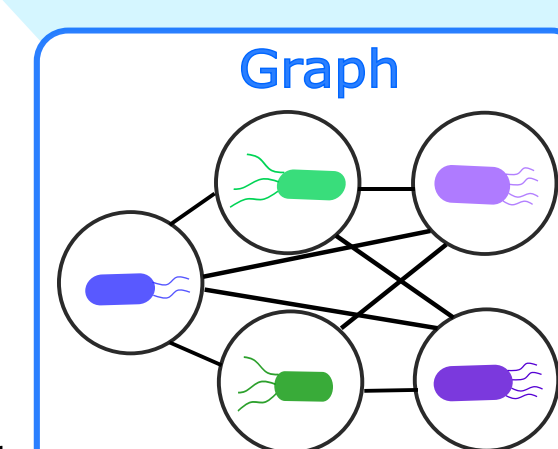


Up to millions of possible **minimal communities** for a set of targets.

How visualize them?

• Association graph
 → Not easily readable on thousands minimal communities.

- **Graph compression**
 → shows **groups of equivalence**.



1. K. C. H. van der Ark, R. G. A. van Heek, V. A. P. Martins Dos Santos, C. Belzer, and W. M. de Vos. "More than just a gut feeling: constraint-based genome-scale metabolic models for predicting functions of human intestinal microbes." *Microbiome*, vol. 5, no. 1. BioMed Central, p. 78, Jul. 14, 2017. doi: 10.1186/s40168-017-0299-x.

2. M. Terzer, N. D. Maynard, M. W. Covert, and J. "Og Stelling. "Genome-scale metabolic networks LARGE-SCALE NETWORK ANALYSIS." *In: WIREs Syst Biol Med*, vol. 1, pp. 285-297, 2009, doi: 10.1002/wsbm.037.

3. Belcour A, Frioux C, Aite M, Hildebrand F, Siegel A. Metabolic Complementarity for the Identification of Key Species. *ELife*, 9, 1-33.

4. M. Gebser, R. Kaminski, B. Kaufmann, and T. Schaub. Answer set solving in practice.