



**HAL**  
open science

## Reasoning approaches for the characterization of cooperation and competition in large-scale microbial communities

Maxime Lecomte, David James Sherman, H el ene Falentin, Cl emence Frioux

► **To cite this version:**

Maxime Lecomte, David James Sherman, H el ene Falentin, Cl emence Frioux. Reasoning approaches for the characterization of cooperation and competition in large-scale microbial communities. Journ ee GT Bioss 2022, Nov 2022, Nantes, France. hal-03857781

**HAL Id: hal-03857781**

**<https://hal.inrae.fr/hal-03857781>**

Submitted on 17 Nov 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 destin ee au d ep ot et  a la diffusion de documents scientifiques de niveau recherche, publi es ou non,  emanant des  tablissements d'enseignement et de recherche franais ou  trangers, des laboratoires publics ou priv es.



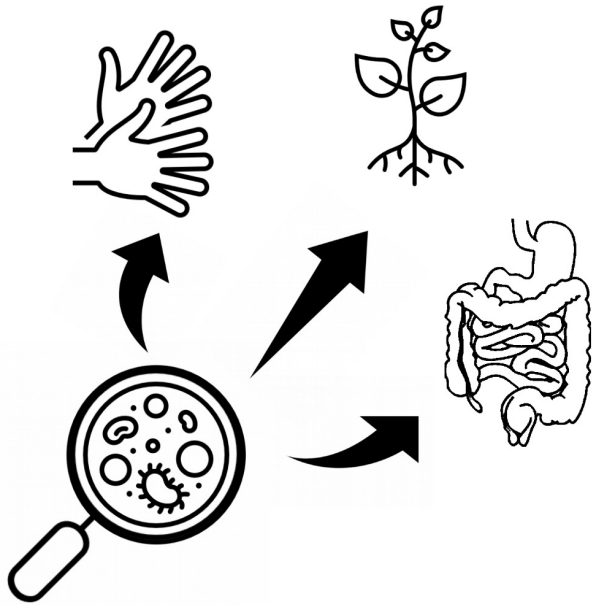
➤ Reasoning approaches for the characterization of cooperation and competition in large-scale microbial communities

Maxime Lecomte – David Sherman – Hélène Falentin – Clémence Frioux

GT-BIOSS NANTES November, 17 2022

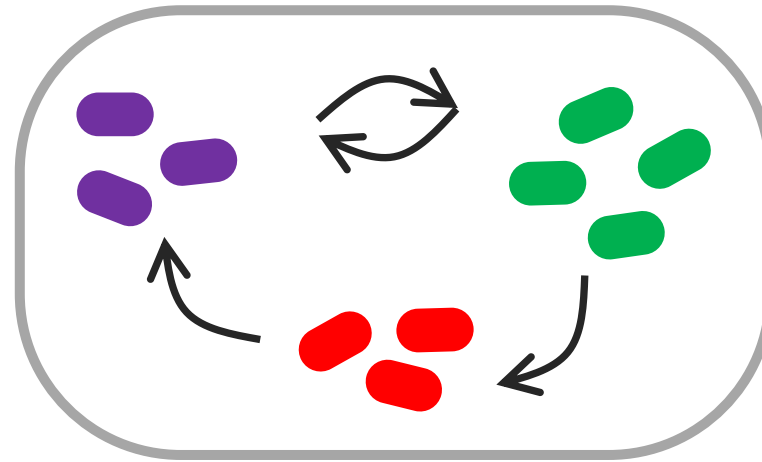
## > Motivation

Bacterial communities ?



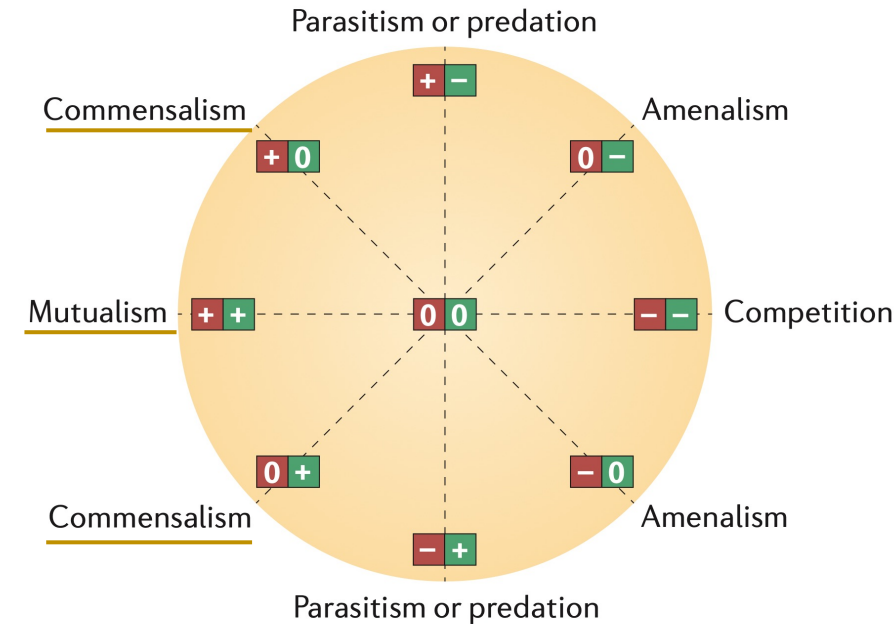
Microbes are essential in ecosystems

System biology



Bacterial interactions as a key mechanism

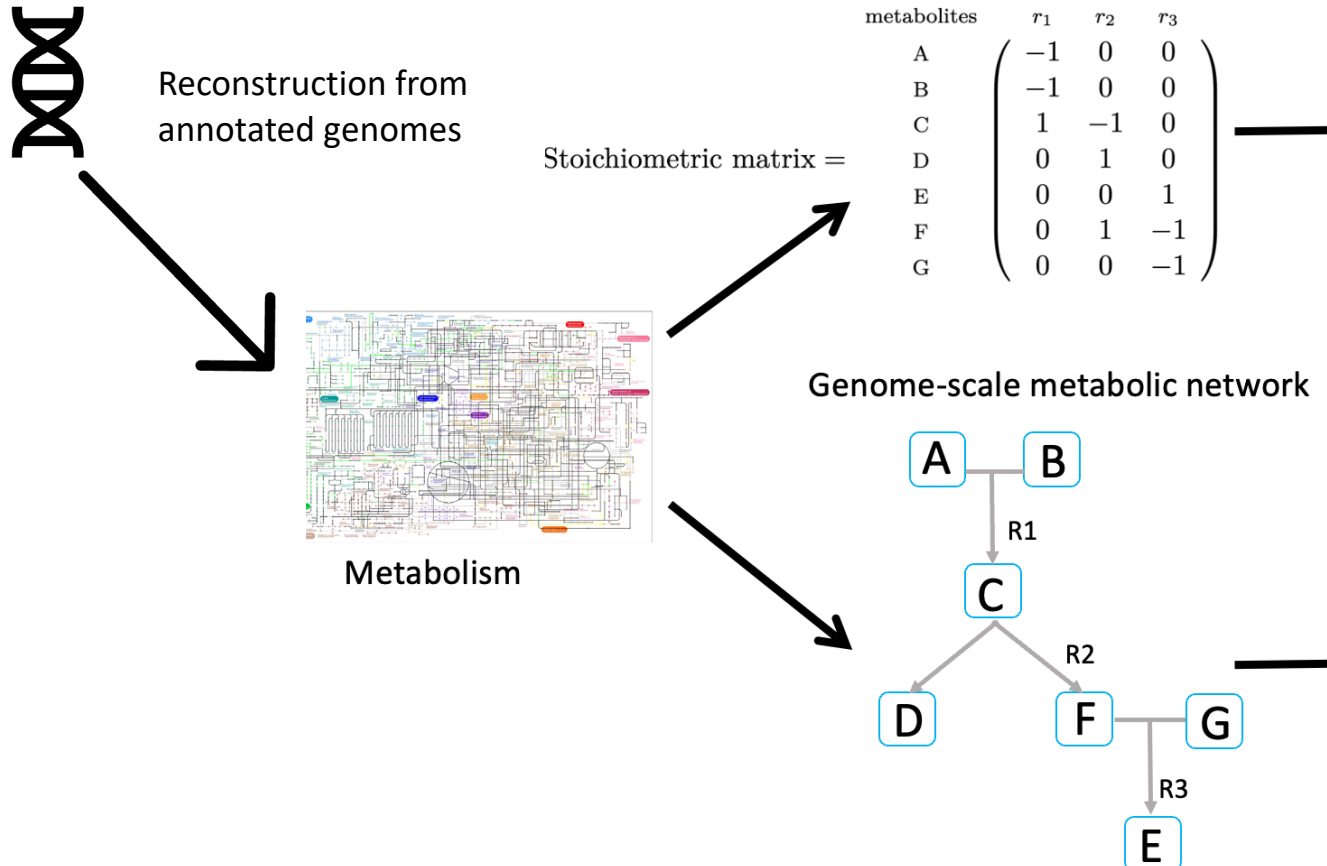
Interaction types



Cooperation and competition

Metabolism enable the understanding of interaction-based mechanisms in microbial communities

## ➤ State-of-the art for modeling bacterial communities



Genome-scale metabolic networks describe all functions associated to genomes

# ➤ State-of-the art for modeling bacterial communities



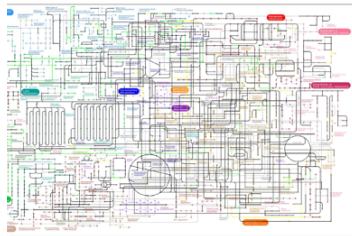
Reconstruction from annotated genomes

Stoichiometric matrix =

metabolites	$r_1$	$r_2$	$r_3$
A	-1	0	0
B	-1	0	0
C	1	-1	0
D	0	1	0
E	0	0	1
F	0	1	-1
G	0	0	-1

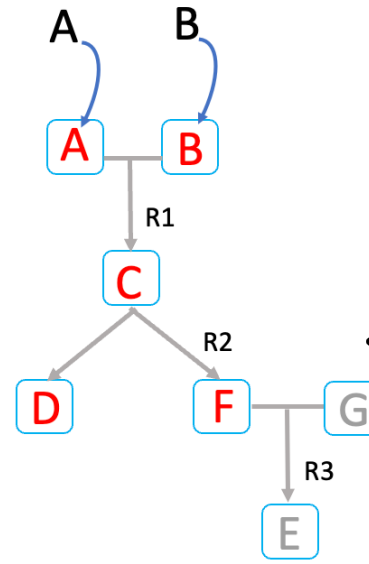
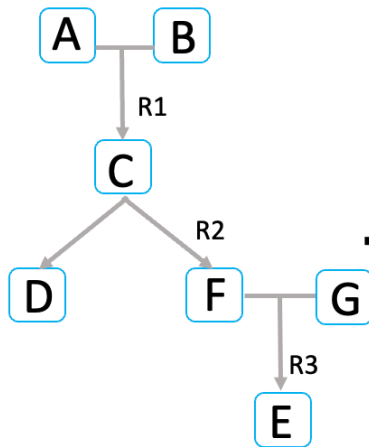
$\max v_{growth}$   
 such that  $S \cdot v = 0$   
 and  $v_{min} \leq v \leq v_{max}$

Numerical methods (e.g., FBA-like)



Metabolism

Genome-scale metabolic network



Discrete method

Metabolite scope from the A,B in the environment

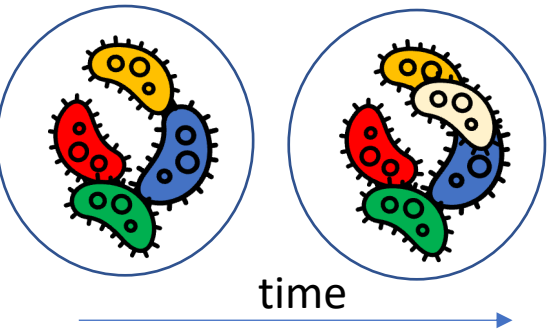
Two mathematical formalisms used for modeling the behavior of an organism in its environment



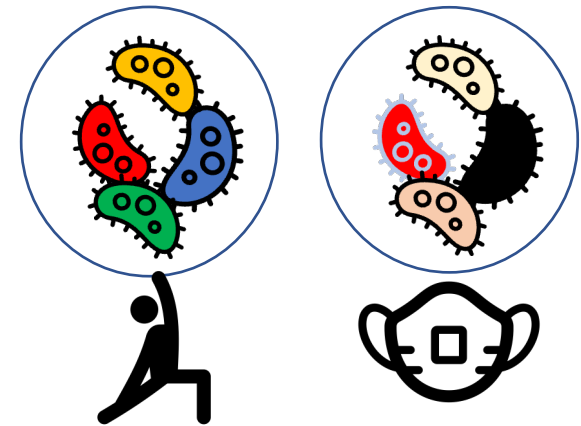
# ➤ Goal : Identify cooperation and competition potential in large scale bacterial communities

Cooperation and competition potential

## Longitudinal analysis



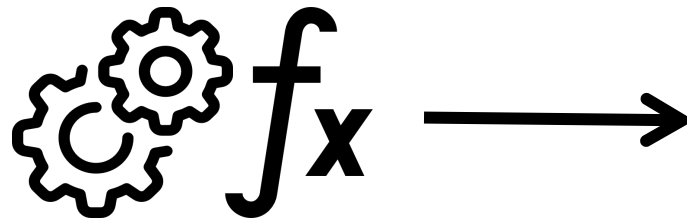
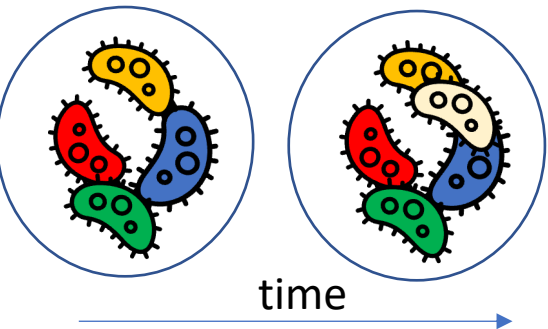
## Cross sectional analysis



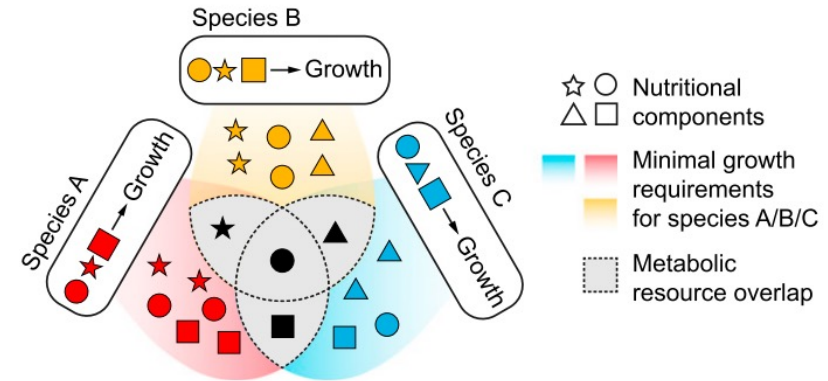
# ➤ Goal : Identify cooperation and competition potential in large scale bacterial communities

Cooperation and competition potential

Longitudinal analysis

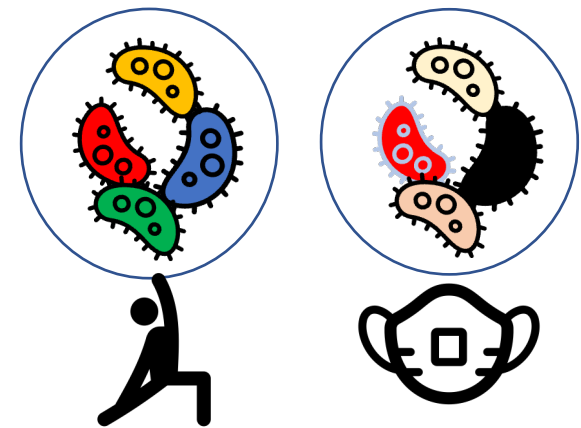


Nutrient point of view



Competition potentials

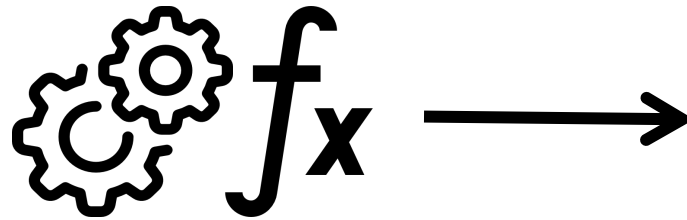
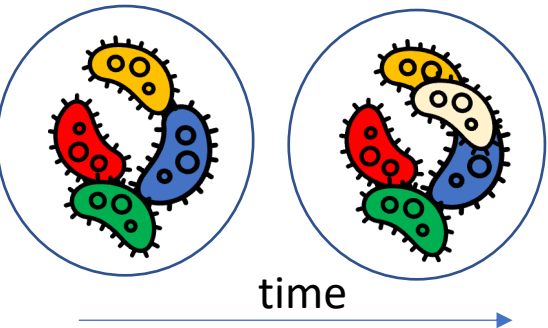
Cross sectional analysis



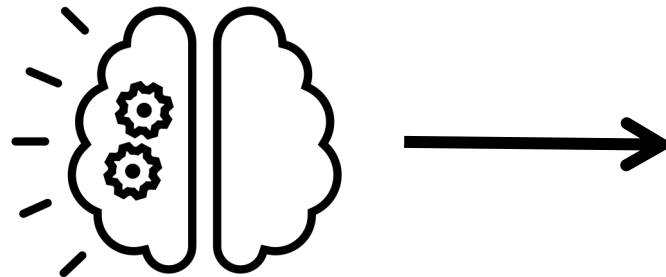
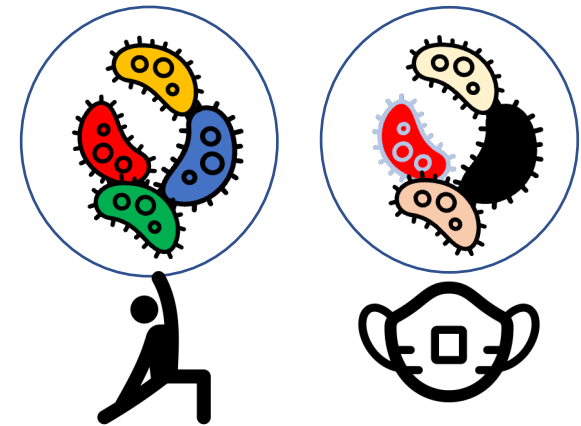
# ➤ Goal : Identify cooperation and competition potential in large scale bacterial communities

Cooperation and competition potential

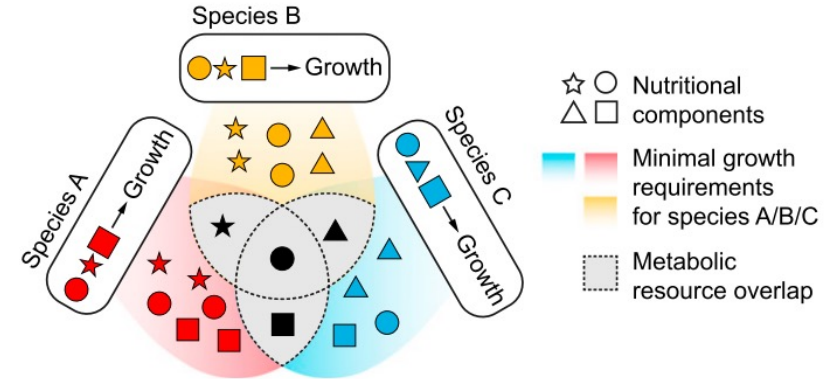
Longitudinal analysis



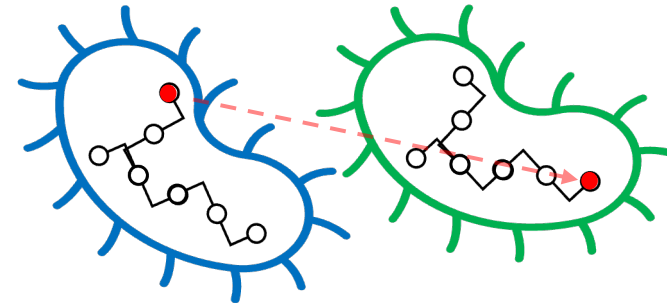
Cross sectional analysis



Nutrient point of view



Competition potentials



Cooperation potentials

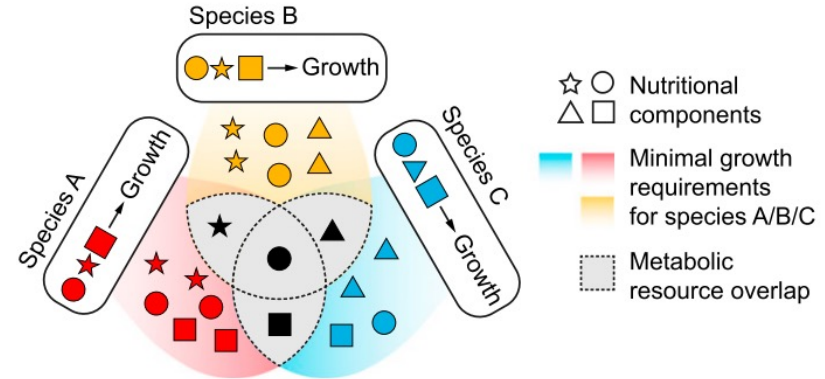
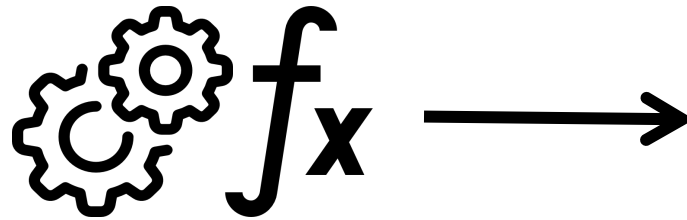
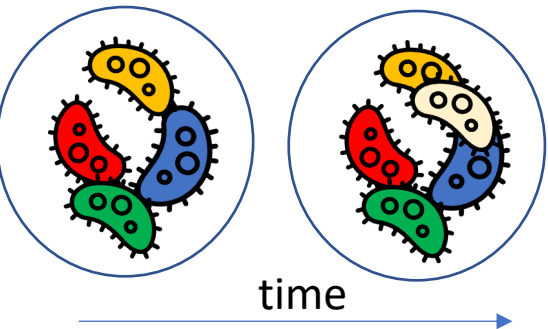
Either numerical or discrete methods highlight cooperation and competition potentials



# ➤ Goal : Identify cooperation and competition potential in large scale bacterial communities

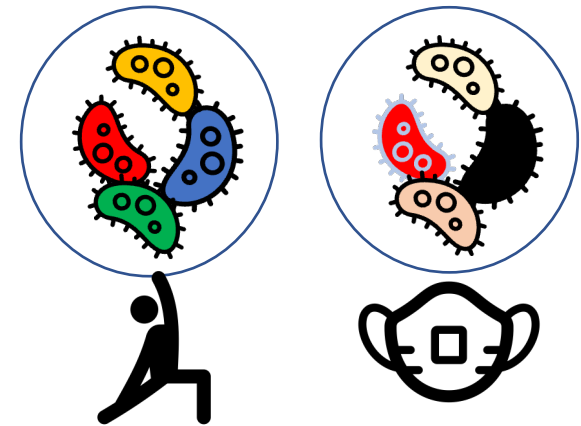
Scale-up to large scale bacterial communities

## Longitudinal analysis



Community size up to 18

## Cross sectional analysis

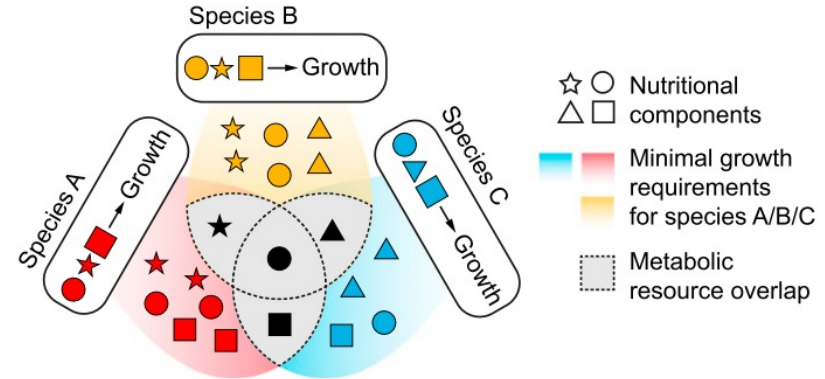
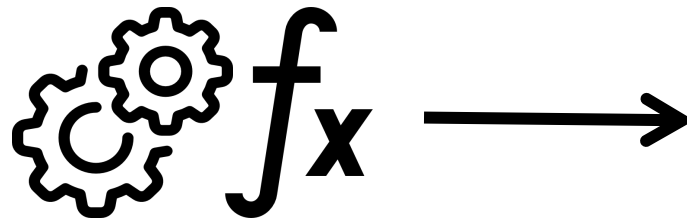
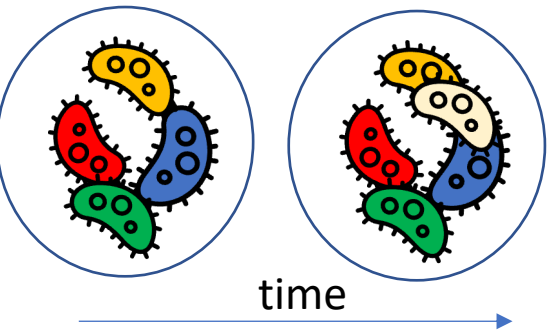


Cost in computational time

# ➤ Goal : Identify cooperation and competition potential in large scale bacterial communities

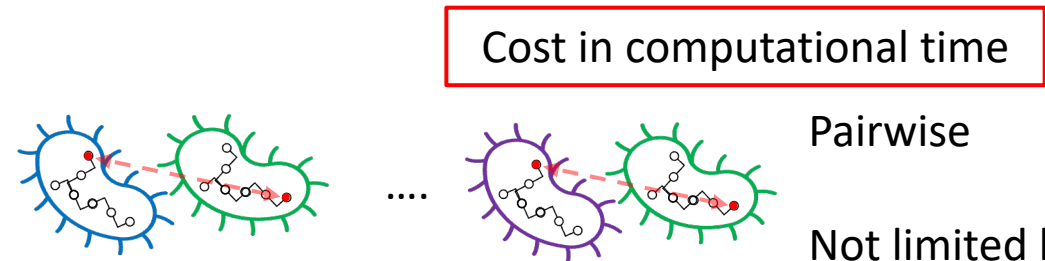
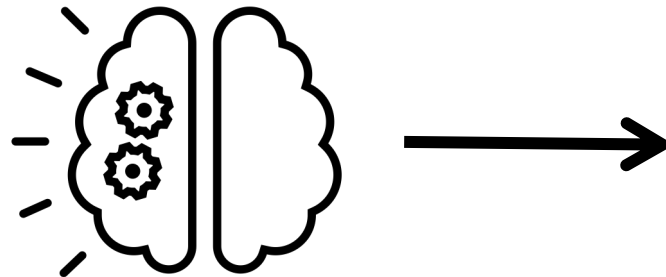
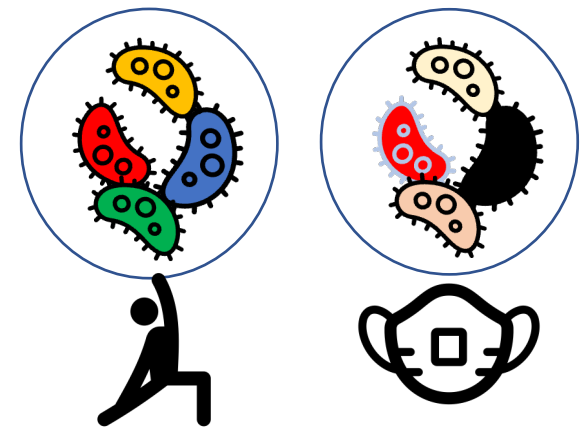
Scale-up to large scale bacterial communities

## Longitudinal analysis



Community size up to 18

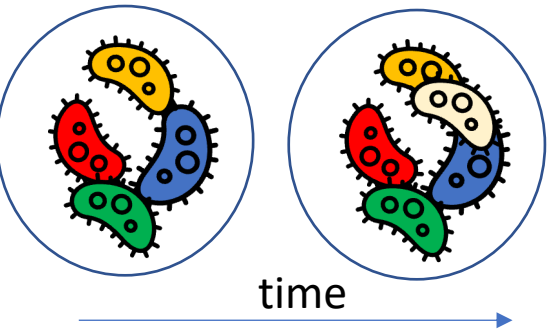
## Cross sectional analysis



Pairwise  
Not limited by the community size

# ➤ Avoid pairwise analysis for characterizing cooperation and competition in microbial communities

Longitudinal analysis



Characterize community

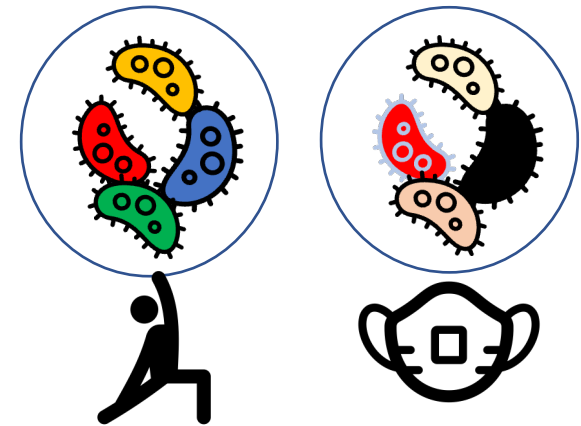


150 bacteria

Pairwise analysis

$$(150 * (150-1))/2 = 11\ 375 \text{ combinations}$$

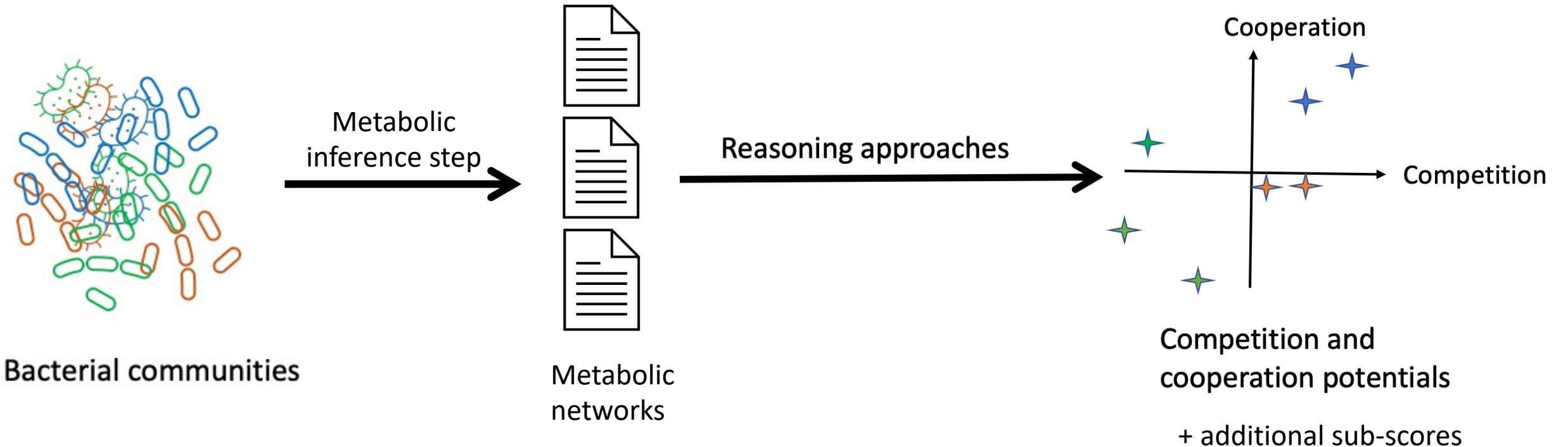
Cross sectional analysis



Cost in computational time + tedious analysis

How to characterize cooperation and competition potentials? → trade-off between scalability and accuracy

# ➤ Avoid pairwise analysis for characterizing cooperation and competition in microbial communities



Calculation of scores for characterizing the whole community with Answer Set Programming

# ➤ Answer Set Programming

Logic paradigm and Knowledge representation & reasoning

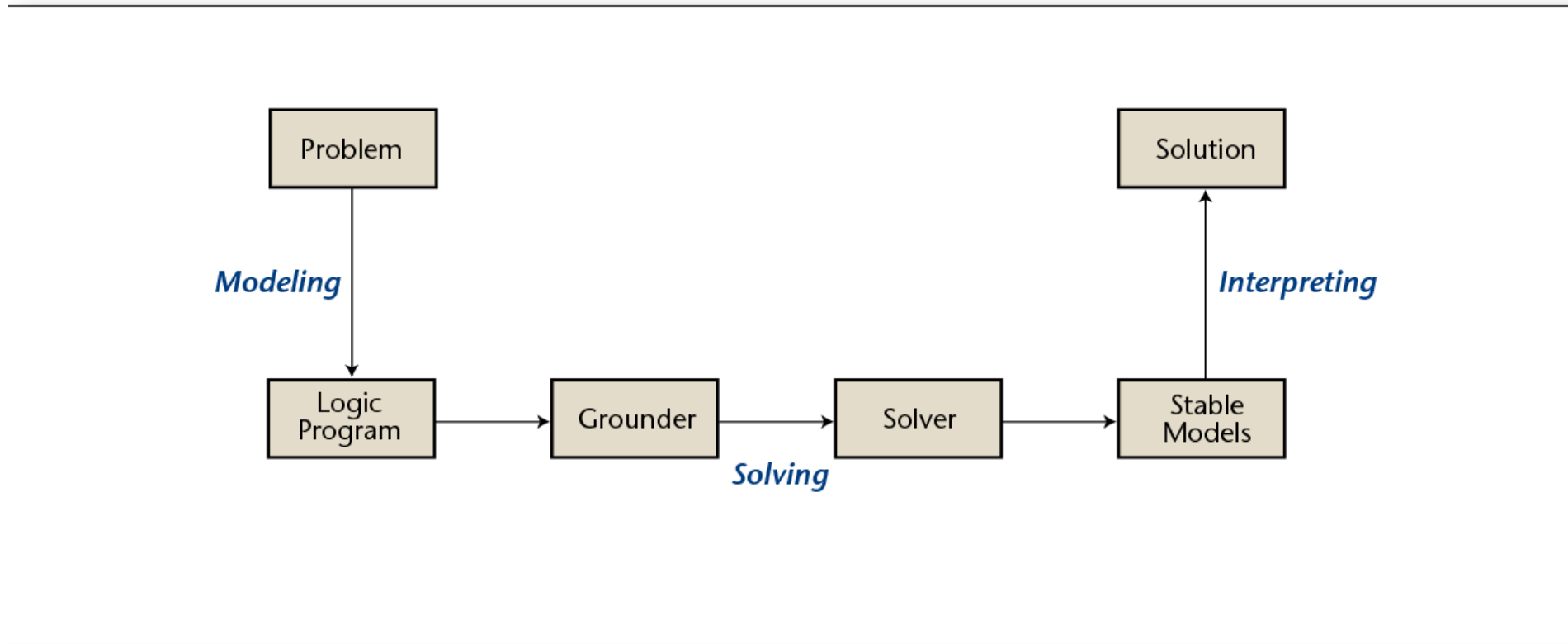
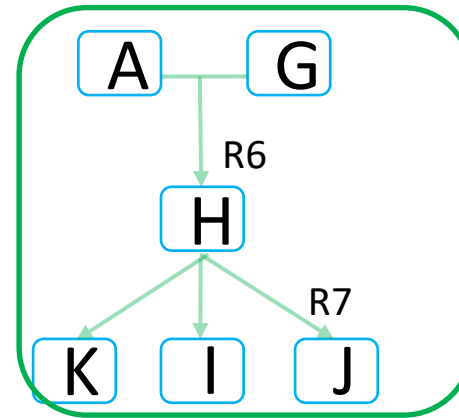
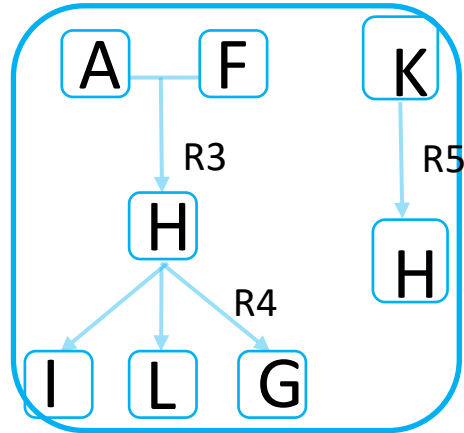
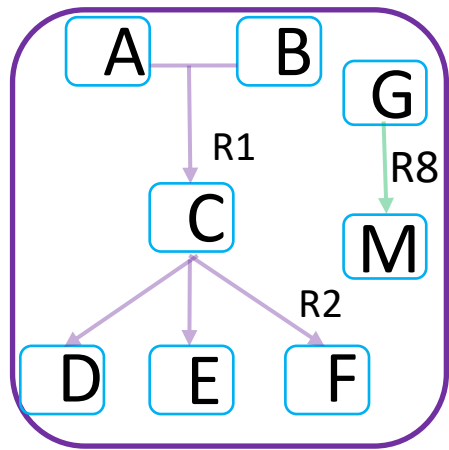


Figure 1. The Work Flow of Answer Set Programming.

Kaufmann, Benjamin et al. "Grounding and Solving in Answer Set Programming." *AI Mag.* 37 (2016): 25-32.

➤ Cooperation potential based on exchanged metabolites using ASP

Seed : A,B

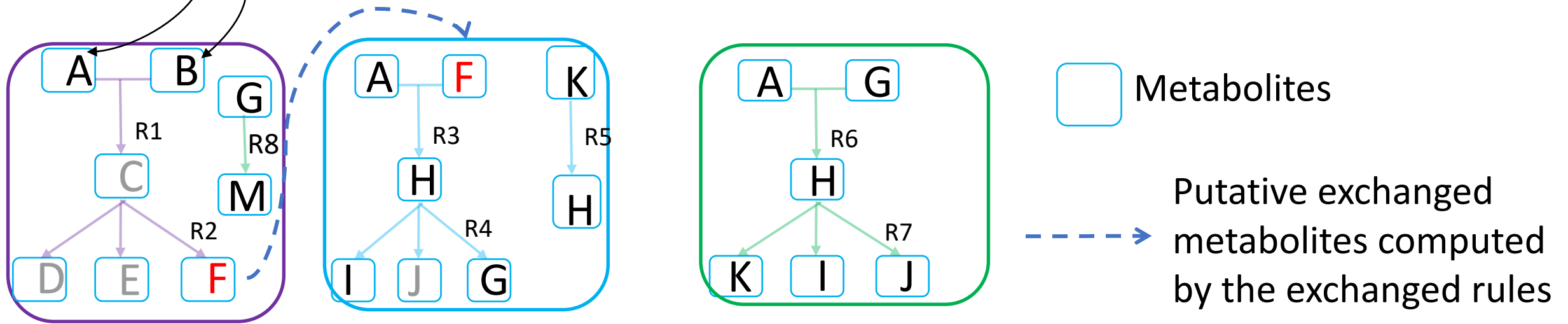


 Metabolites

$exchanged_{metabolites} = scope(G_s, S), not indivProducible(S, G_t), products(S, G_s)$ . Where  $S \in G$  and  $T \in G$ , and  $S \neq T$ .

➤ Cooperation potential based on exchanged metabolites using ASP

Seed : A,B

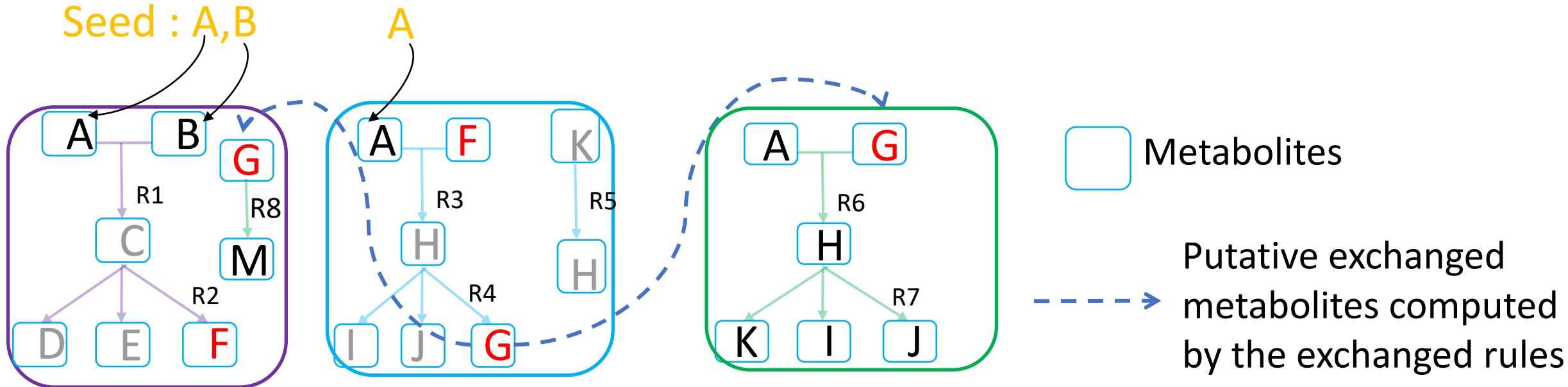


From	What	To
	F	



# ➤ Cooperation potential based on exchanged metabolites using ASP

Seed : A,B



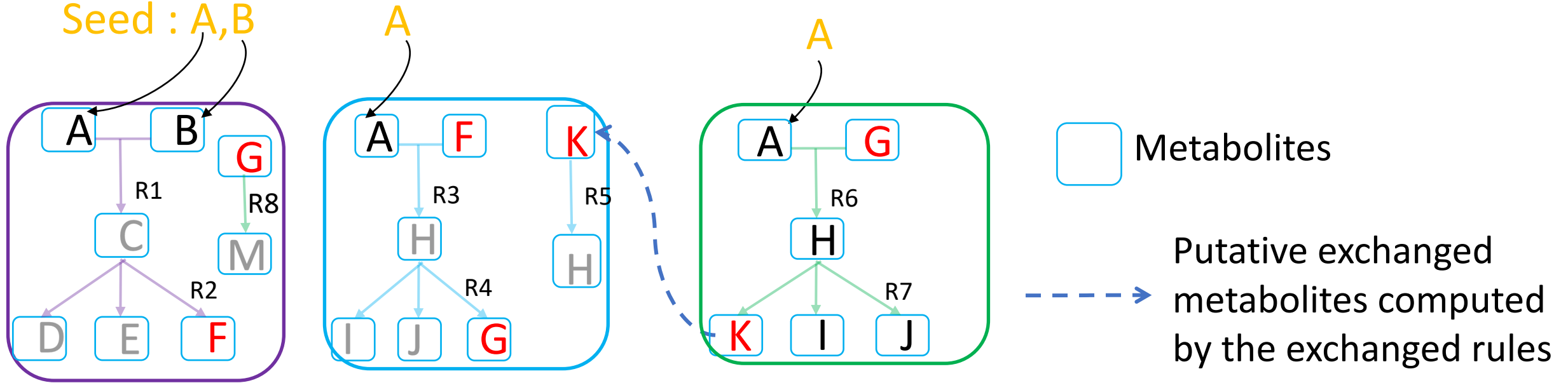
From	What	To
<input type="checkbox"/>	F	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>





# ➤ Cooperation potential based on exchanged metabolites using ASP

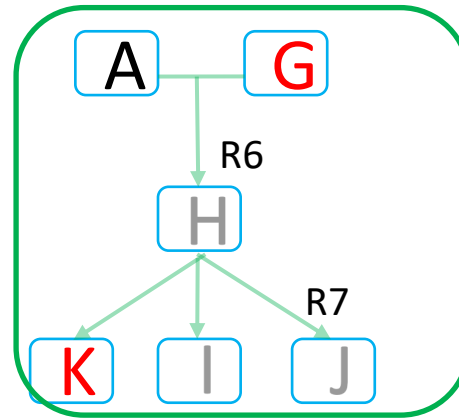
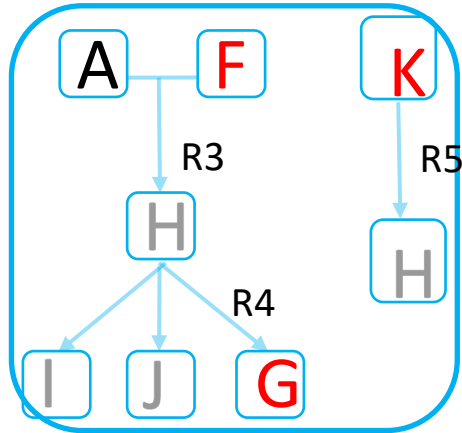
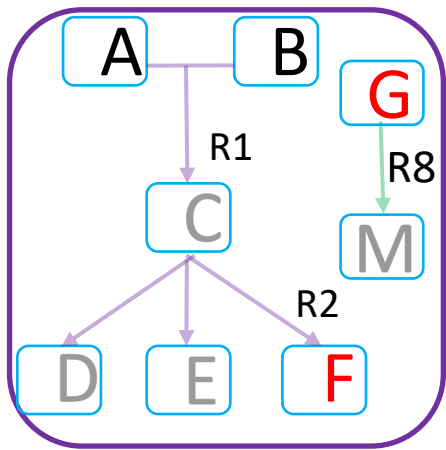
Seed : A,B



From	What	To
<input type="checkbox"/>	F	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	K	<input type="checkbox"/>

# ➤ Exponential bonus (python)

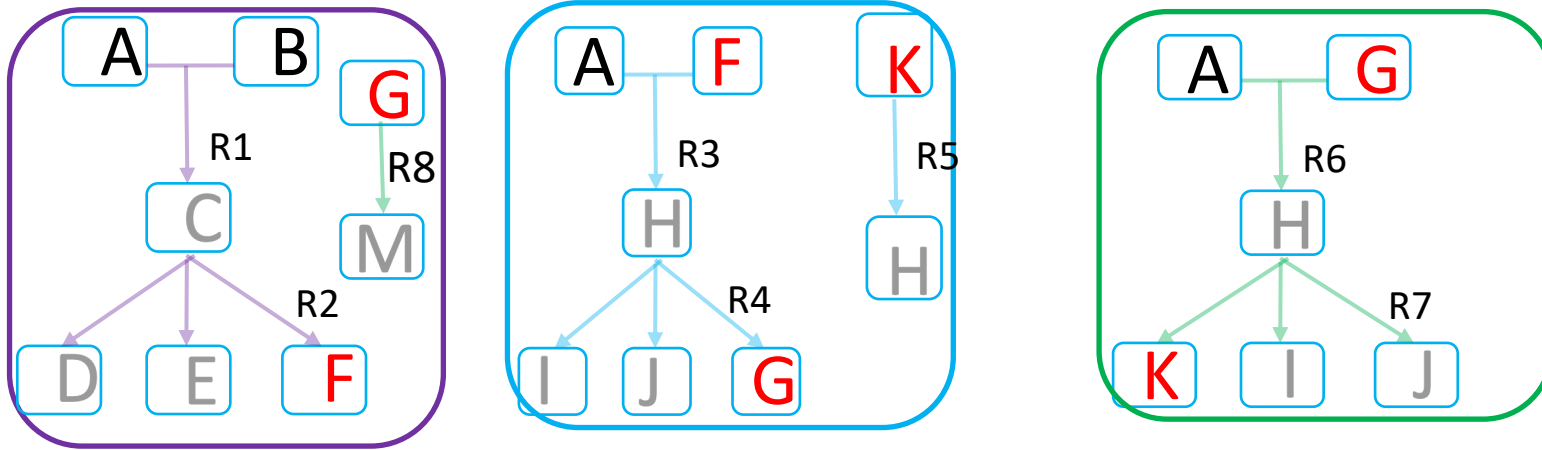
hypothesis : each species contributes differently



From	What	To
<input type="checkbox"/>	F	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	K	<input type="checkbox"/>

# ➤ Exponential bonus (python)

hypothesis : each species contributes differently



From	What	To
<input type="checkbox"/>	F	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	K	<input type="checkbox"/>



$$cooperation = \sum_{i=1}^m \sum_{k=2}^n 1 + 2^{-(k-1)}$$

Number of metabolites

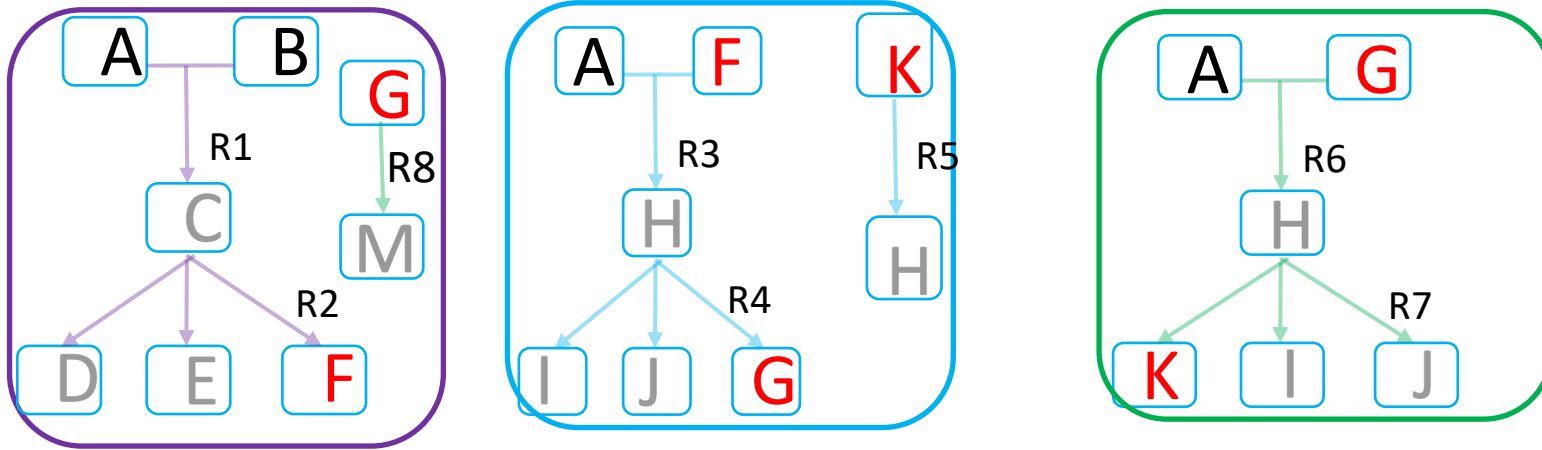
Number of different producers / consumers



INRAE

# Exponential bonus (python)

hypothesis : each species contributes differently



Metabolites	Producers	consumers
F	1	1

From	What	To
<input type="checkbox"/>	F	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	K	<input type="checkbox"/>



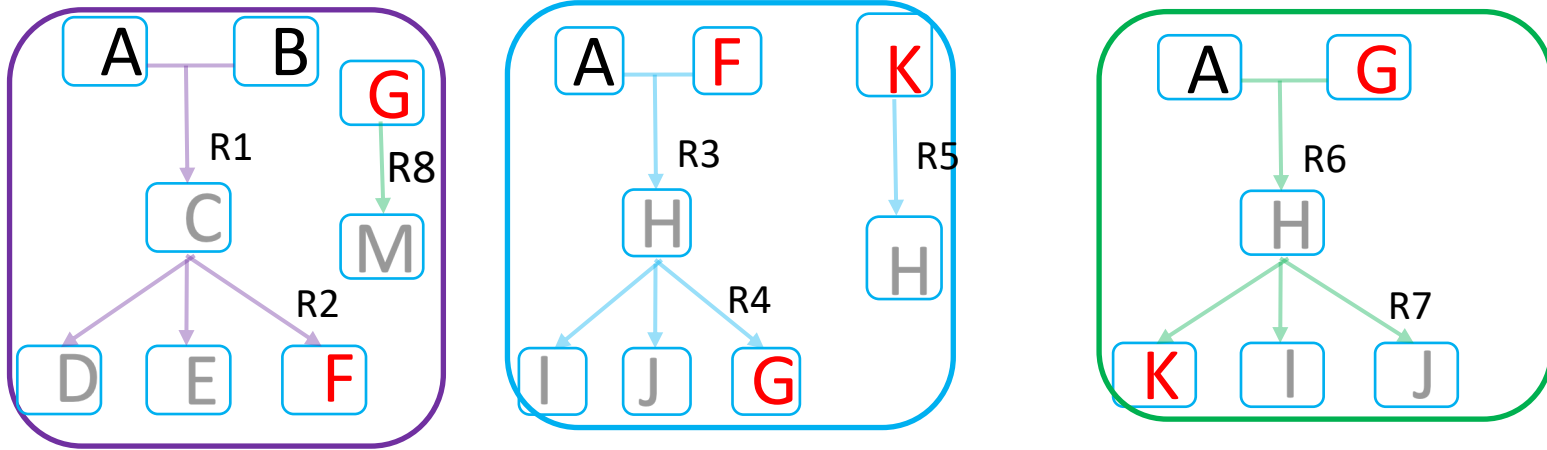
$$cooperation = \sum_{i=1}^m \sum_{k=2}^n 1 + 2^{-(k-1)}$$

Number of metabolites

Number of different producers / consumers

# Exponential bonus (python)

hypothesis : each species contributes differently



Metabolites	Producers	consumers
F	1	1
G	1	1 + 2 <sup>1</sup> =1.5

From	What	To
<input type="checkbox"/>	F	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	K	<input type="checkbox"/>



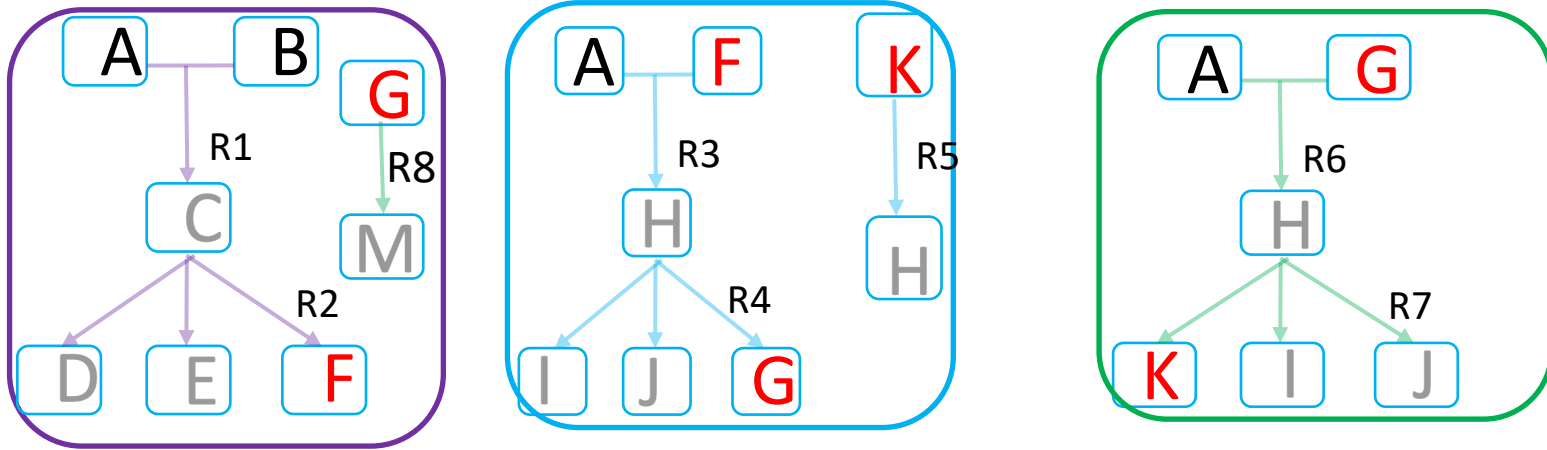
$$cooperation = \sum_{i=1}^m \sum_{k=2}^n 1 + 2^{-(k-1)}$$

Number of metabolites

Number of different producers / consumers

# Exponential bonus (python)

hypothesis : each species contributes differently



Metabolites	Producers	consumers
F	1	1
G	1	1 + 2 <sup>1</sup> =1.5
K	1	1

Cooperation = F + G + K = 6.5

From	What	To
<input type="checkbox"/>	F	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	K	<input type="checkbox"/>



$$cooperation = \sum_{i=1}^m \sum_{k=2}^n 1 + 2^{-(k-1)}$$

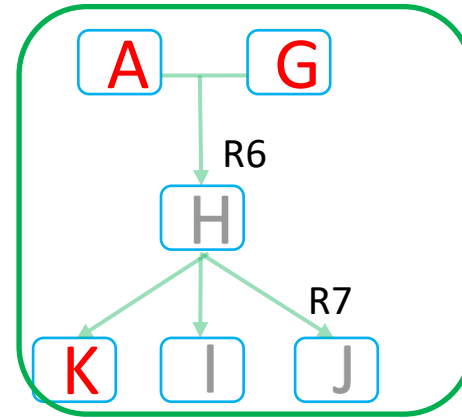
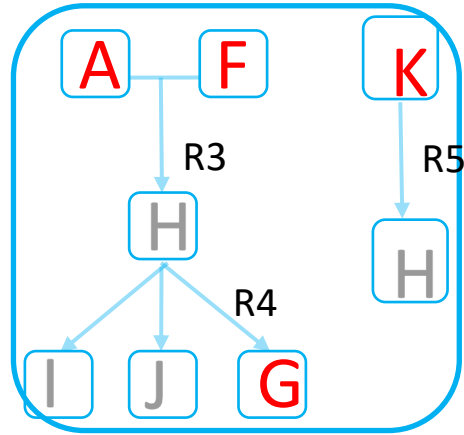
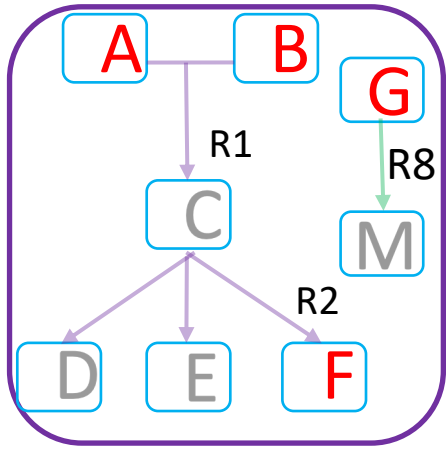
Number of metabolites

Number of different producers / consumers






# Competition potential based on limiting substrate using ASP

Seed : A,B



**G** Limiting substrates

-  A,B,F
-  A,B,G,K
-  A,G,K



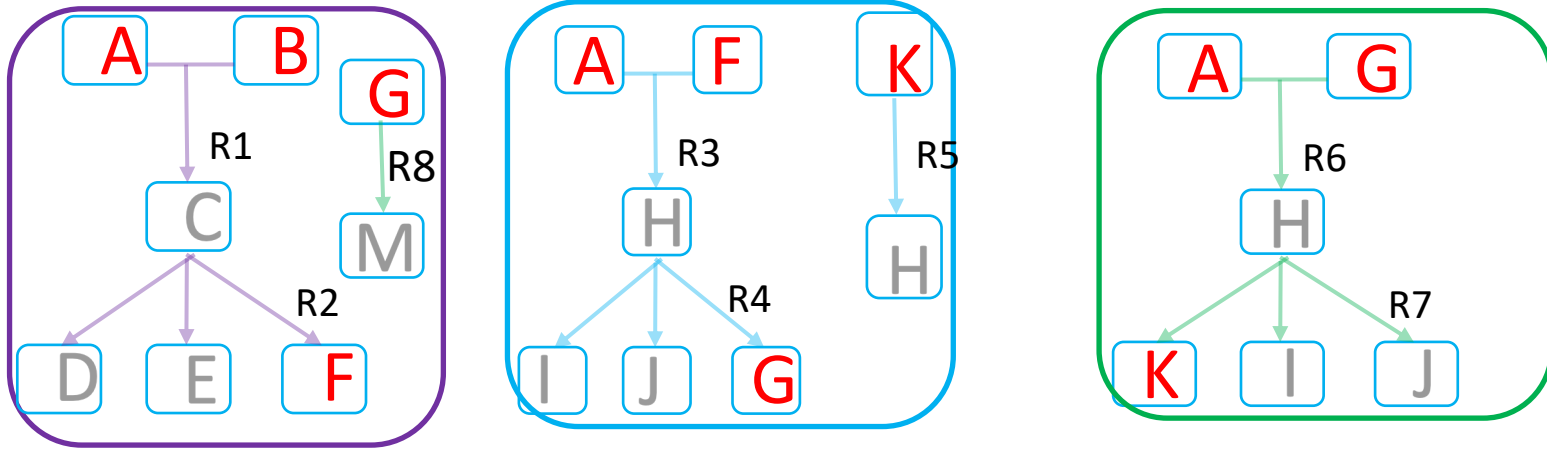
INRAE

Reasoning approaches for the characterization of cooperation and competition in large-scale microbial communities

November 17 2022 / [maxime.lecomte@inrae.fr](mailto:maxime.lecomte@inrae.fr) / Maxime Lecomte 3<sup>rd</sup> PhD student

➤ Calculation of the competition potential (python)

Seed : A,B



- A,B,F
- A,B,G,K
- A,G,K



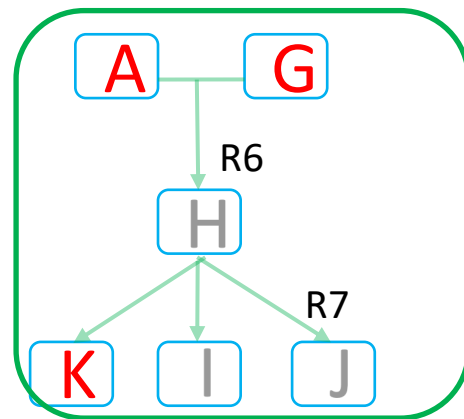
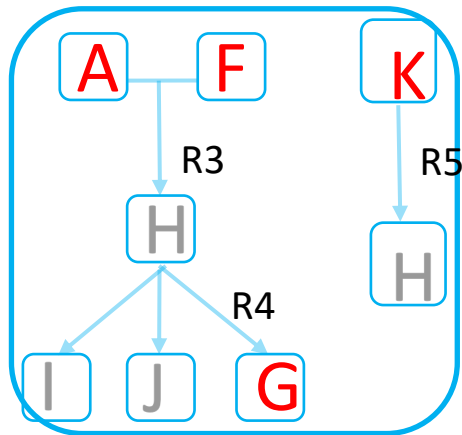
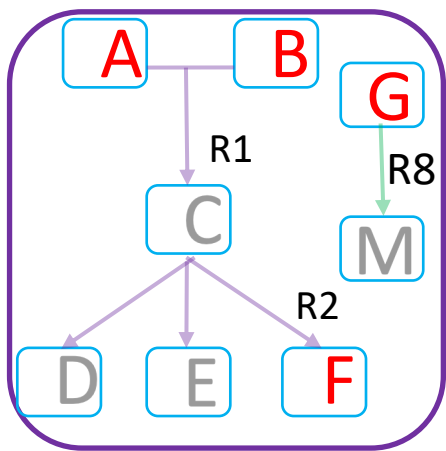
$$competition = \sum_{i=1}^m \frac{count(i)}{size\_community}$$





# ➤ Calculation of the competition potential (python)

Seed : A,B



A : 3  
B : 2  
G : 2  
K : 2  
F : 1

Metabolites

Number of consumers

- A,B,F
- A,B,G,K
- A,G,K

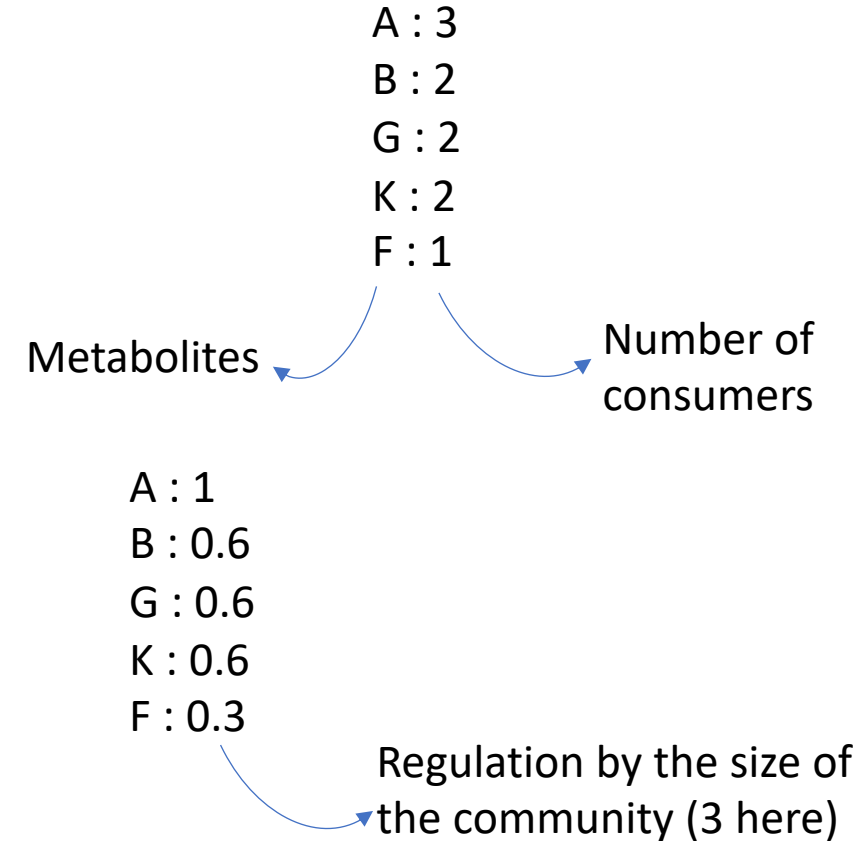
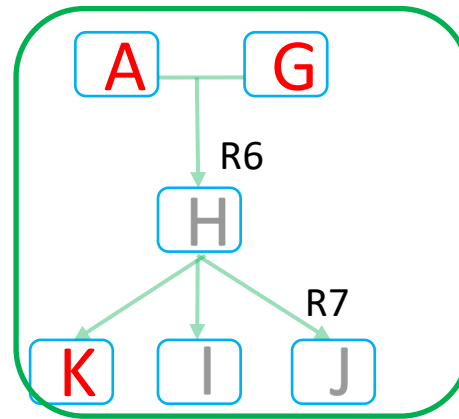
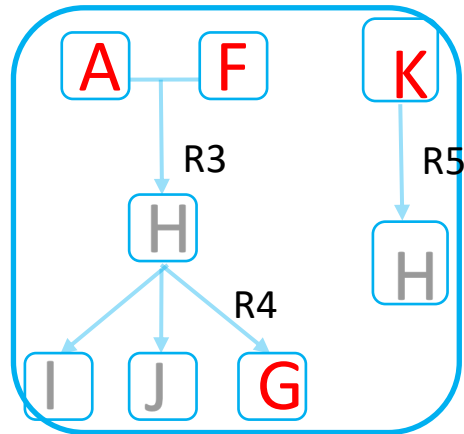
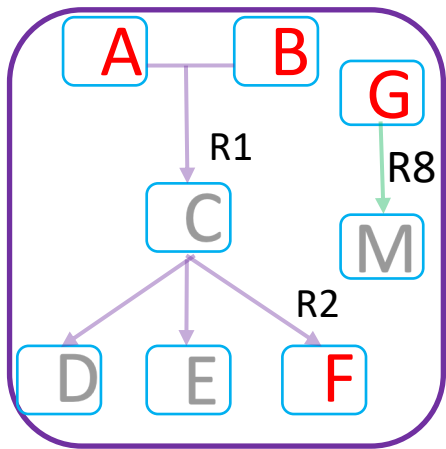


$$competition = \sum_{i=1}^m \frac{count(i)}{size\_community}$$



# ➤ Calculation of the competition potential (python)

Seed : A,B



- A,B,F
- A,B,G,K
- A,G,K

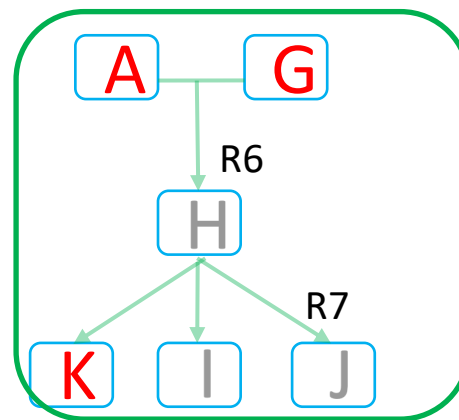
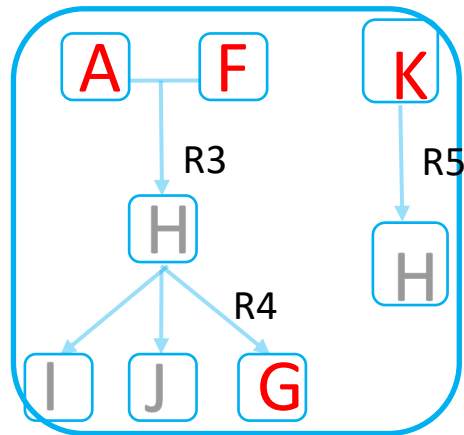
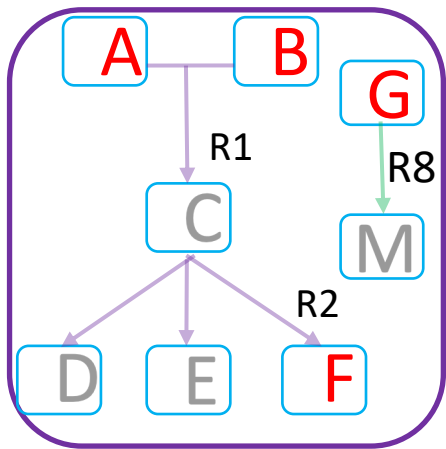


$$competition = \sum_{i=1}^m \frac{count(i)}{size\_community}$$



# ➤ Calculation of the competition potential (python)

Seed : A,B



A : 3  
B : 2  
G : 2  
K : 2  
F : 1

Metabolites

Number of consumers

A : 1  
B : 0.6  
G : 0.6  
K : 0.6  
F : 0.3

Regulation by the size of the community (3 here)

- A,B,F
- A,B,G,K
- A,G,K



$$competition = \sum_{i=1}^m \frac{count(i)}{size\_community}$$

Competition = 1 + 0.6 + 0.6 + 0.6 + 0.3 = **3.1**



## ➤ Benchmarks for testing scores

Scores in function of the ecosystem



gut



Leaf



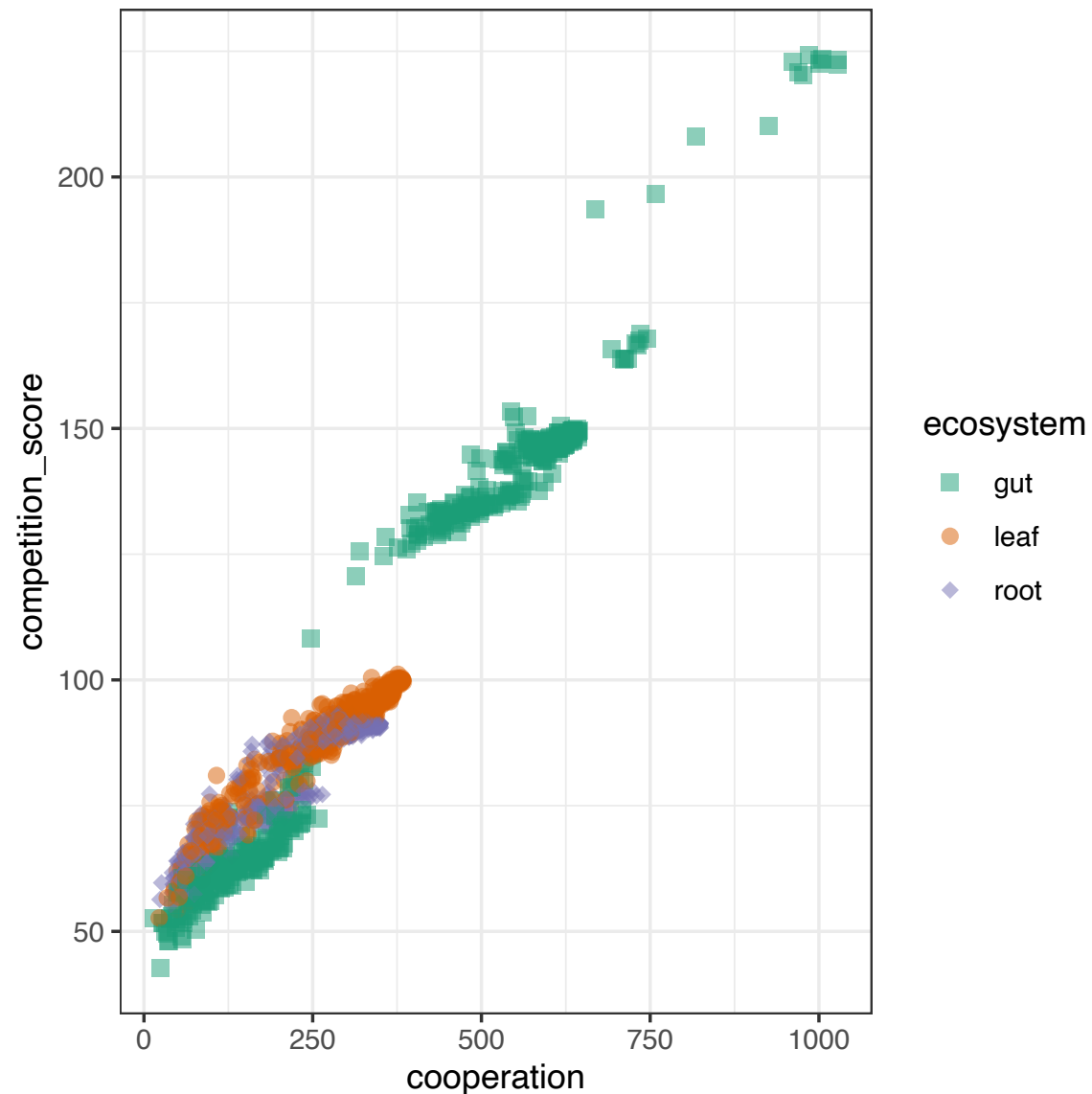
root



50 communities of size X

Reference  
genomes of  
cultivable species  
from 3 ecosystems

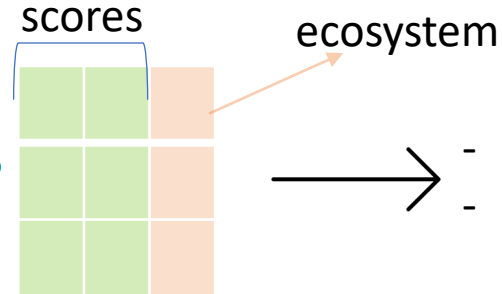
Different scores in function of the ecosystems



INRAE

# ➤ Ecosystem prediction from scores

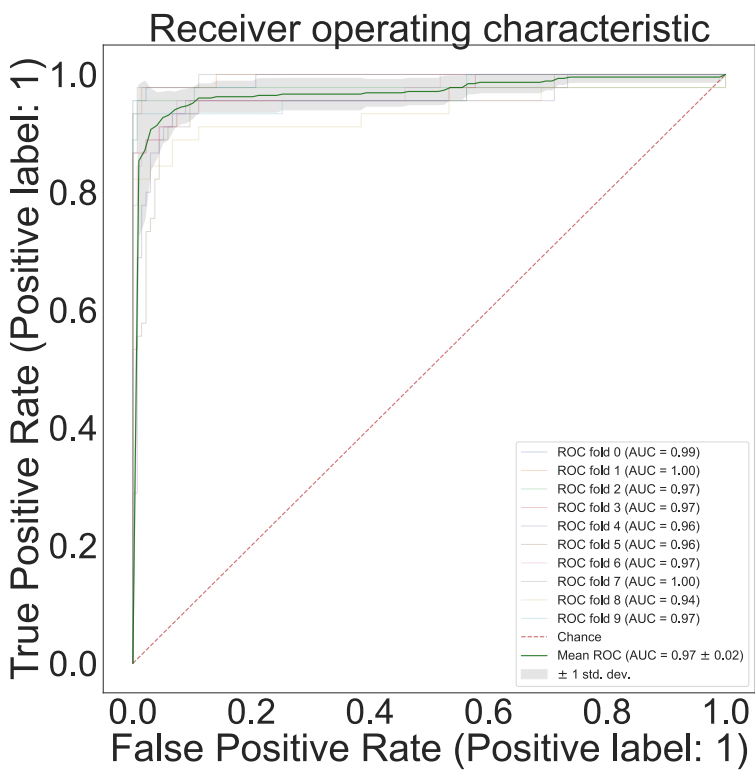
Prediction of gut ecosystem (SVM)



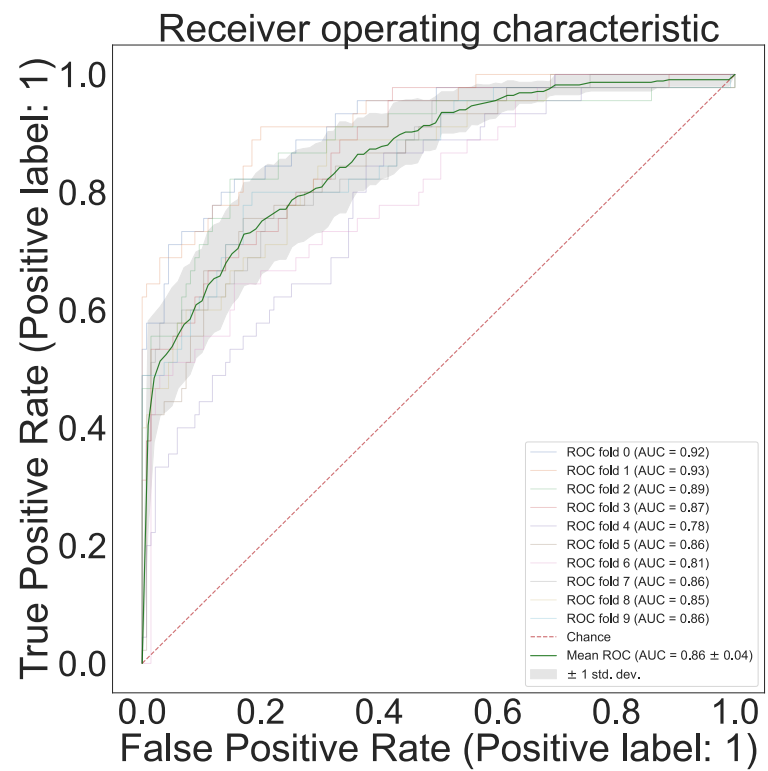
➔ - Noise  
- Cross validation ➔ Ecosystem?

Up to 3 features = training

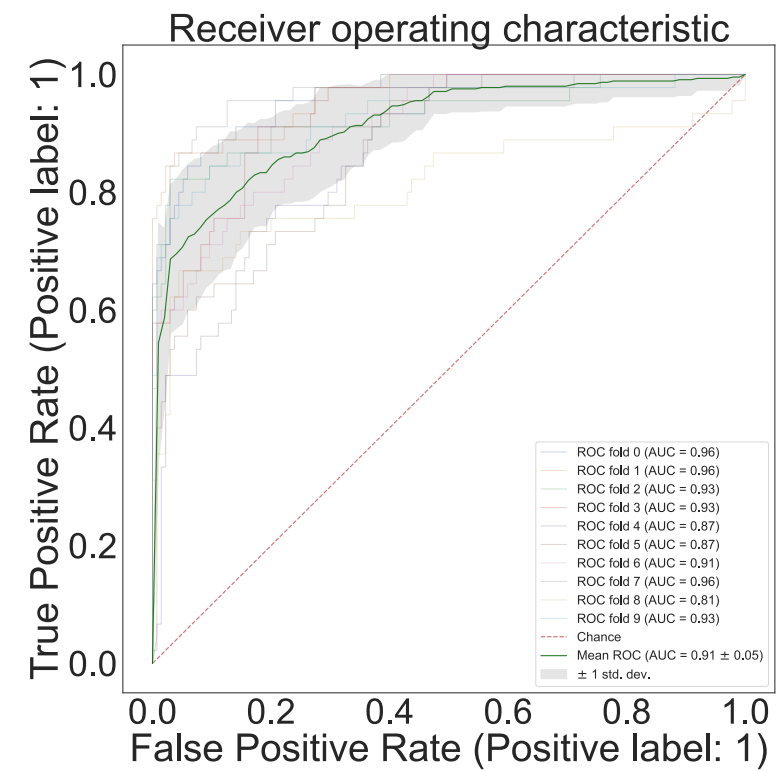
Up to 4



Only competition



Only cooperation



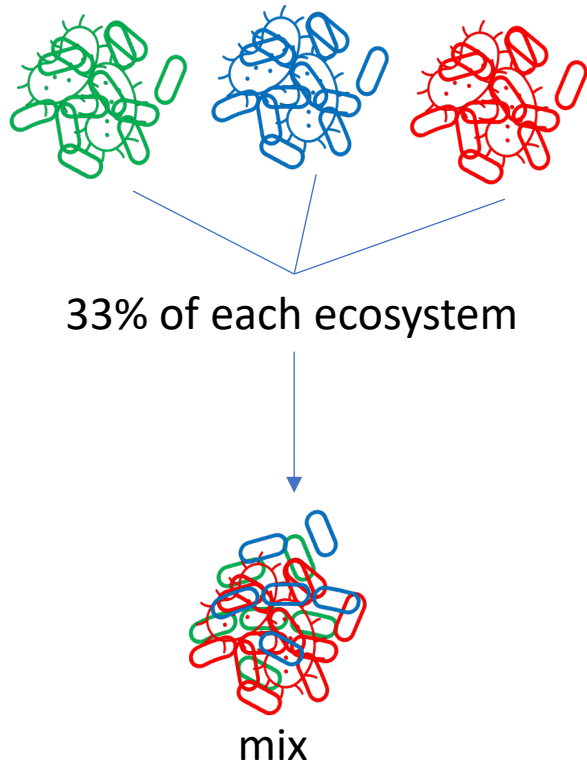
Both

Competition score seems to be enough for predicting ecosystem



## ➤ Benchmarks for testing scores

Do scores differ between ecosystems ?



Cooperation and competition scores significantly differ between non-realistic and *ecosystem-consistent* communities



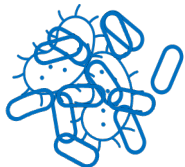
INRAE

## ➤ Benchmarks for testing scores

Scores in function of the ecosystem



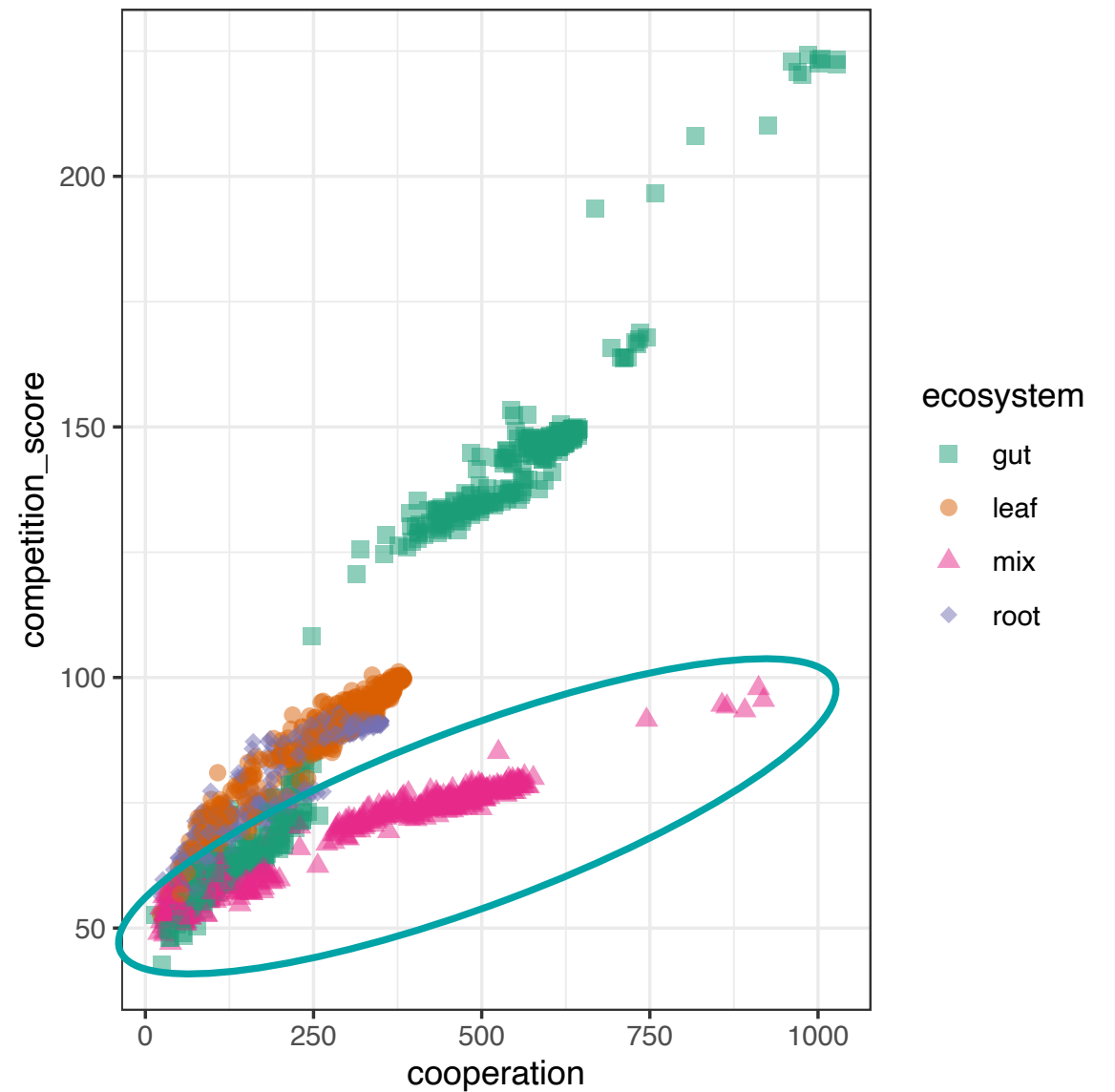
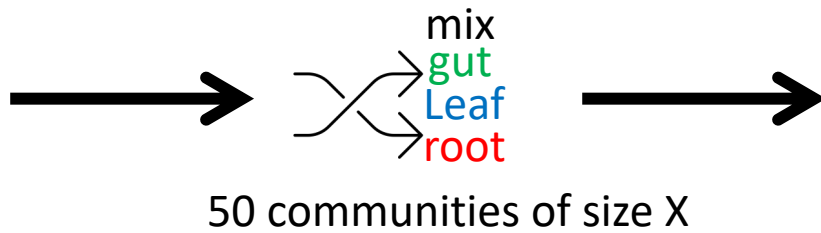
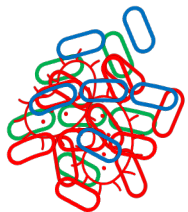
gut



Leaf



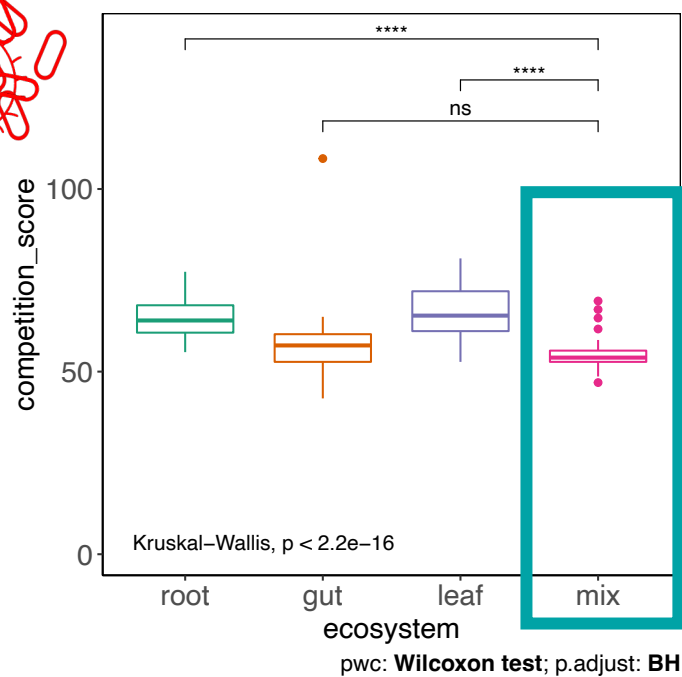
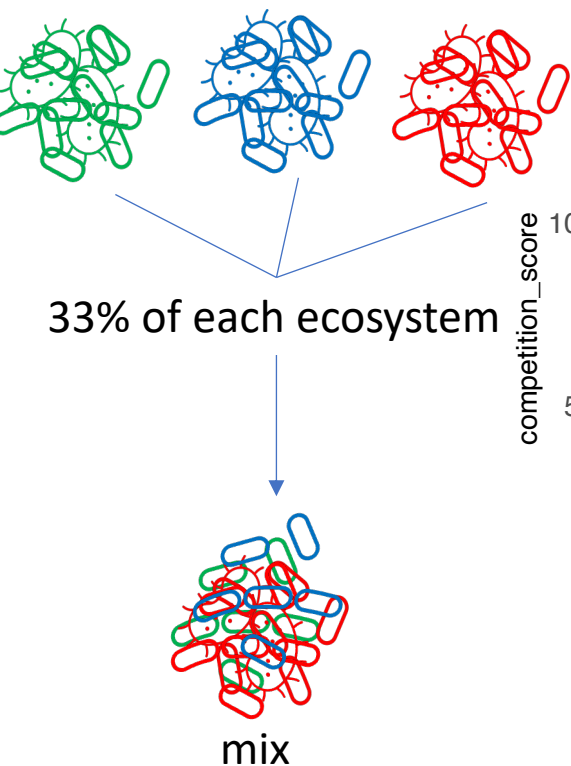
mix



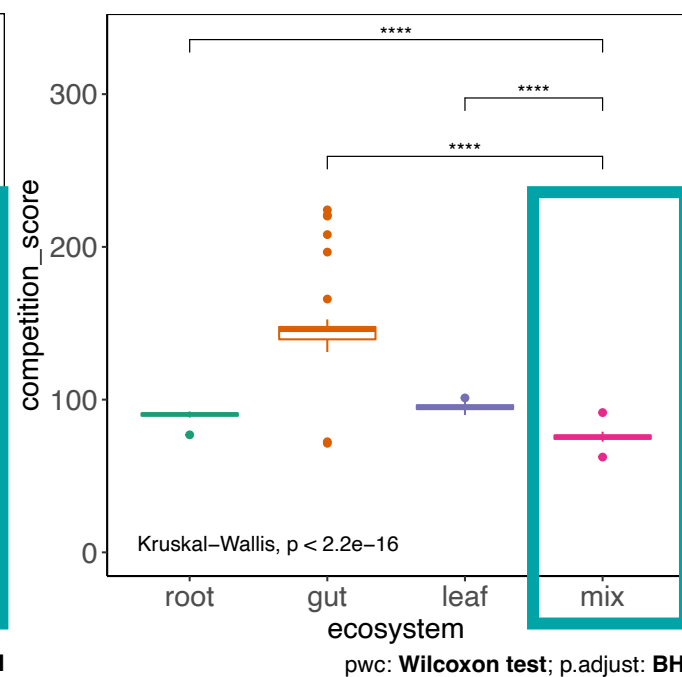
Cooperation and competition scores significantly differ between non-realistic and *ecosystem-consistent* communities

# ➤ Benchmarks for testing scores

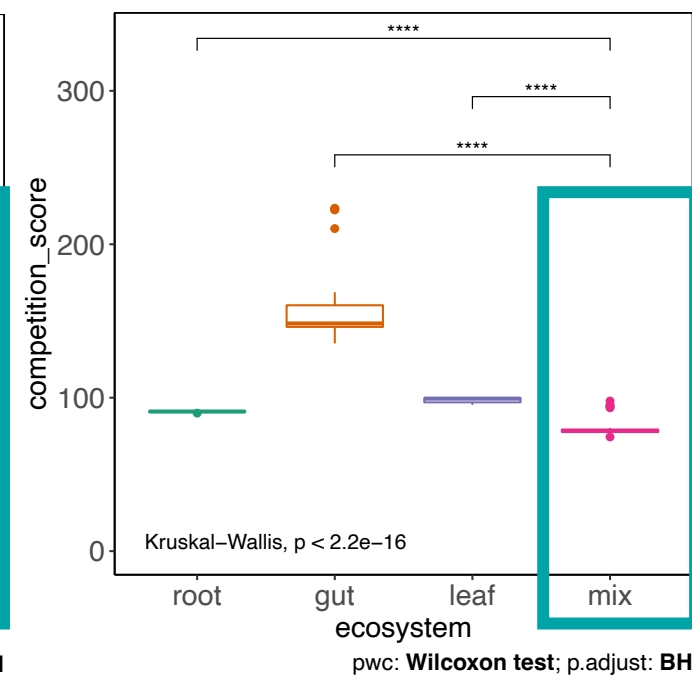
Do competition score differ between ecosystems ?



Size = 3



Size = 75



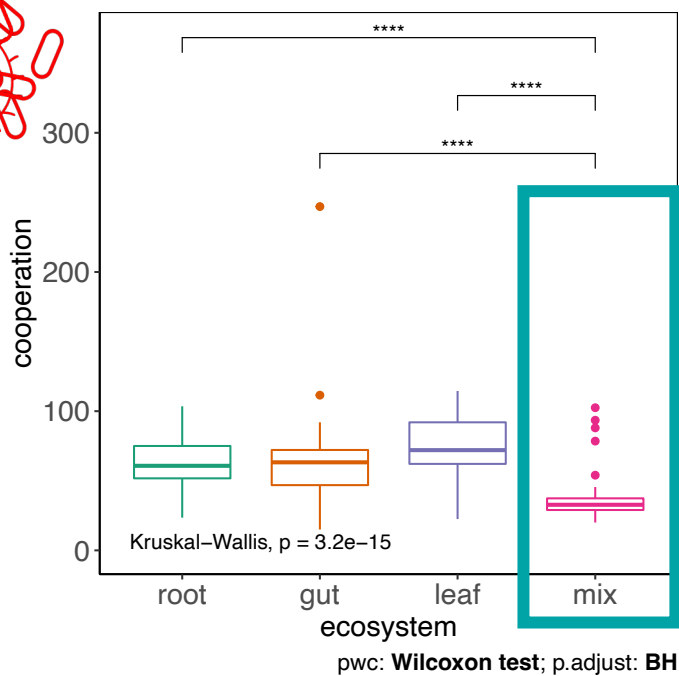
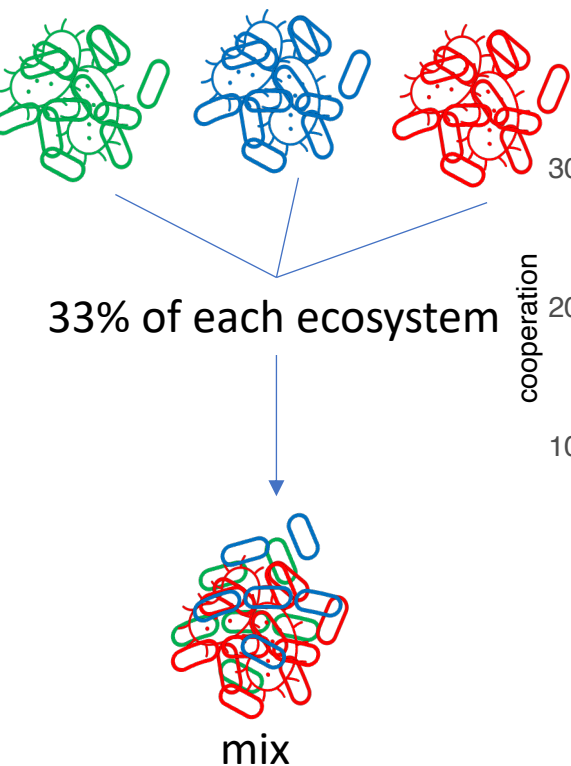
Size = 150

Cooperation and competition scores significantly differ between non-realistic and *ecosystem-consistent* communities

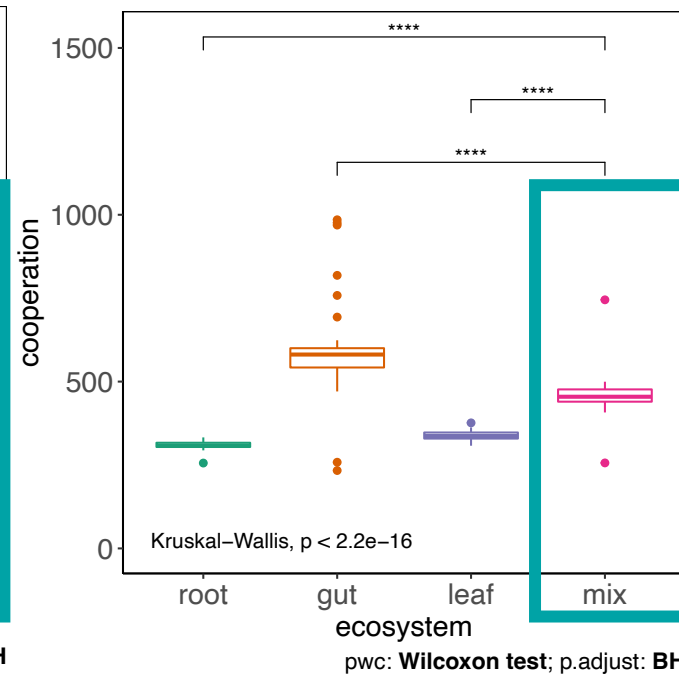


# ➤ Benchmarks for testing scores

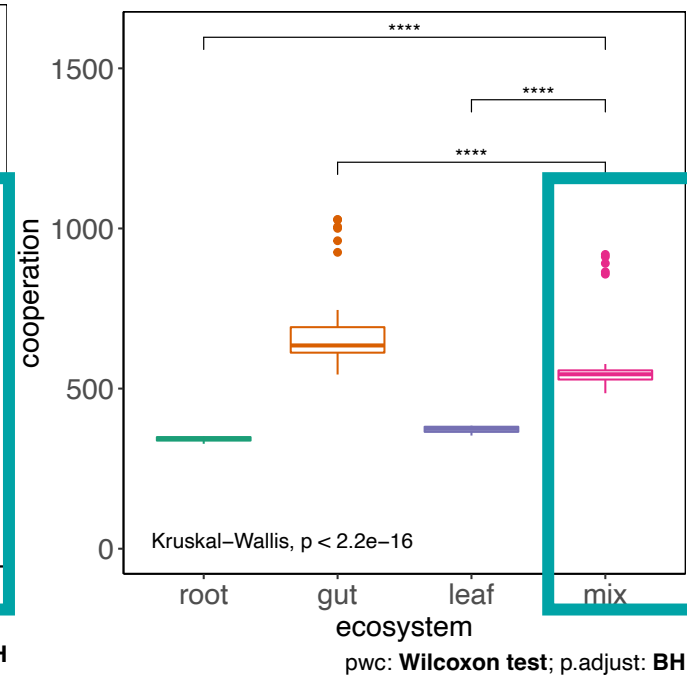
Do cooperation score differ between ecosystems ?



Size = 3



Size = 75

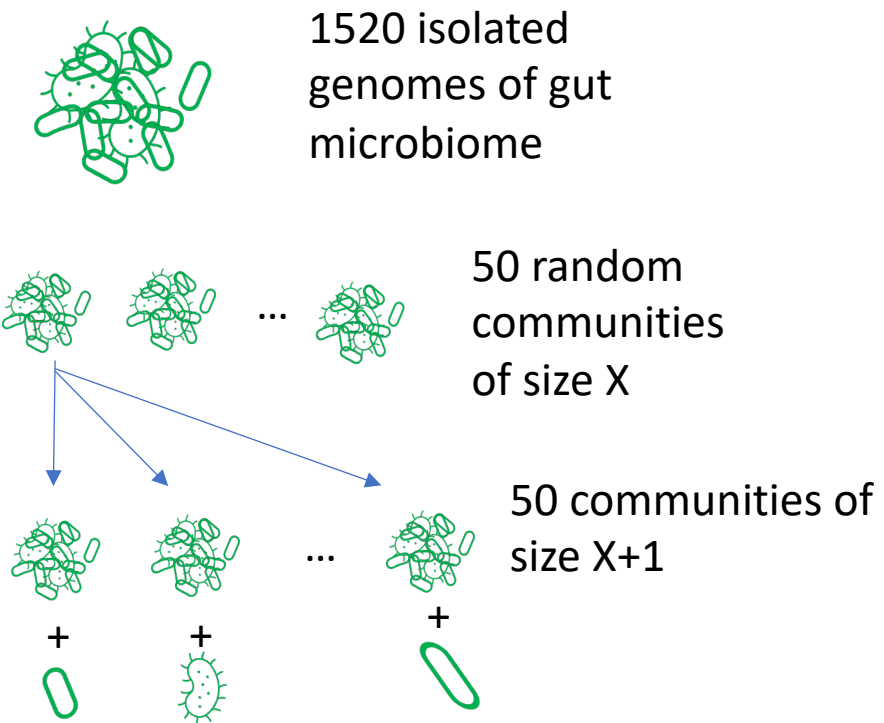


Size = 150

Cooperation and competition scores significantly differ between non-realistic and *ecosystem-consistent* communities

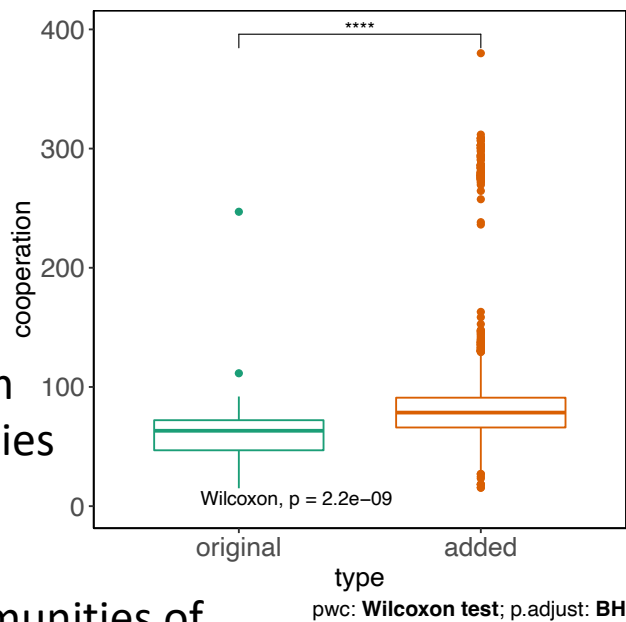
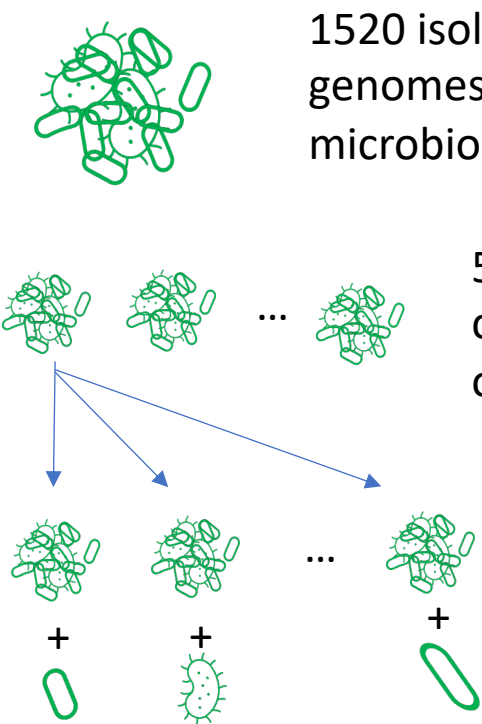
## ➤ Benchmarks for testing scores

Added-value of adding a bacteria in community

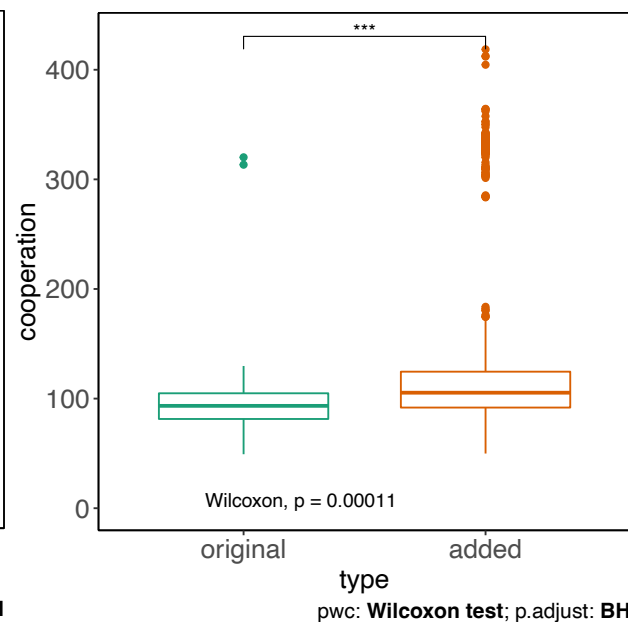


# ➤ Benchmarks for testing scores

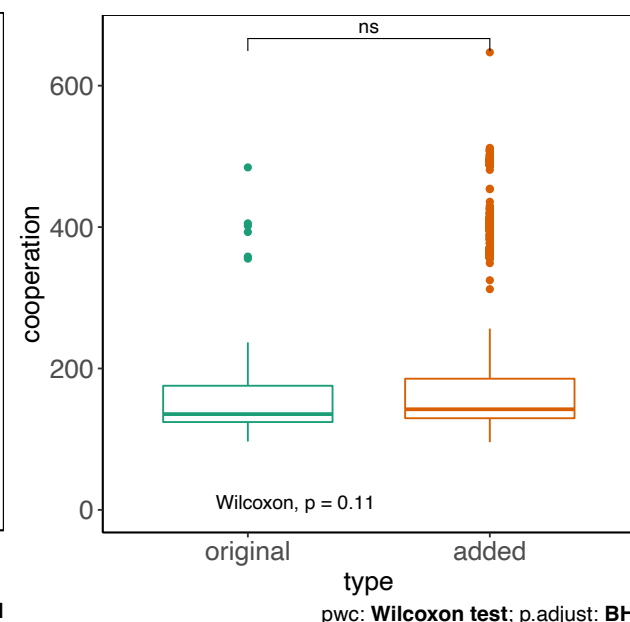
Added-value of adding a bacteria in community based on cooperation score



Size = 3



Size = 5



Size = 10

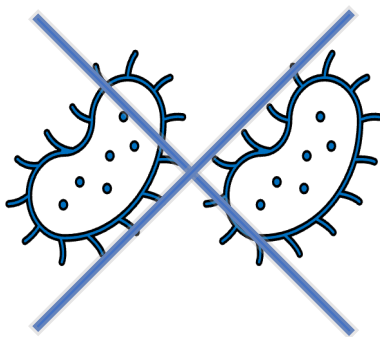
The larger is the community the less the community is disturbed by another species

# ➤ Conclusion

Tradeoff



Scalability



Pairwise



Resilience



Potentials



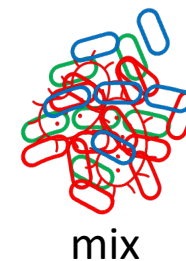
gut



Leaf



Root

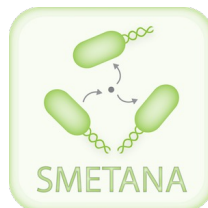


mix

Perspective



Soil



SMETANA



micom

INRAE

Reasoning approaches for the characterization of cooperation and competition in large-scale microbial communities

November 17 2022 / [maxime.lecomte@inrae.fr](mailto:maxime.lecomte@inrae.fr) / Maxime Lecomte 3<sup>rd</sup> PhD student



INRAE



- David Sherman
- Clémence Frioux
- Simon Labarthe
- Coralie Muller

- Hélène Falentin

Thanks for your attention



INRAE

Reasoning approaches for the characterization of cooperation and competition in large-scale microbial communities

November 17 2022 / [maxime.lecomte@inrae.fr](mailto:maxime.lecomte@inrae.fr) / Maxime Lecomte 3<sup>rd</sup> PhD student

# ➤ Benchmarks for testing scores

Scores in function the community size



gut



Leaf

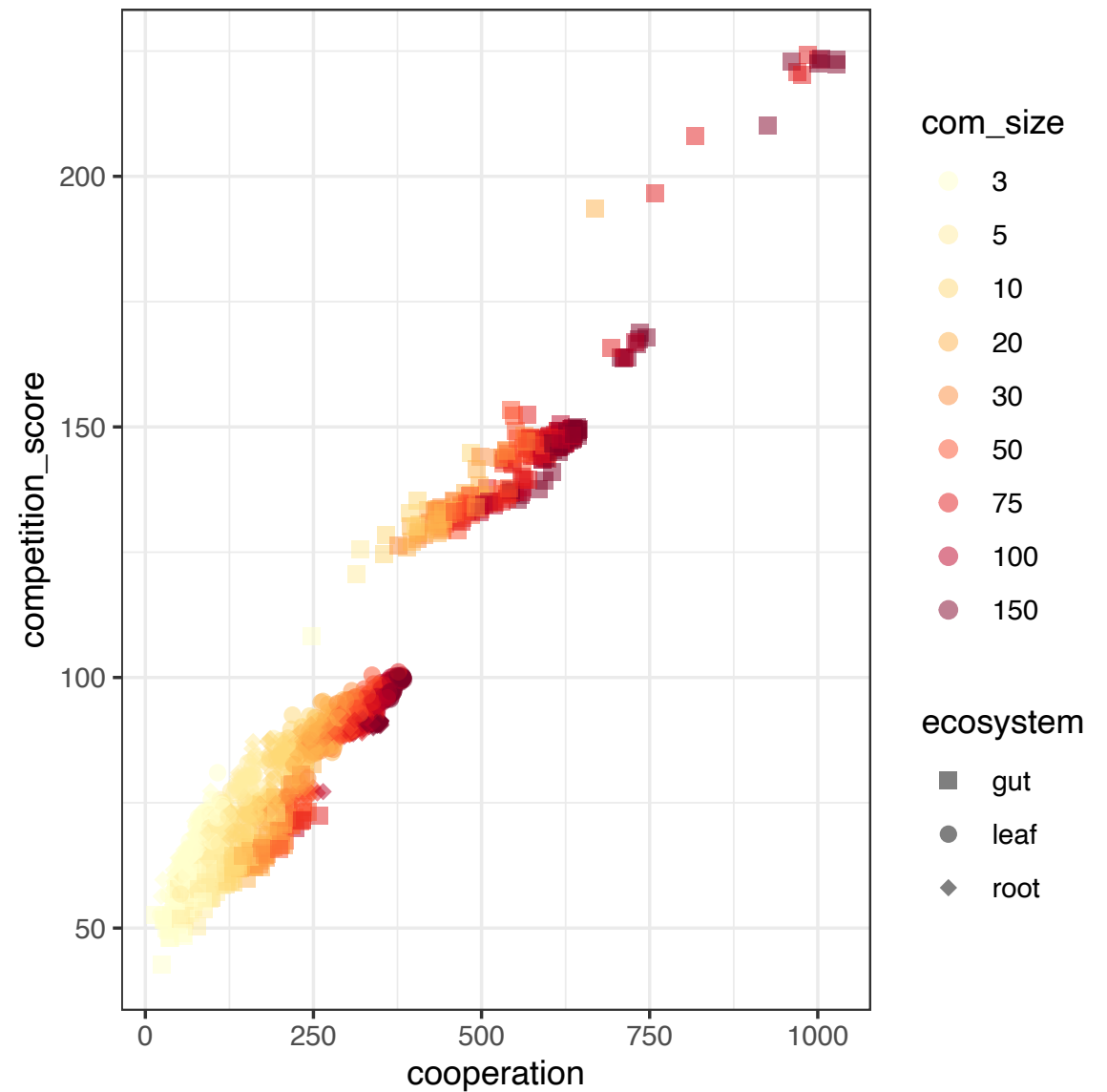


root



Reference genomes of cultivable species from 3 ecosystems

Community size is not the main actor in the score variations



Zou, Y., et al, 2019, *Nature Biotechnology*