



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

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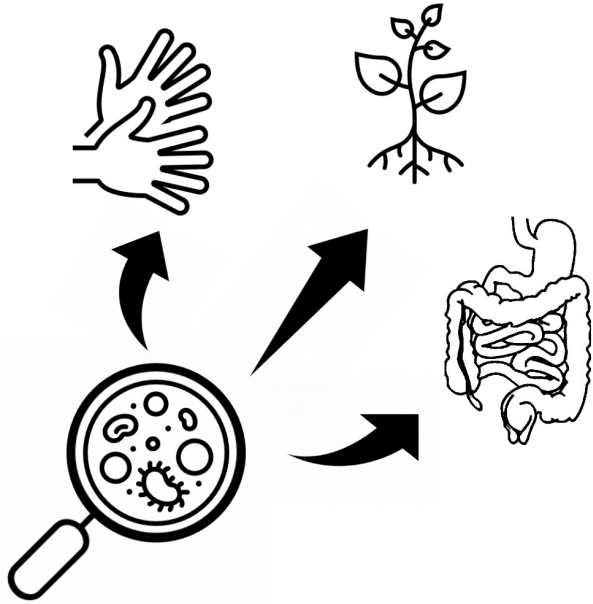
➤ Reasoning approaches for the characterization of cooperation and competition in large-scale microbial communities

Maxime Lecomte – David Sherman – Hélène Falentin – Clémence Frioux

GT-BIOSS NANTES November, 17 2022

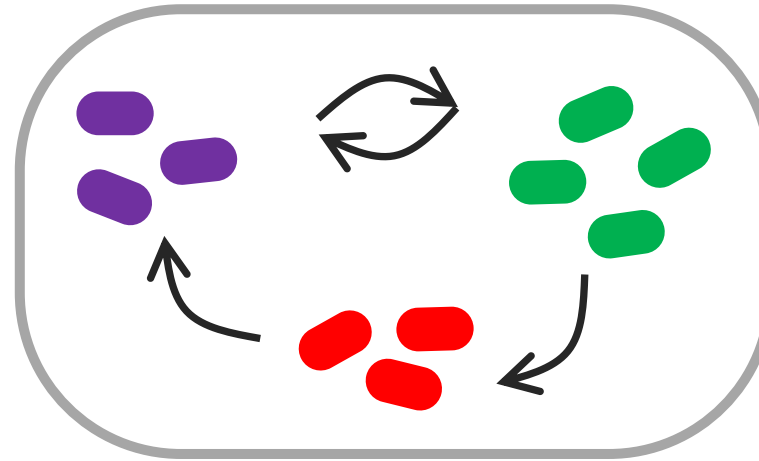
> Motivation

Bacterial communities ?



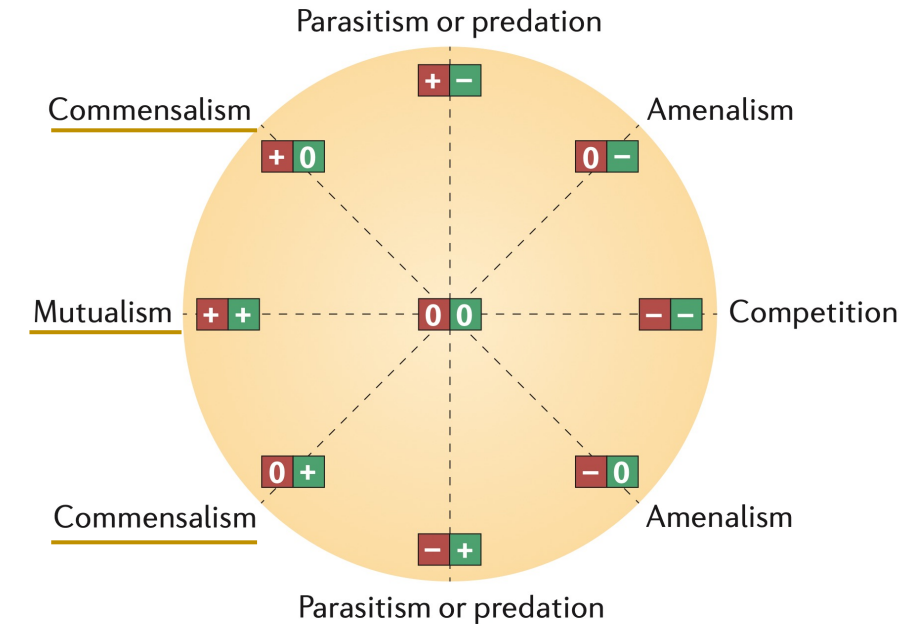
Microbes are essential in ecosystems

System biology



Bacterial interactions as a key mechanism

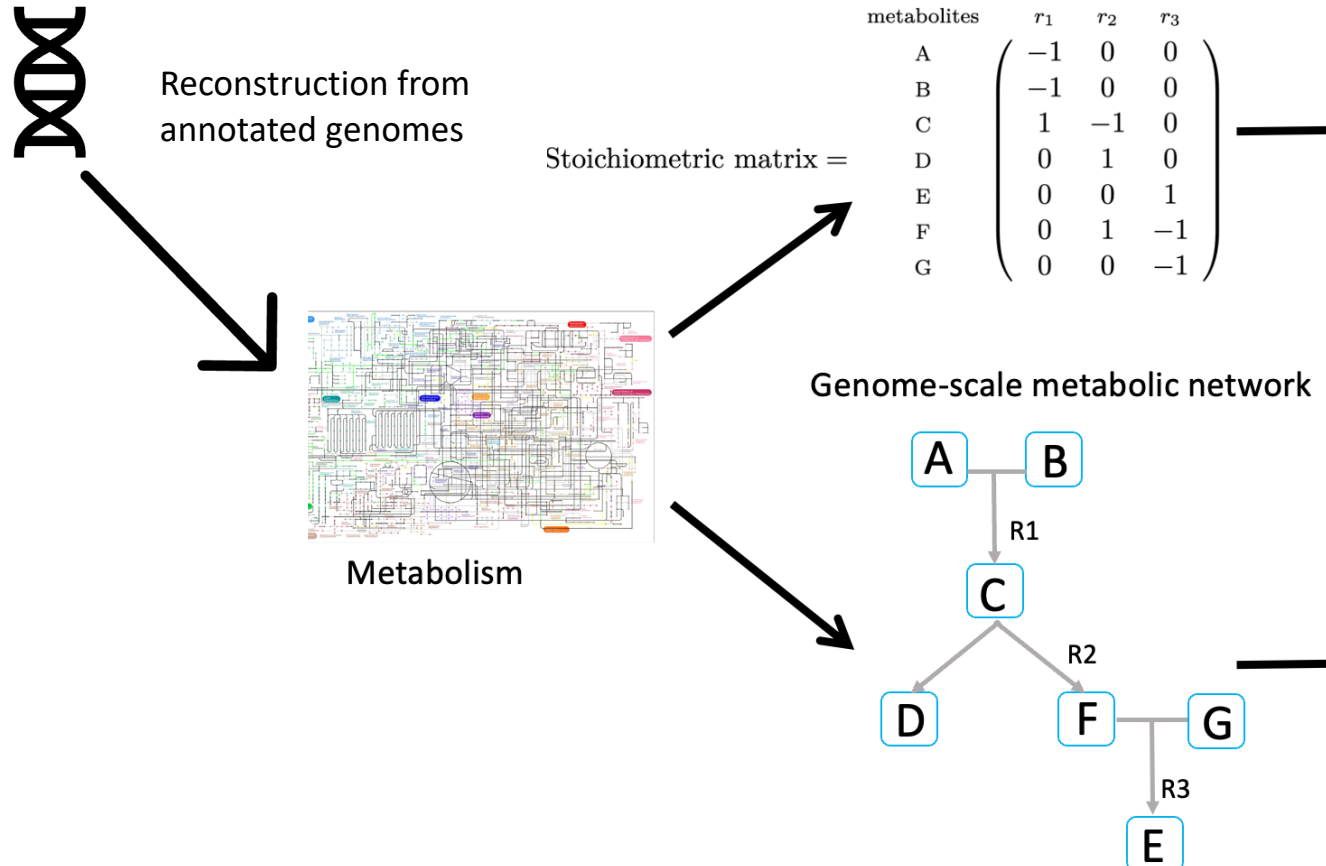
Interaction types



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



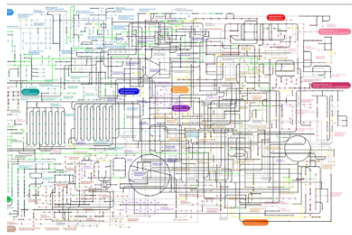
Reconstruction from
annotated genomes

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

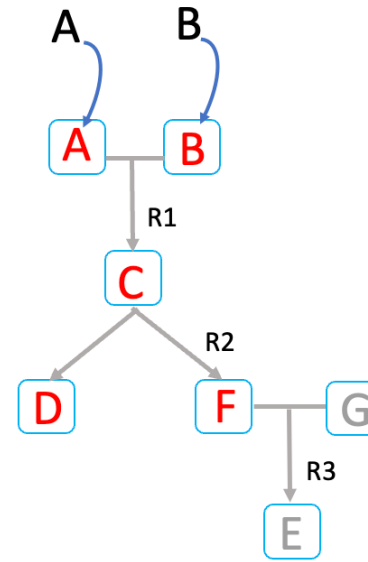
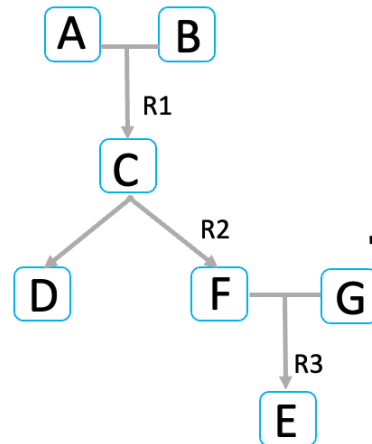
$$\begin{aligned} &\max v_{growth} \\ &\text{such that } S.v = 0 \\ &\text{and } v_{min} \leq v \leq v_{max} \end{aligned}$$

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



Metabolism

Genome-scale metabolic network



Metabolite scope from the A,B in
the environment

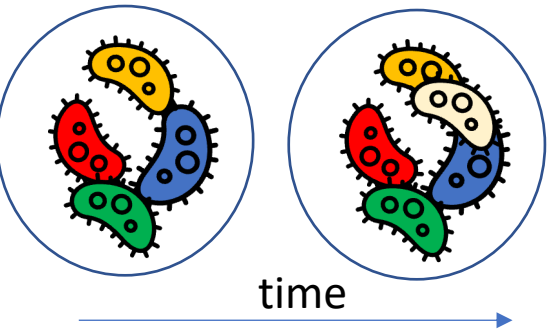
Discrete method

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

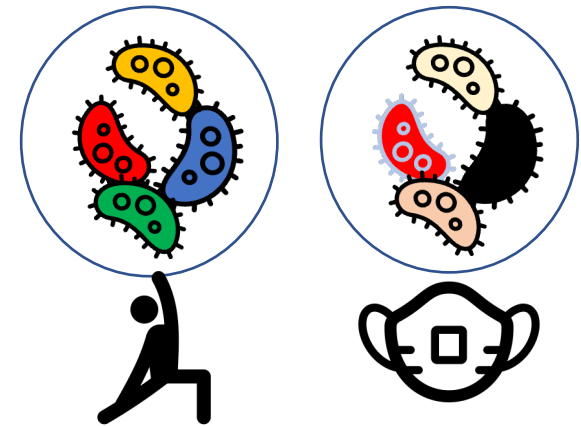
➤ Goal : Identify cooperation and competition potential in large scale bacterial communities

Cooperation and competition potential

Longitudinal analysis



Cross sectional analysis



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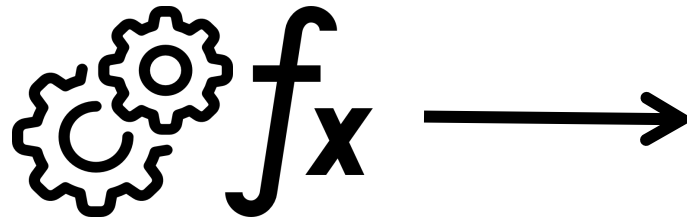
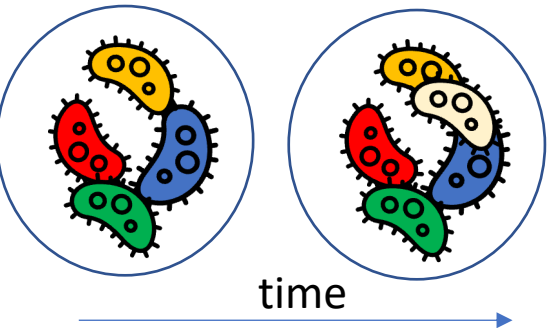
Reasoning approaches for the characterization of cooperation and competition in large-scale microbial communities

November 17 2022 / maxime.lecomte@inrae.fr / Maxime Lecomte 3rd PhD student

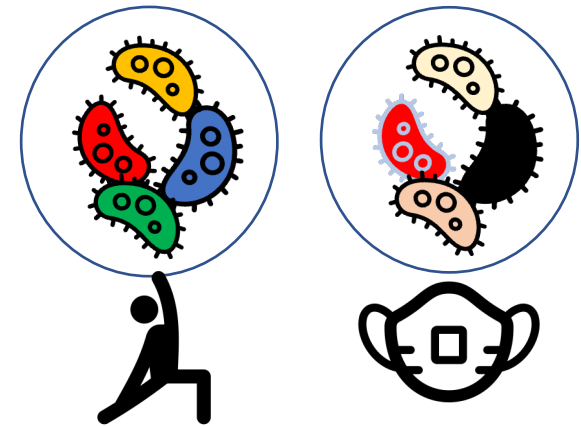
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Cooperation and competition potential

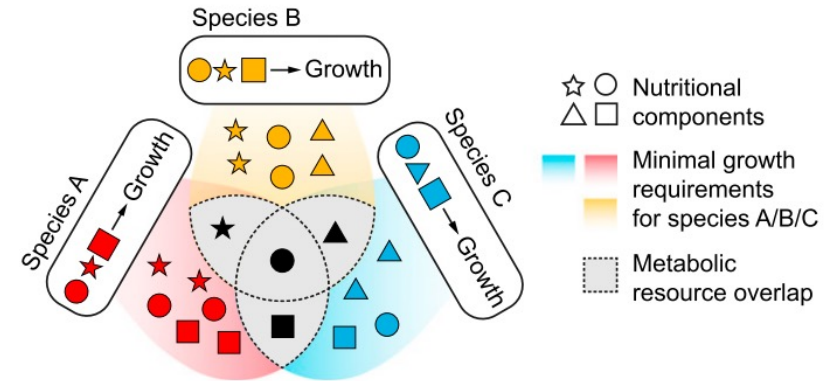
Longitudinal analysis



Cross sectional analysis



Nutrient point of view

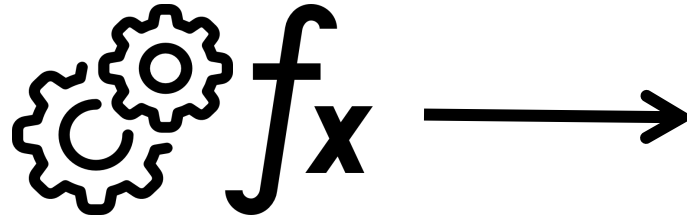
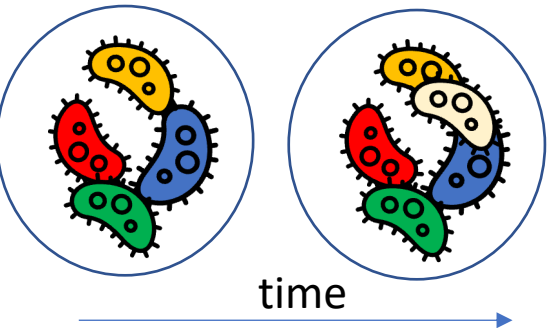


Competition potentials

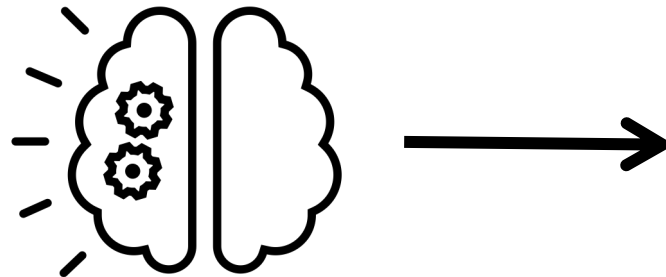
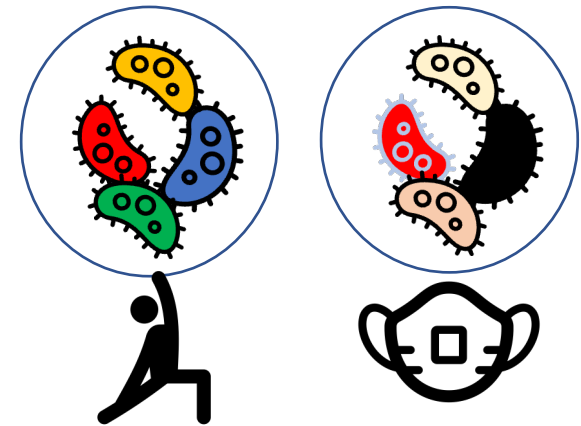
➤ Goal : Identify cooperation and competition potential in large scale bacterial communities

Cooperation and competition potential

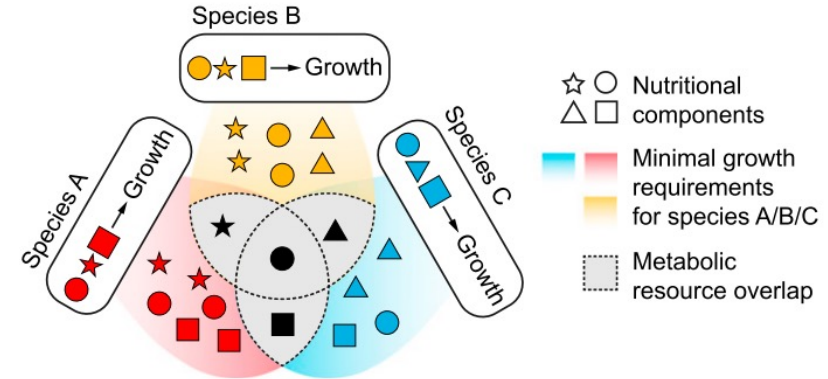
Longitudinal analysis



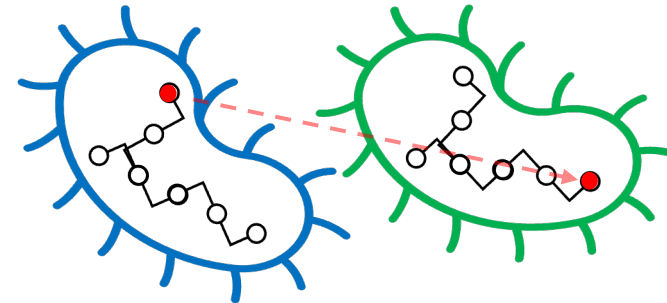
Cross sectional analysis



Nutrient point of view



Competition potentials



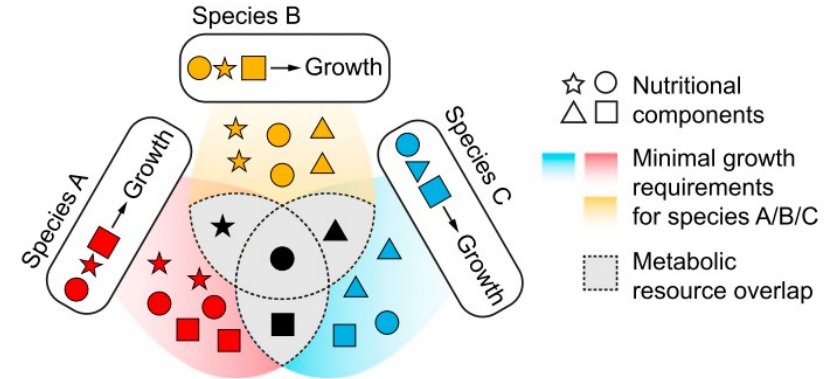
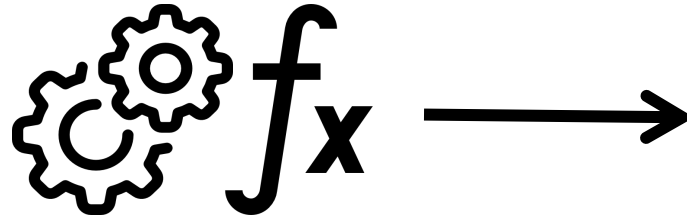
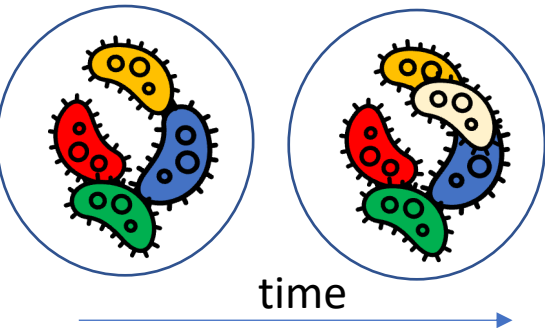
Cooperation potentials

Either numerical or discrete methods highlight cooperation and competition potentials

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

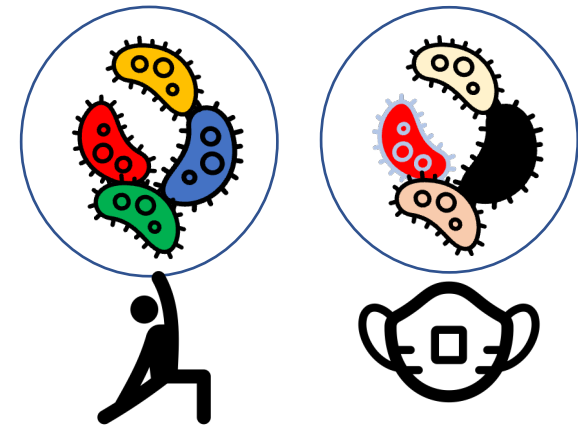
Scale-up to large scale bacterial communities

Longitudinal analysis



Community size up to 18

Cross sectional analysis

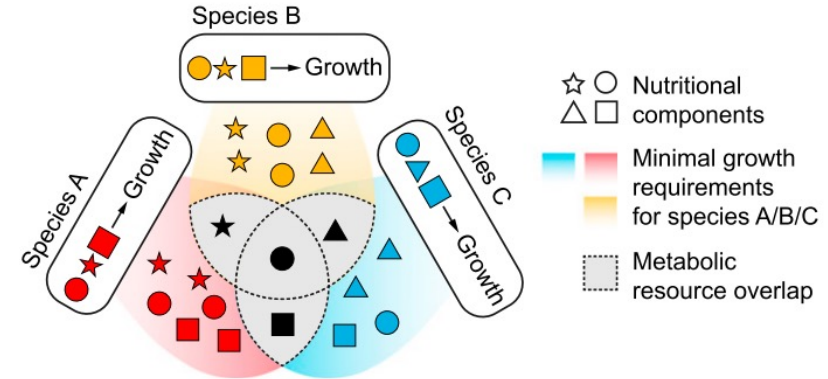
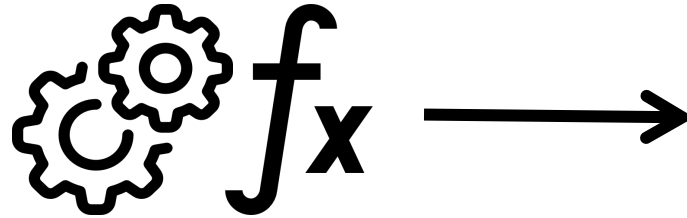
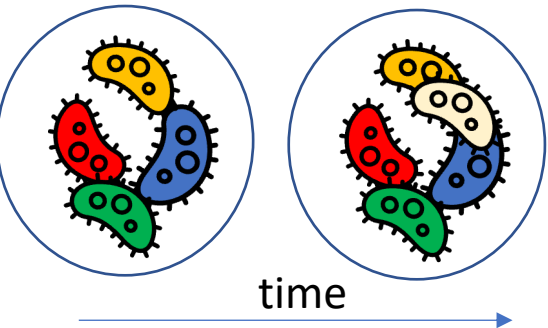


Cost in computational time

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

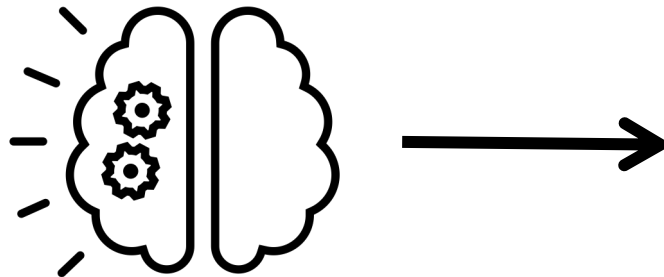
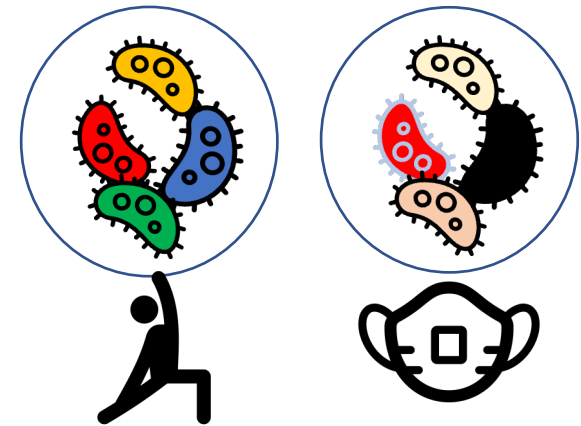
Scale-up to large scale bacterial communities

Longitudinal analysis



Community size up to 18

Cross sectional analysis



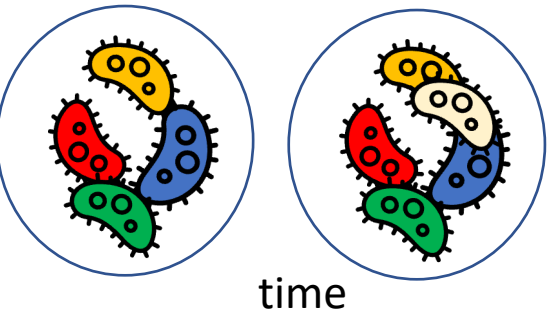
Cost in computational time

Pairwise

Not limited by the community size

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

Longitudinal analysis



Characterize community

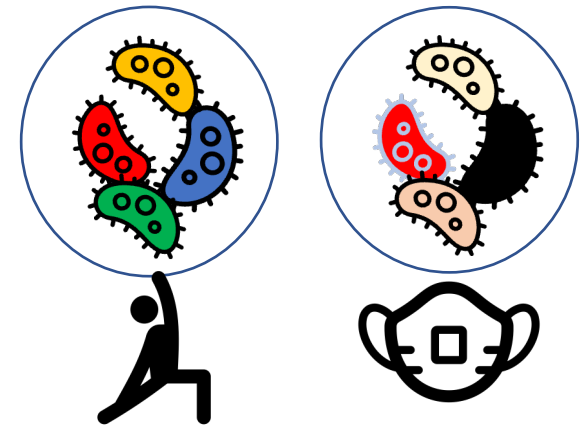


150 bacteria

Pairwise analysis

$(150 * (150-1))/2 = 11\,375$ combinations

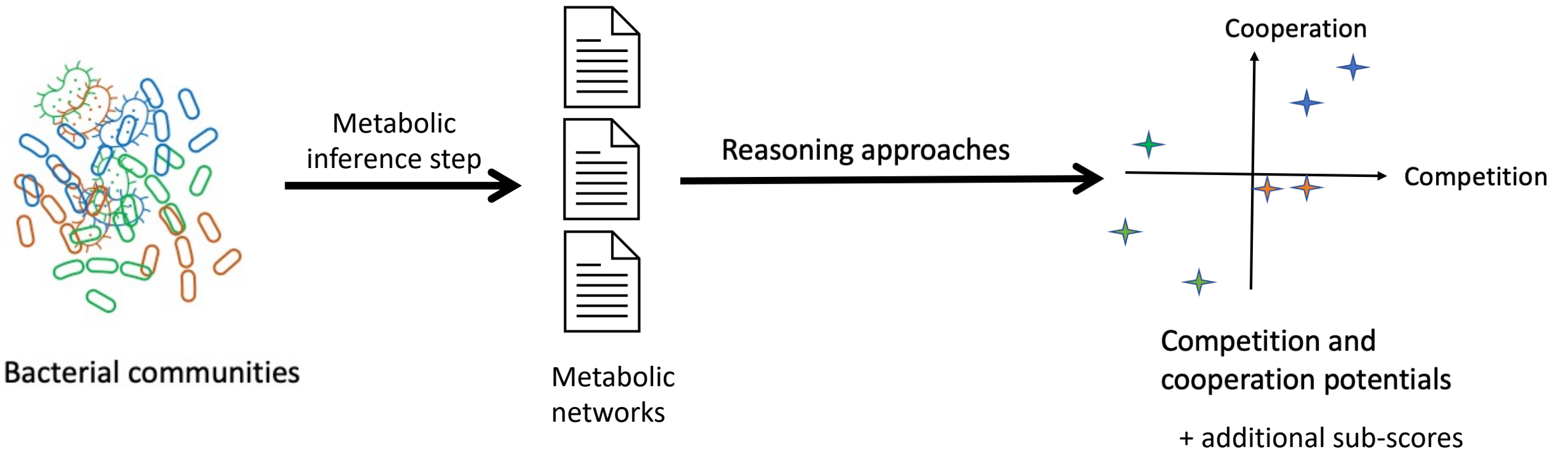
Cross sectional analysis



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

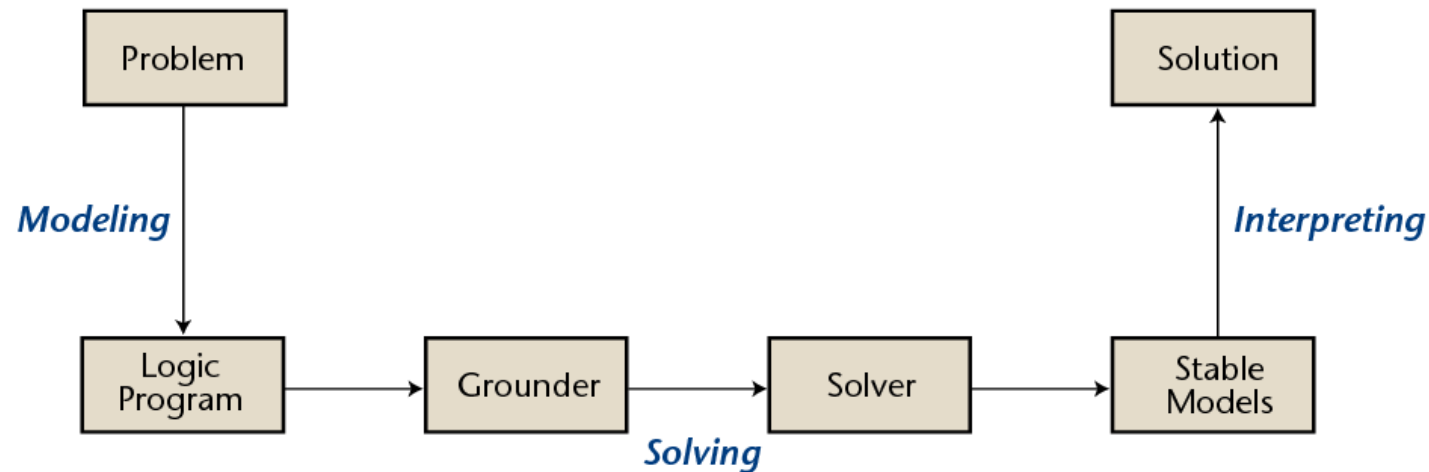
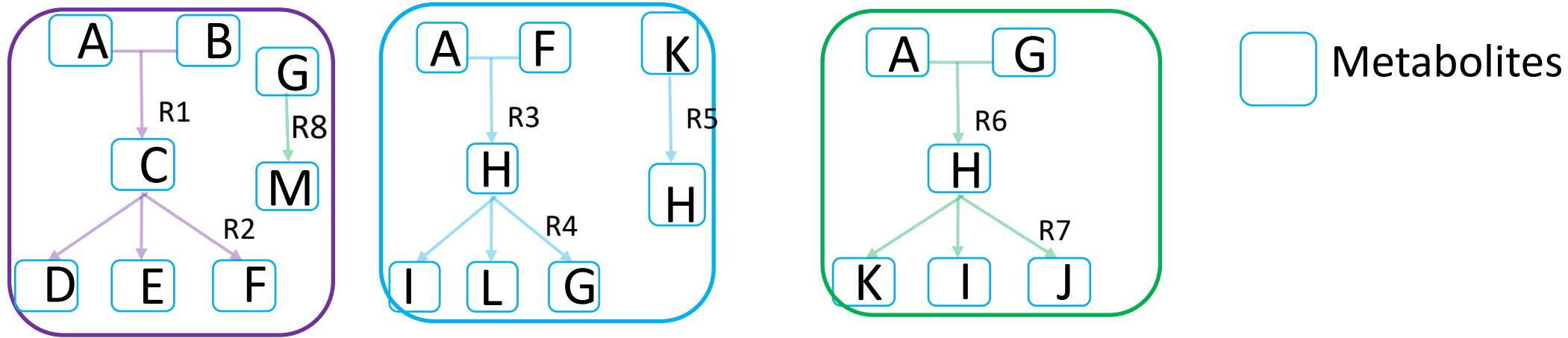


Figure 1. The Work Flow of Answer Set Programming.

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

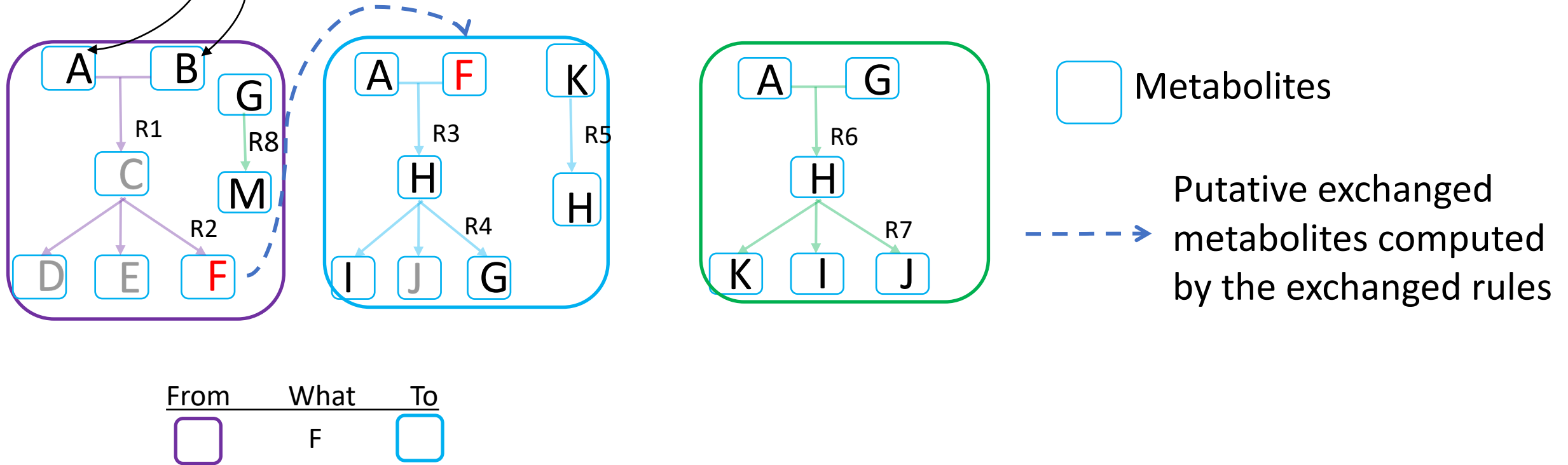
Seed : A,B



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

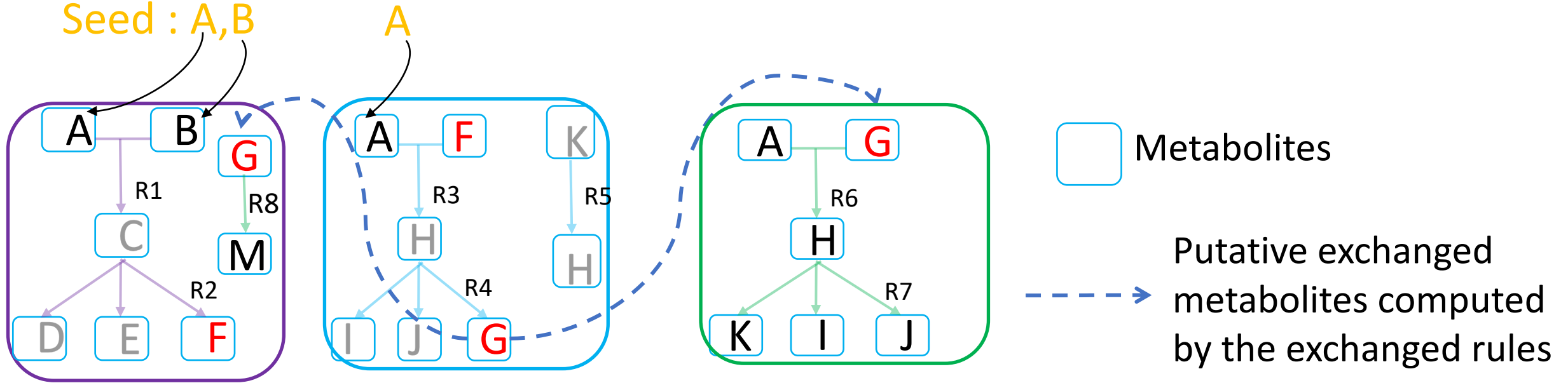
➤ Cooperation potential based on exchanged metabolites using ASP

Seed : A,B



➤ Cooperation potential based on exchanged metabolites using ASP

Seed : A, B



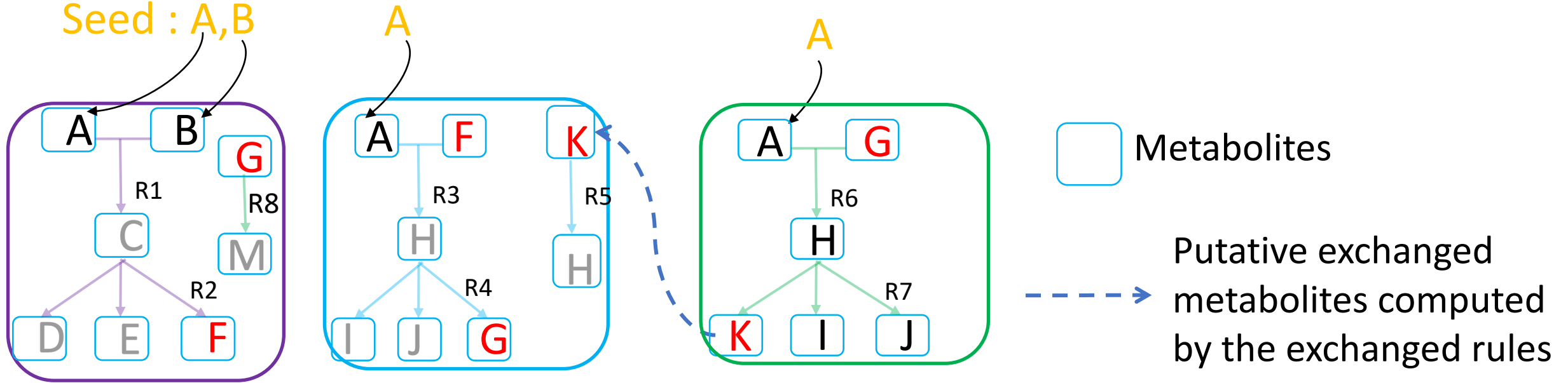
From	What	To
	F	
	G	
	G	



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➤ Cooperation potential based on exchanged metabolites using ASP

Seed : A,B

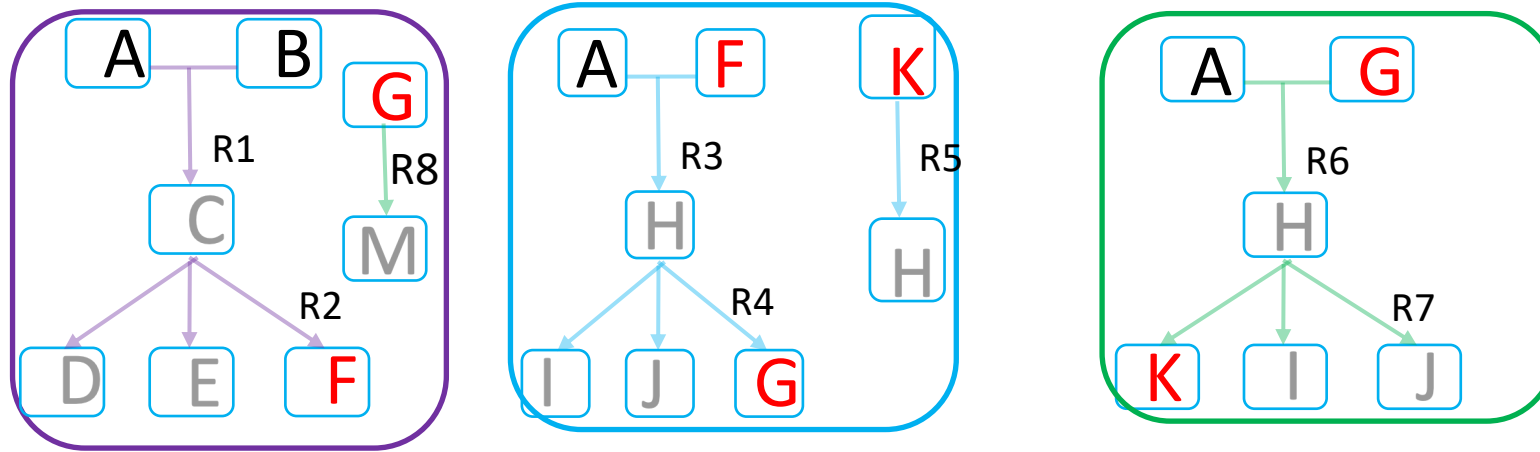


From	What	To
<input type="checkbox"/>	F	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	G	<input type="checkbox"/>
<input type="checkbox"/>	K	<input type="checkbox"/>

INRAE

➤ Exponential bonus (python)

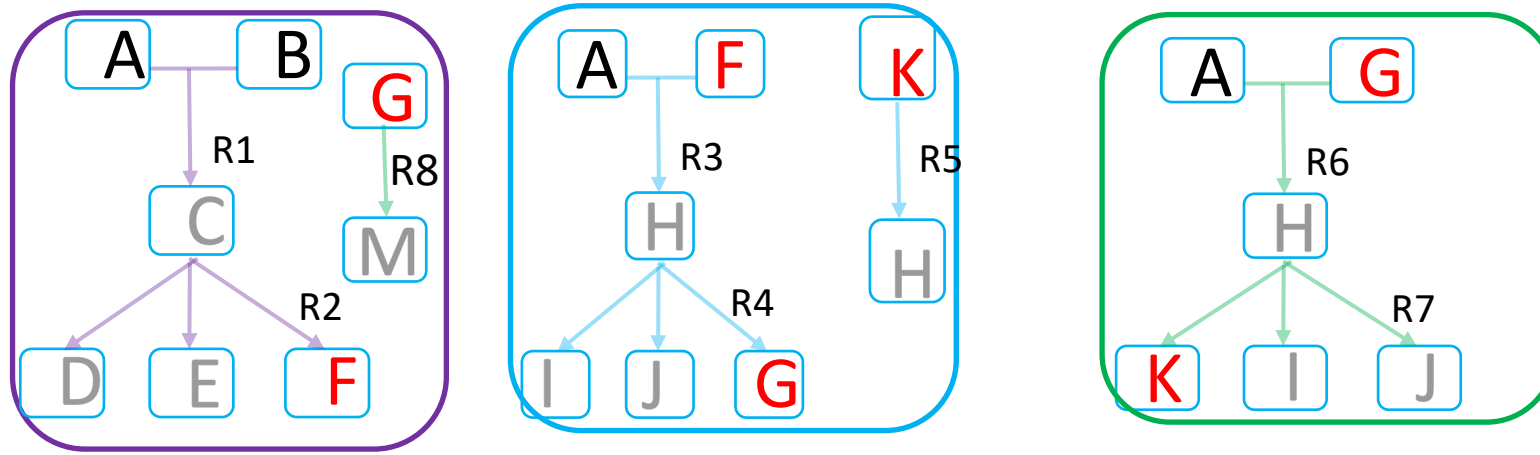
hypothesis : each species contributes differently



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"/>



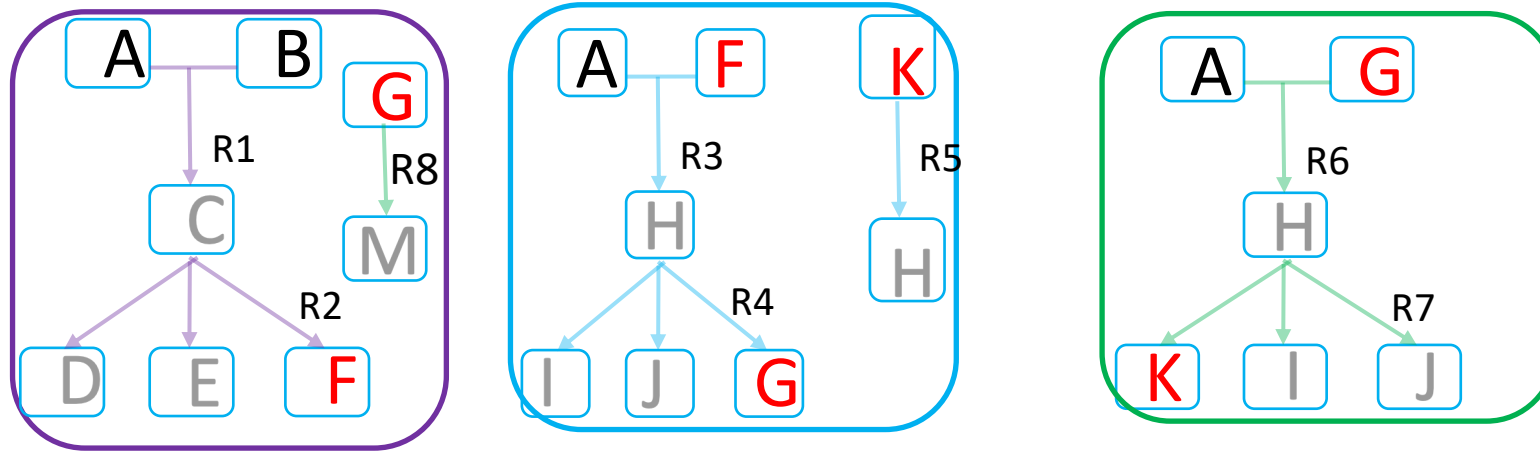
$$cooperation = \sum_{i=1}^m \sum_{k=2}^n 1 + 2^{-(k-1)}$$

Number of metabolites

Number of different
producers / consumers

➤ 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"/>



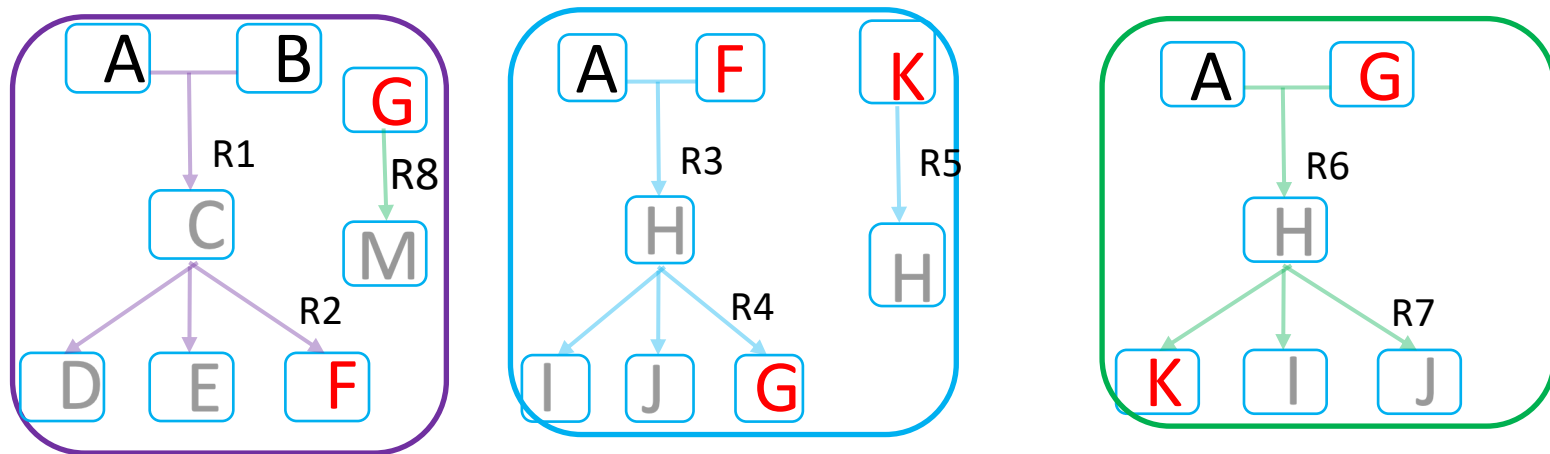
$$cooperation = \sum_{i=1}^m \sum_{k=2}^n 1 + 2^{-(k-1)}$$

Number of metabolites

Number of different
producers / consumers

➤ Exponential bonus (python)

hypothesis : each species contributes differently



Metabolites	Producers	consumers
F	1	1
G	1	$1 + 2^1 = 1.5$

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"/>



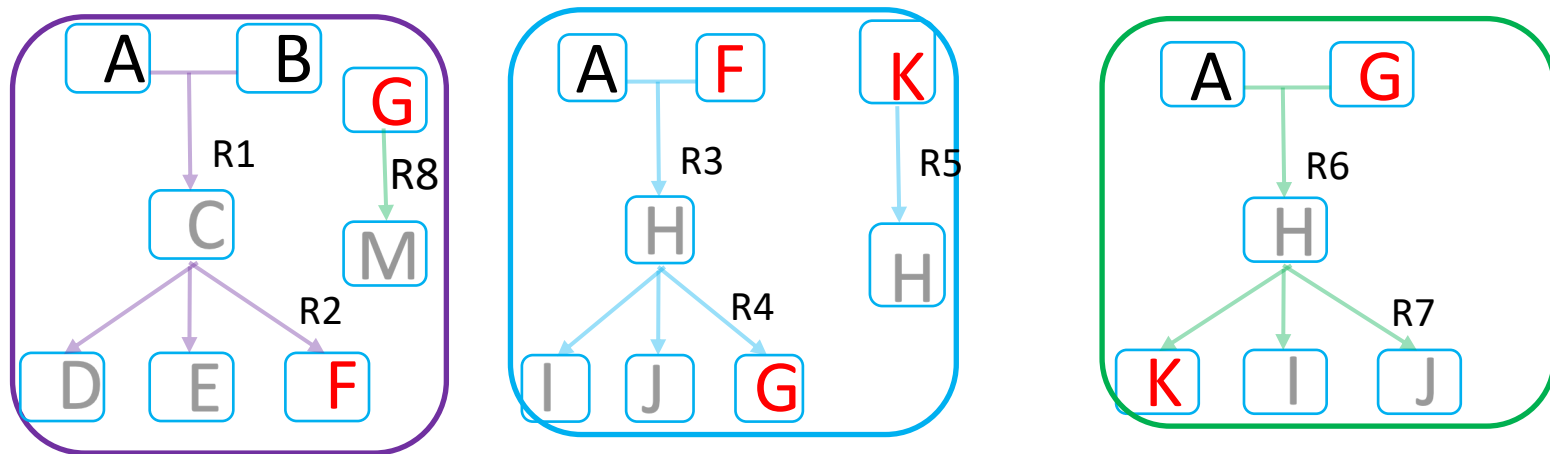
$$cooperation = \sum_{i=1}^m \sum_{k=2}^n 1 + 2^{-(k-1)}$$

Number of metabolites

Number of different
producers / consumers

➤ Exponential bonus (python)

hypothesis : each species contributes differently



Metabolites	Producers	consumers
F	1	1
G	1	$1 + 2^1 = 1.5$
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"/>



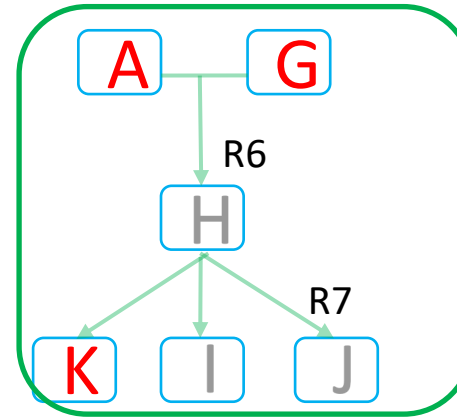
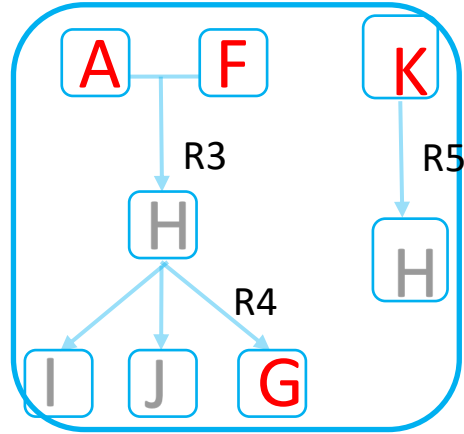
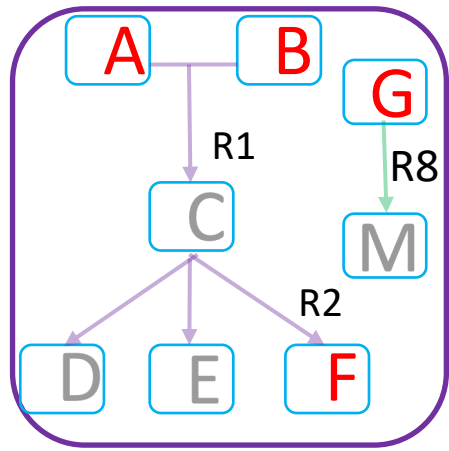
$$cooperation = \sum_{i=1}^m \sum_{k=2}^n 1 + 2^{-(k-1)}$$

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



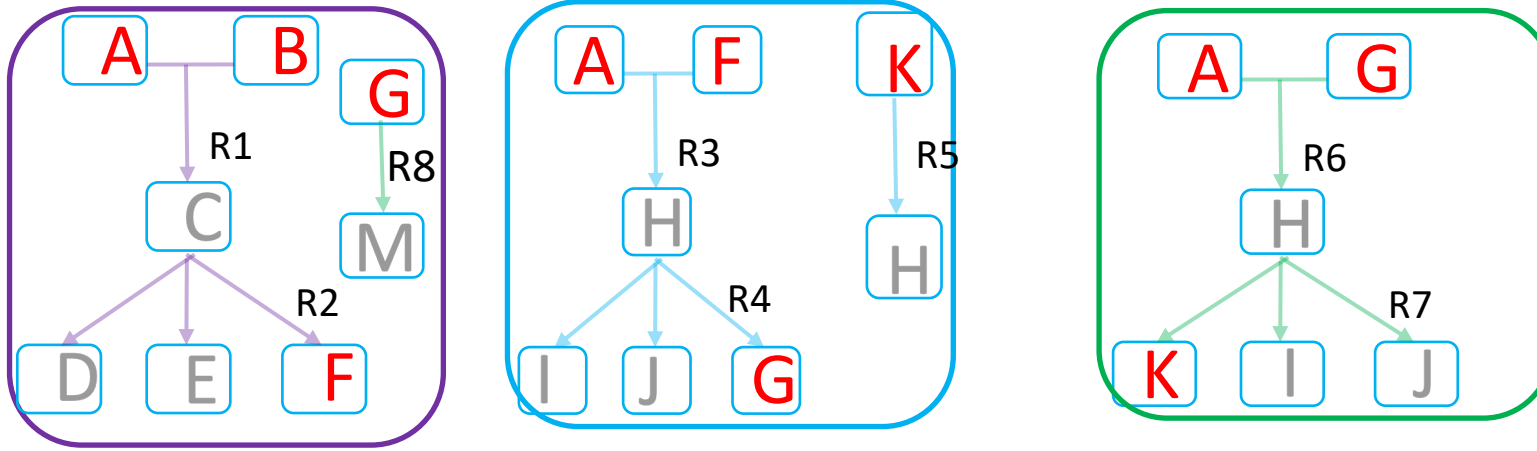
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November 17 2022 / maxime.lecomte@inrae.fr / Maxime Lecomte 3rd PhD student

➤ Calculation of the competition potential (python)

Seed : A,B



A,B,F

A,B,G,K

A,G,K



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



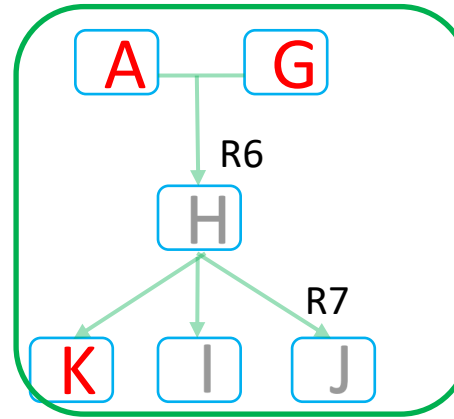
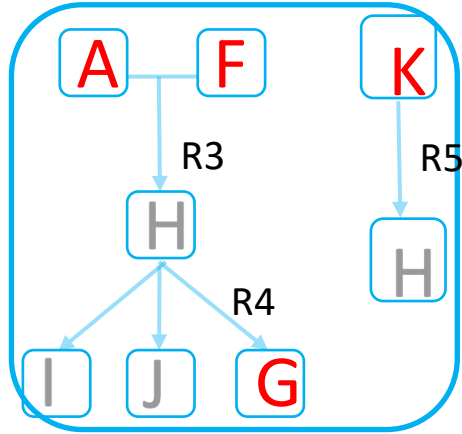
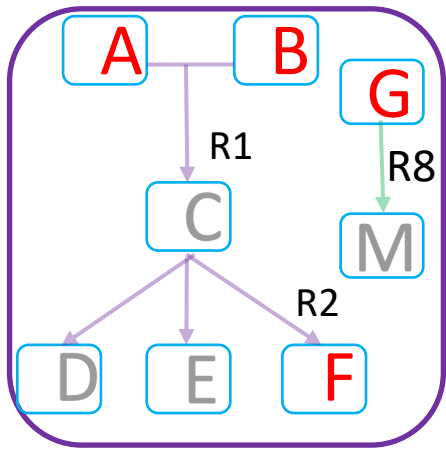
INRAE

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➤ Calculation of the competition potential (python)

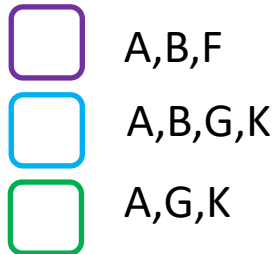
Seed : A,B



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

Metabolites

Number of
consumers

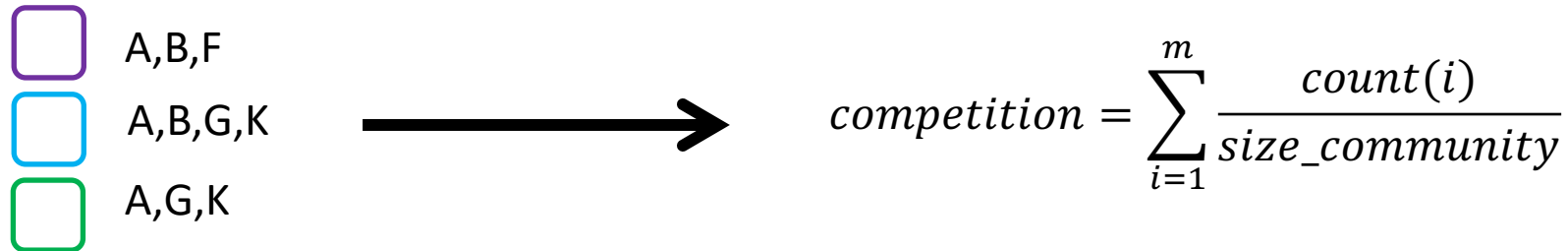
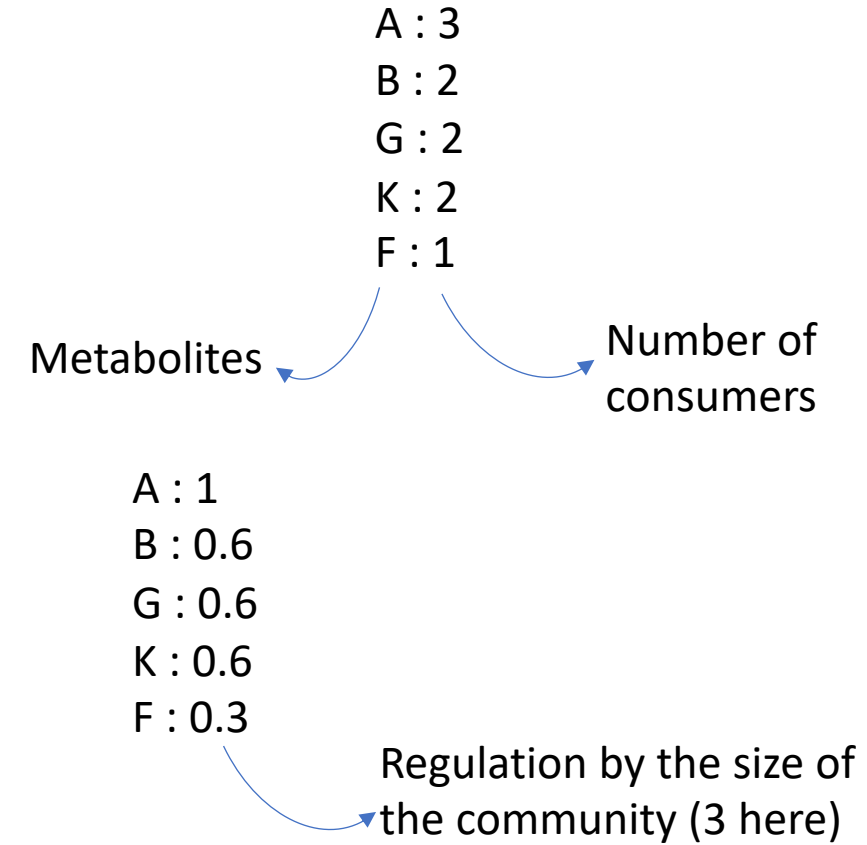
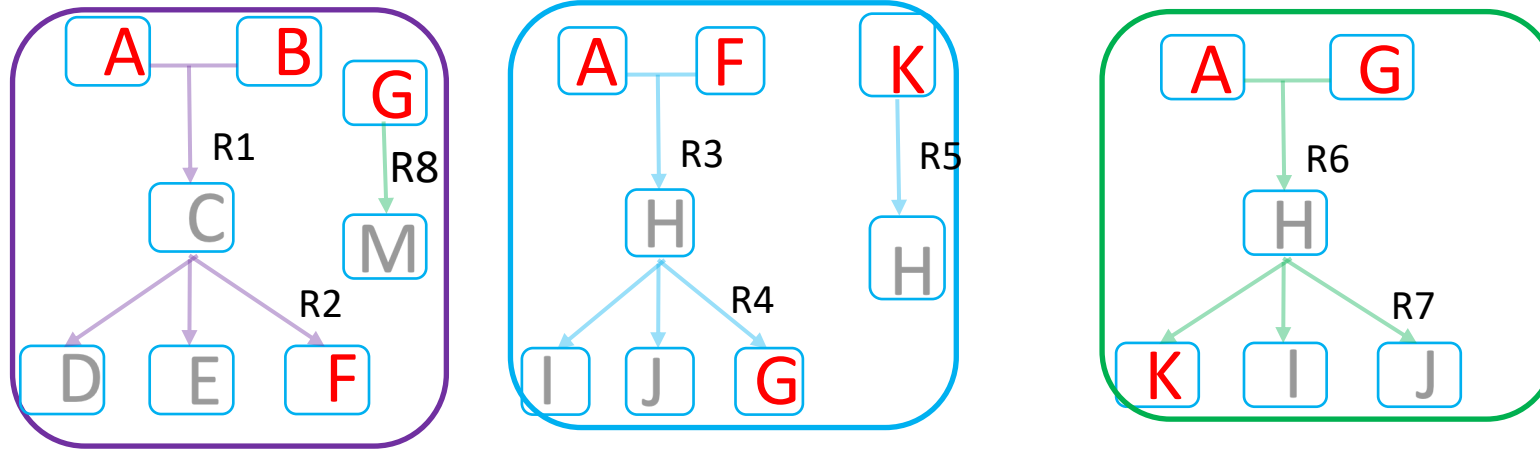


$$competition = \sum_{i=1}^m \frac{count(i)}{size_community}$$



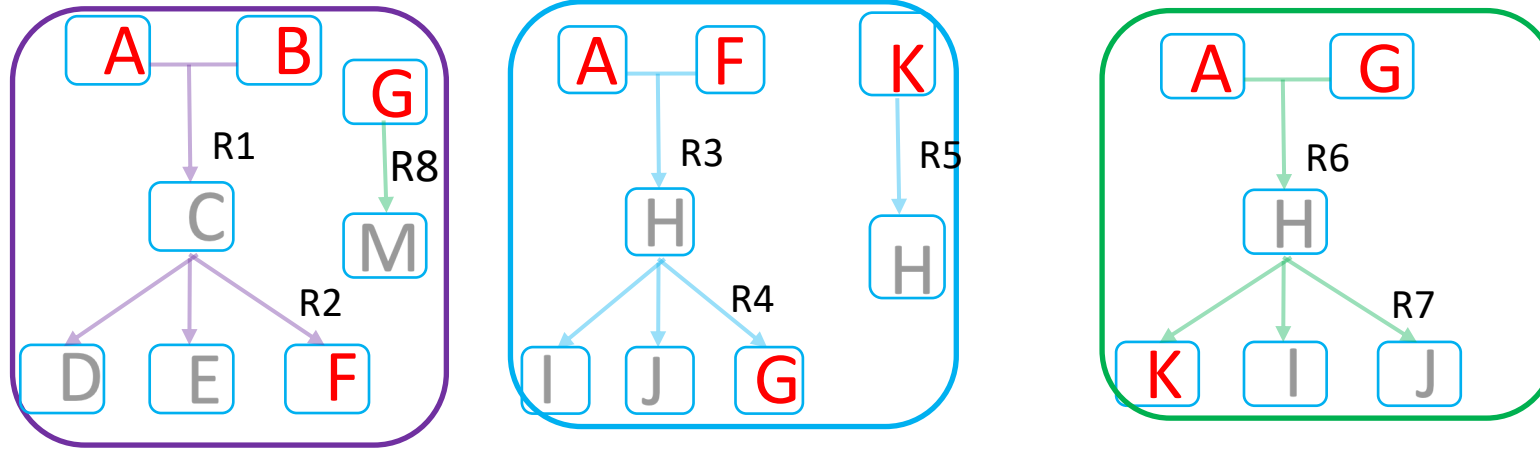
➤ Calculation of the competition potential (python)

Seed : A,B



➤ Calculation of the competition potential (python)

Seed : A,B



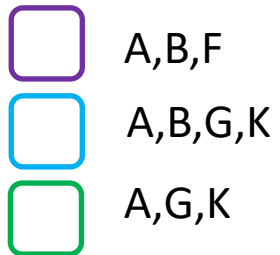
A : 3
B : 2
G : 2
K : 2
F : 1

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)



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

$$Competition = 1 + 0.6 + 0.6 + 0.6 + 0.3 = 3.1$$

➤ Benchmarks for testing scores

Scores in function of the ecosystem



gut



Leaf



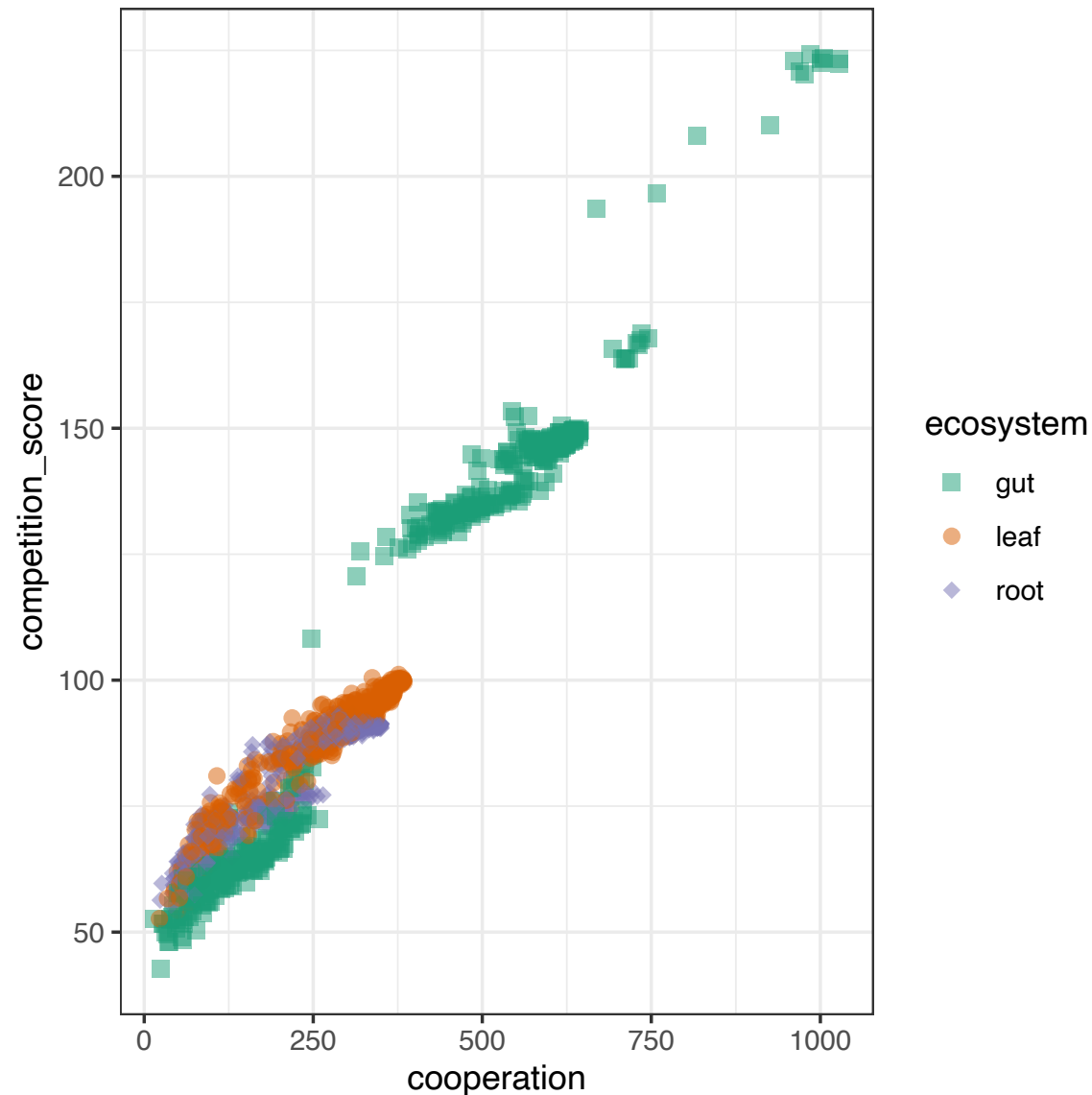
root



50 communities of size X

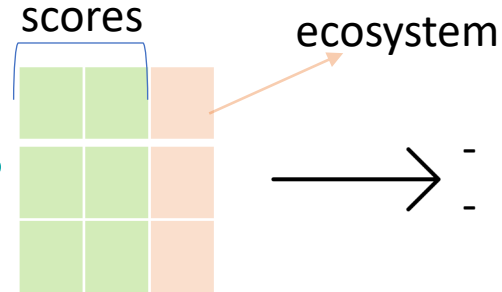
Reference
genomes of
cultivable species
from 3 ecosystems

Different scores in function of the ecosystems



➤ Ecosystem prediction from scores

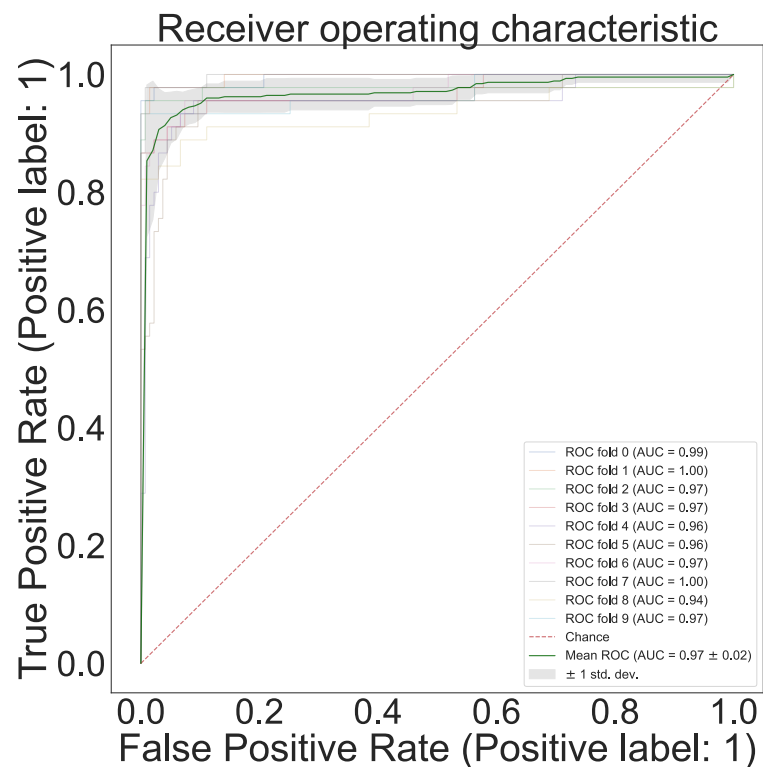
Prediction of gut ecosystem (SVM)



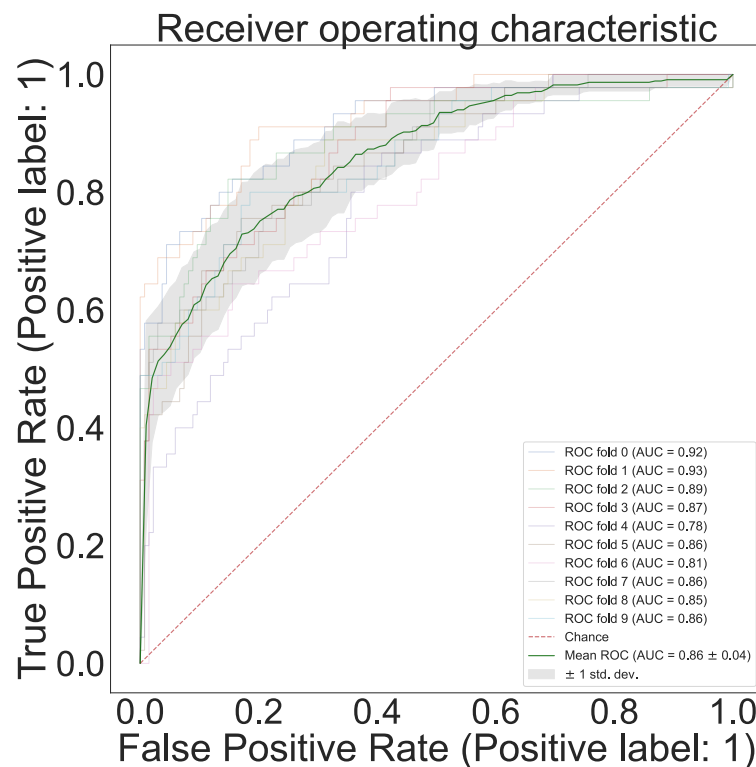
Up to 3 features = training

Up to 4

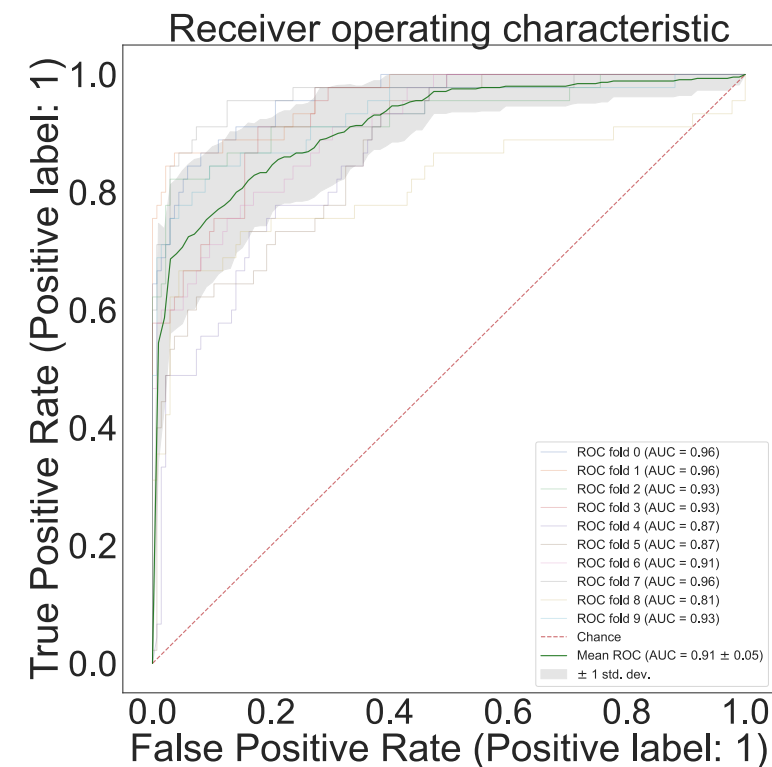
→ Noise
→ Cross validation → Ecosystem?



Only competition



Only cooperation

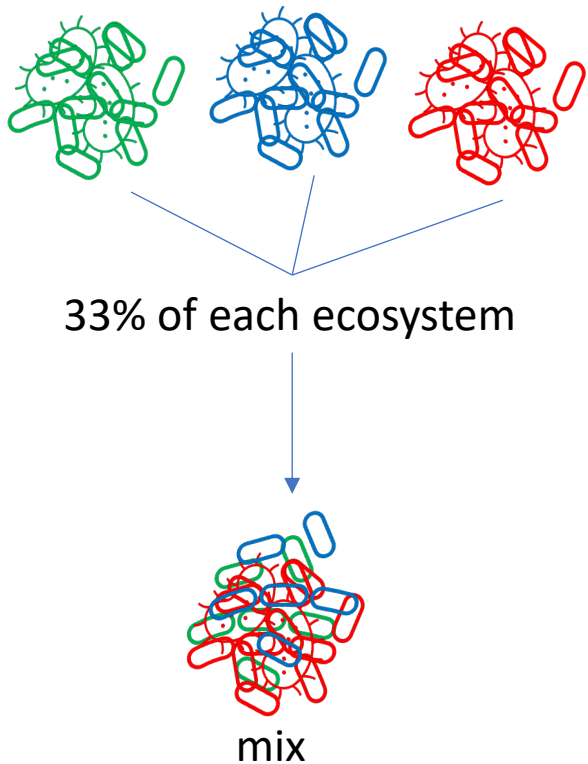


Both

Competition score seems to be enough for predicting ecosystem

➤ Benchmarks for testing scores

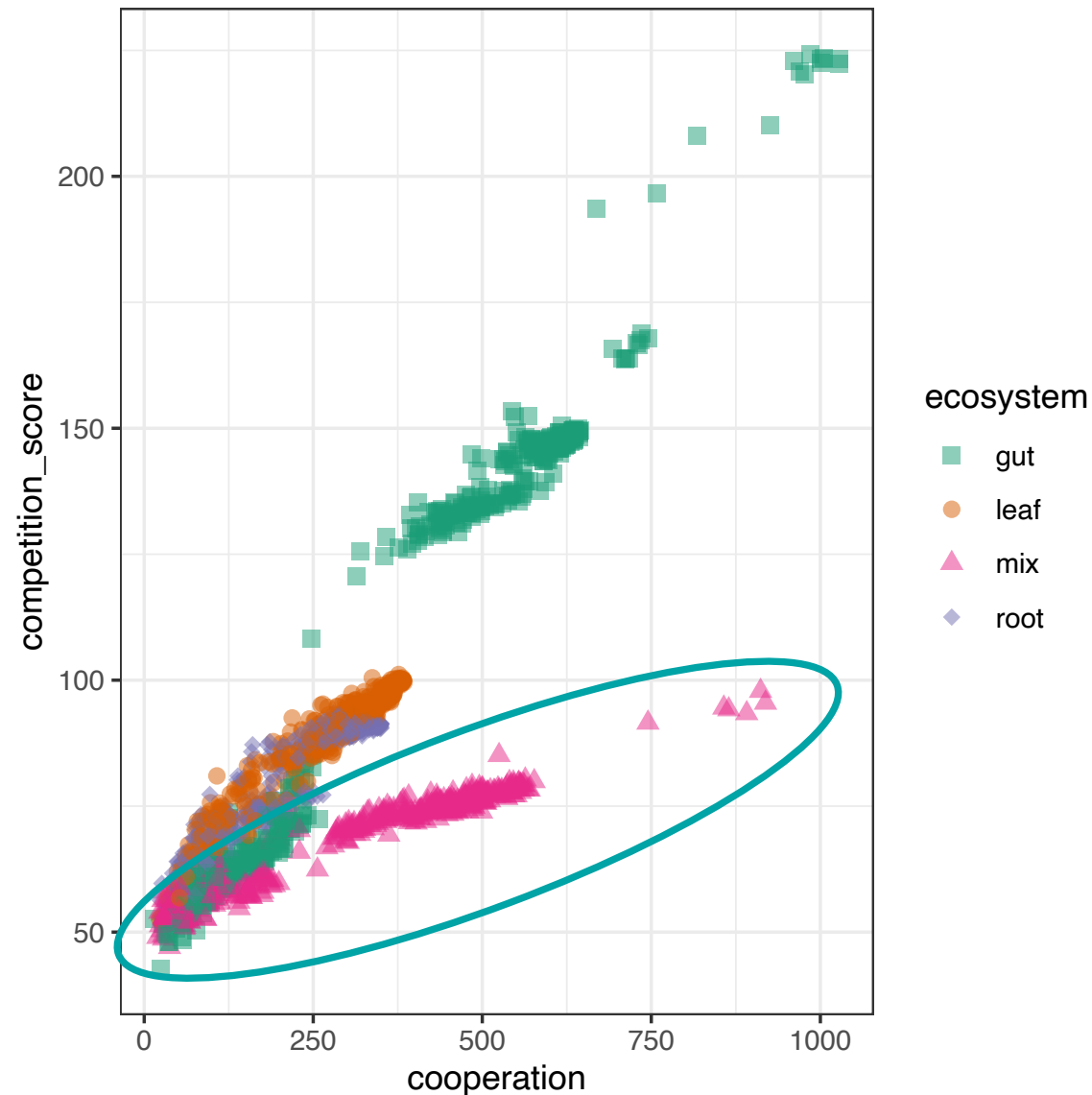
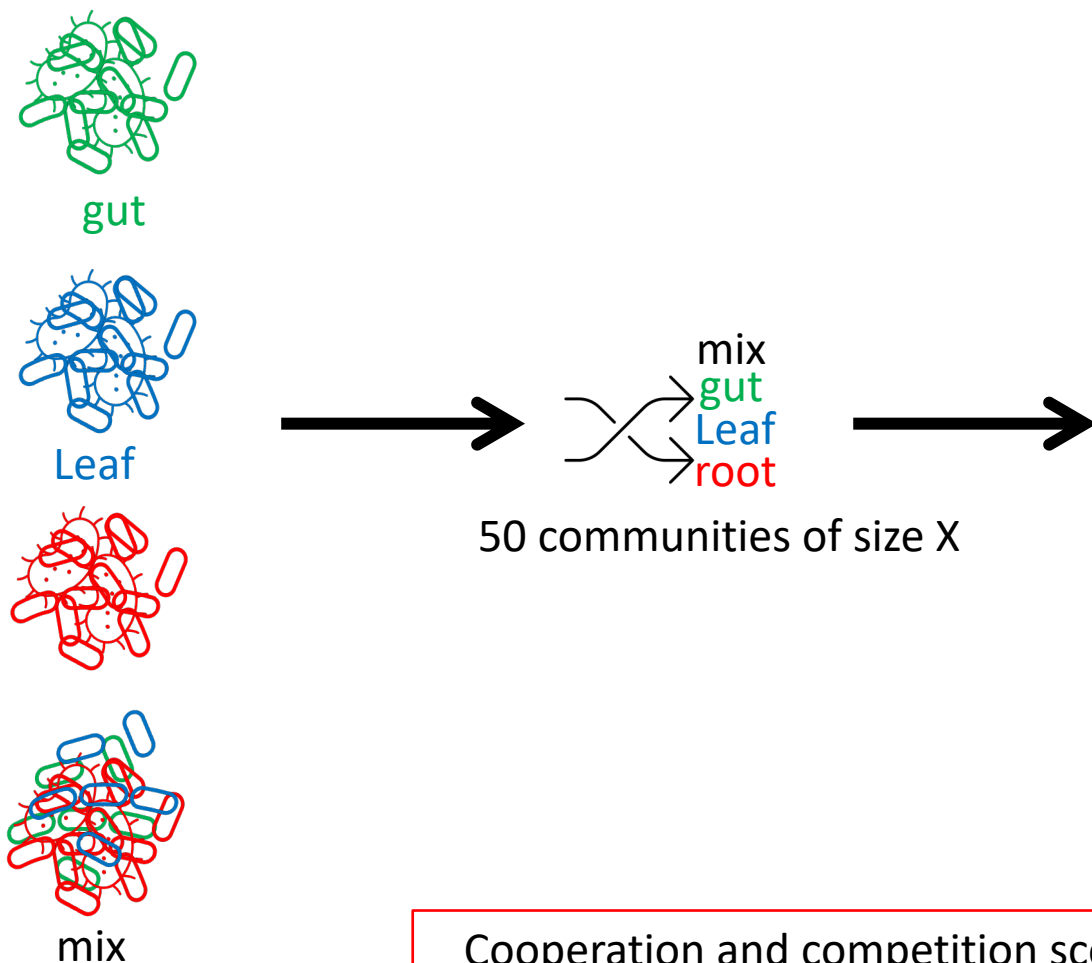
Do scores differ between ecosystems ?



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

➤ Benchmarks for testing scores

Scores in function of the ecosystem



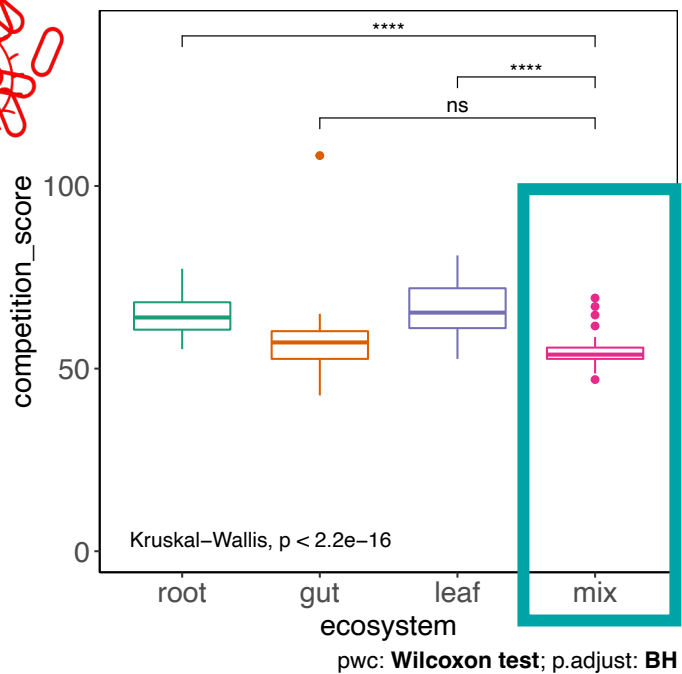
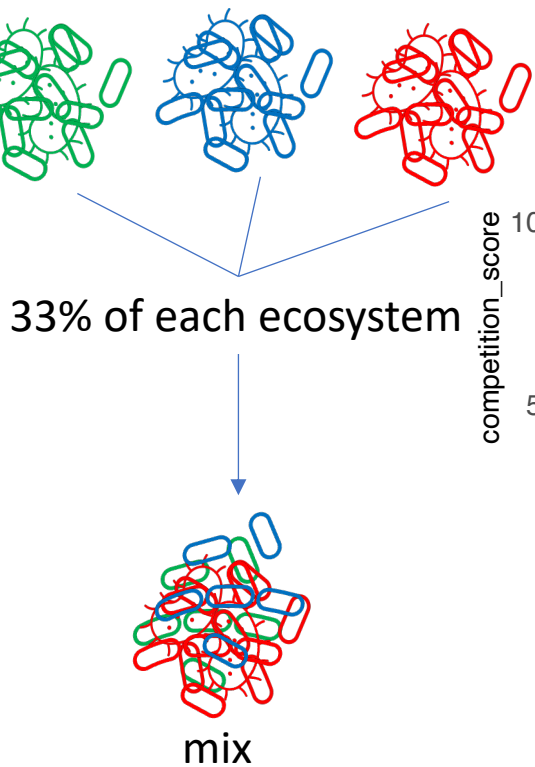
Cooperation and competition scores significantly differ between non-realistic and *ecosystem-consistent* communities

➤ Benchmarks for testing scores

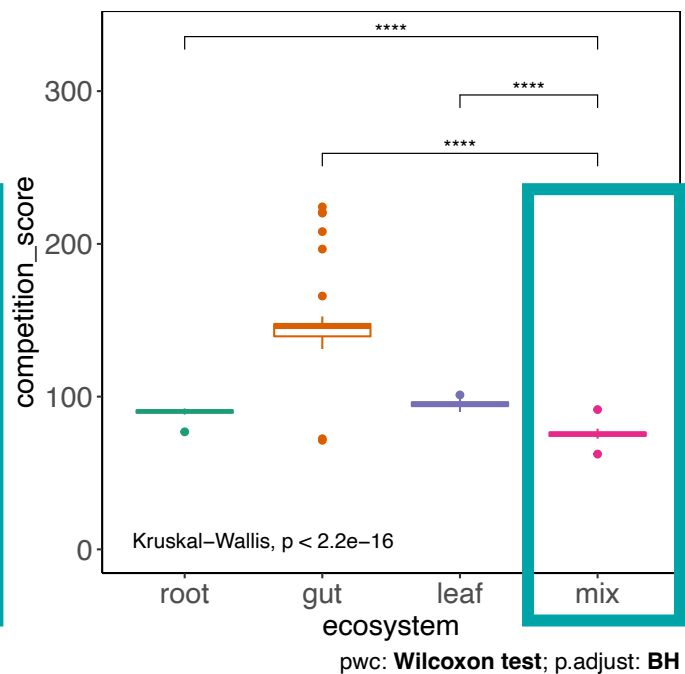
Do competition score differ between ecosystems ?

➤ Benchmarks for testing scores

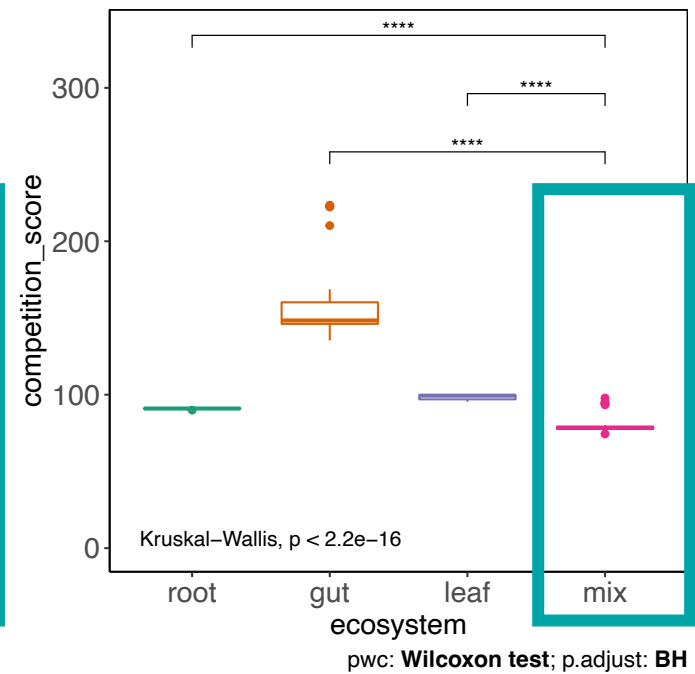
Do competition score differ between ecosystems ?



Size = 3



Size = 75

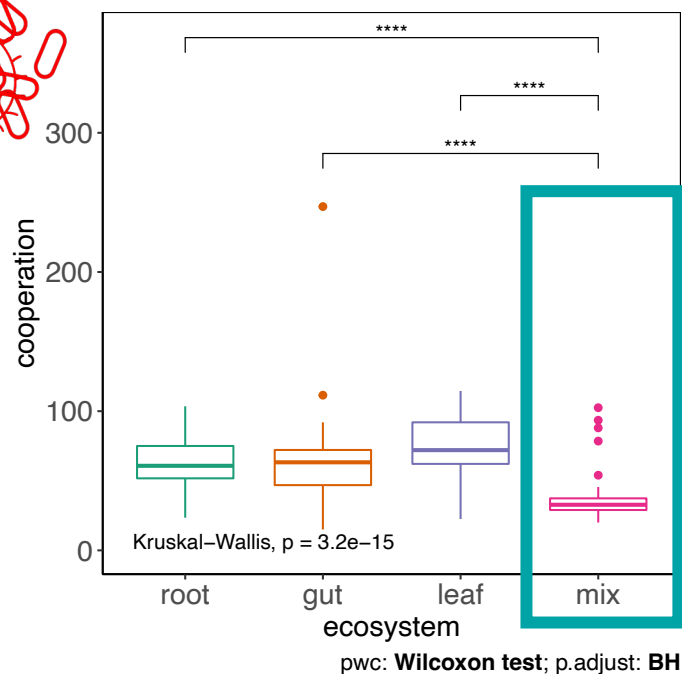
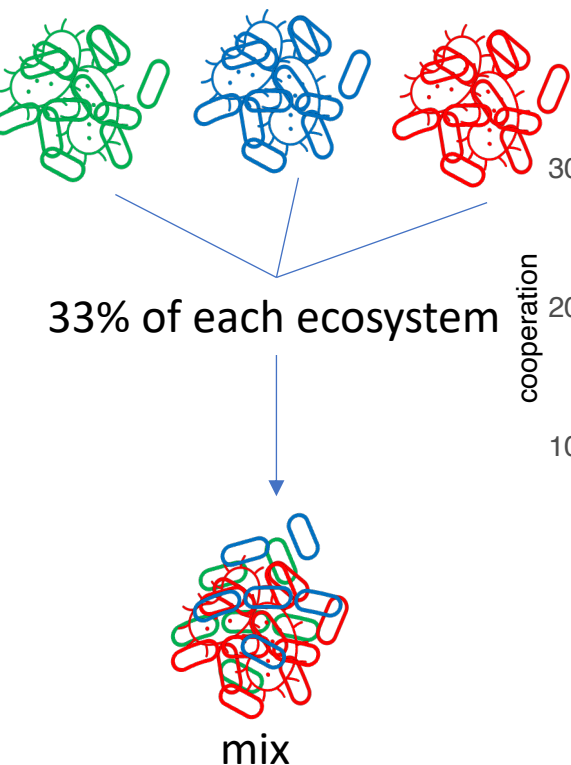


Size = 150

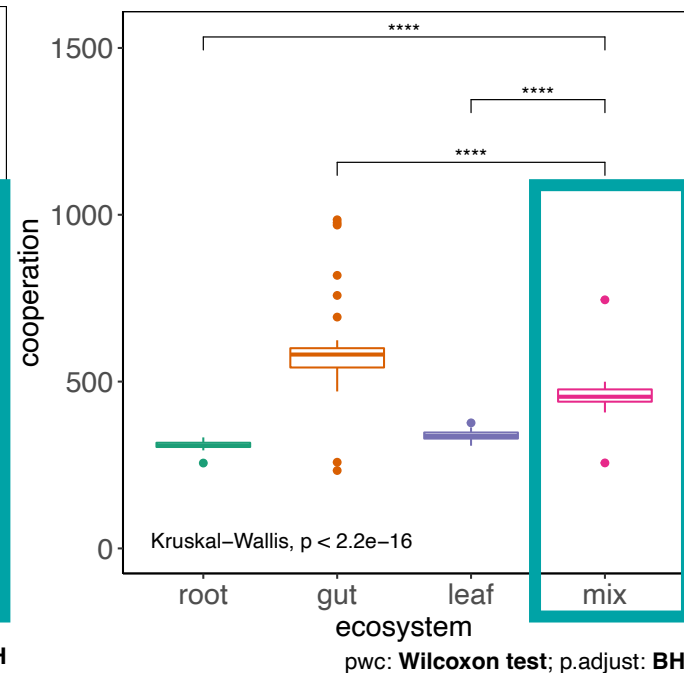
Cooperation and competition scores significantly differ between non-realistic and *ecosystem-consistent* communities

➤ Benchmarks for testing scores

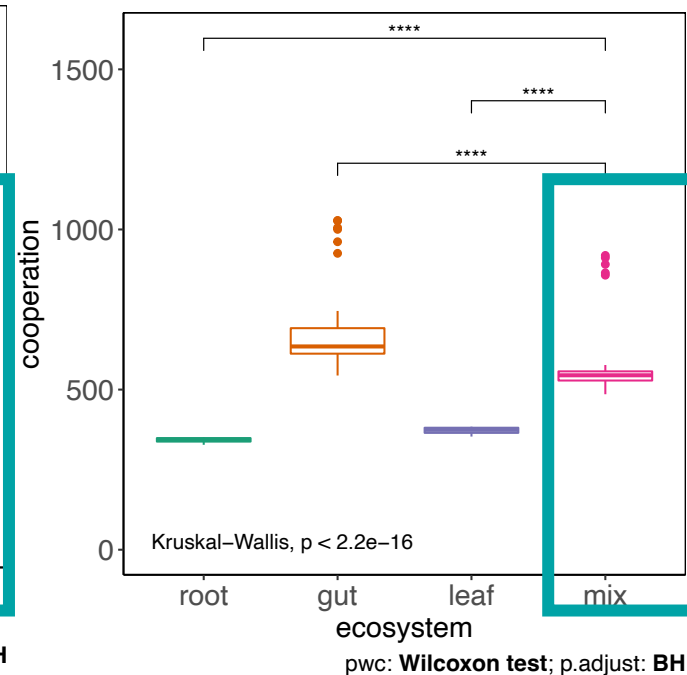
Do cooperation score differ between ecosystems ?



Size = 3



Size = 75

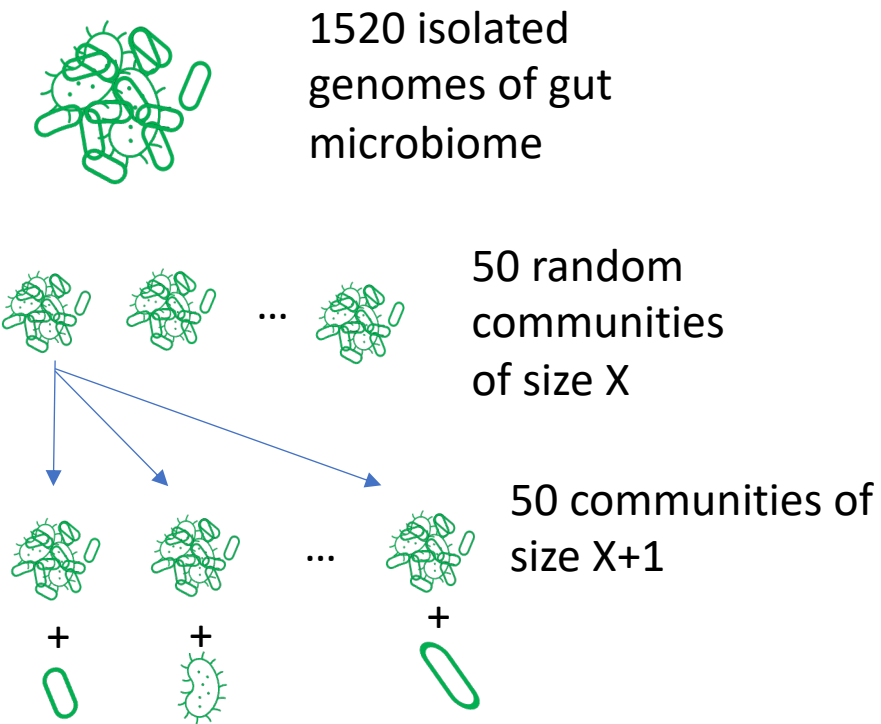


Size = 150

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



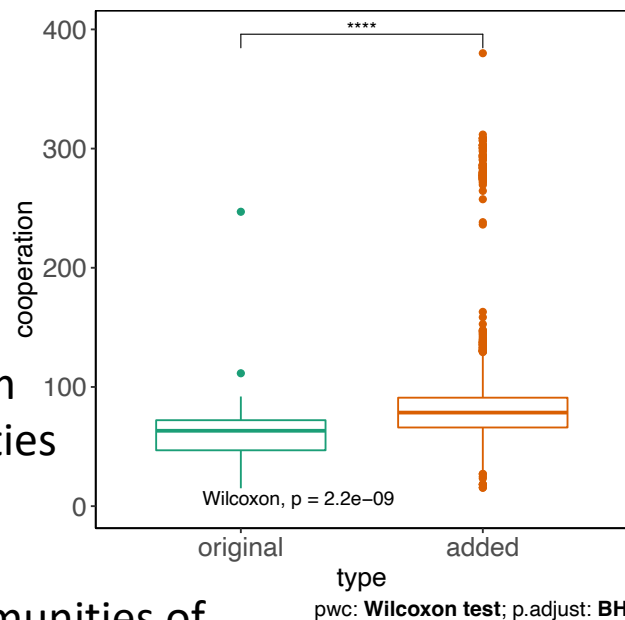
➤ Benchmarks for testing scores

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

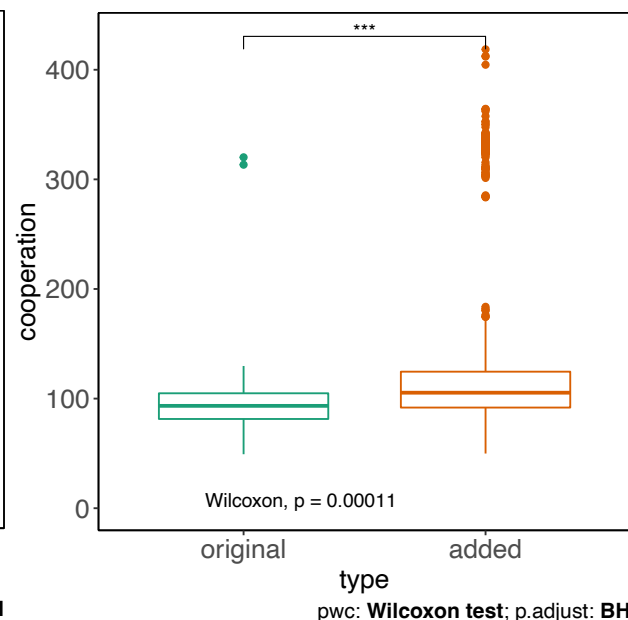
1520 isolated
genomes of gut
microbiome

50 random
communities
of size X

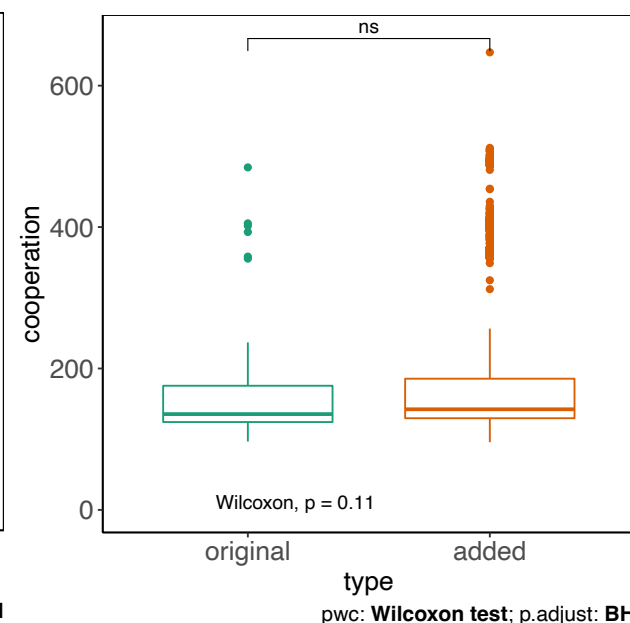
50 communities of
size X+1



Size = 3



Size = 5



Size = 10

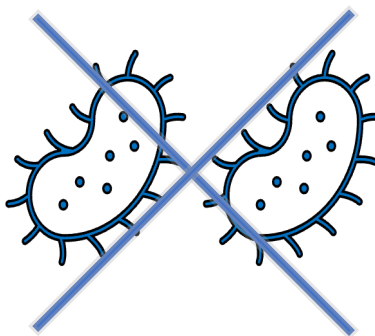
The larger is the community the less the community is disturbed by another species

➤ Conclusion

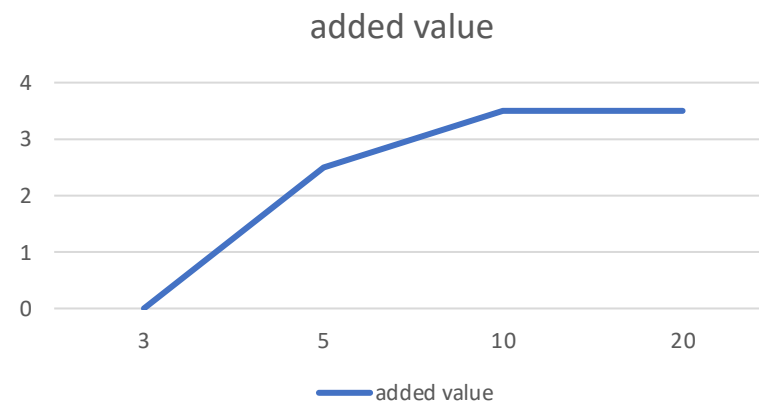
Tradeoff



Scalability



Pairwise



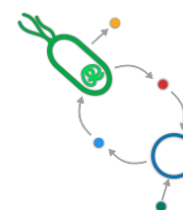
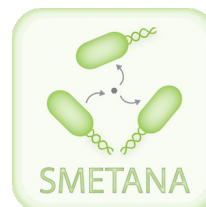
Resilience



Potentials



Perspective



INRAE

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

November 17 2022 / maxime.lecomte@inrae.fr / Maxime Lecomte 3rd PhD student



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- Coralie Muller

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Thanks for your attention



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

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➤ Benchmarks for testing scores

Scores in function the community size



gut



Leaf



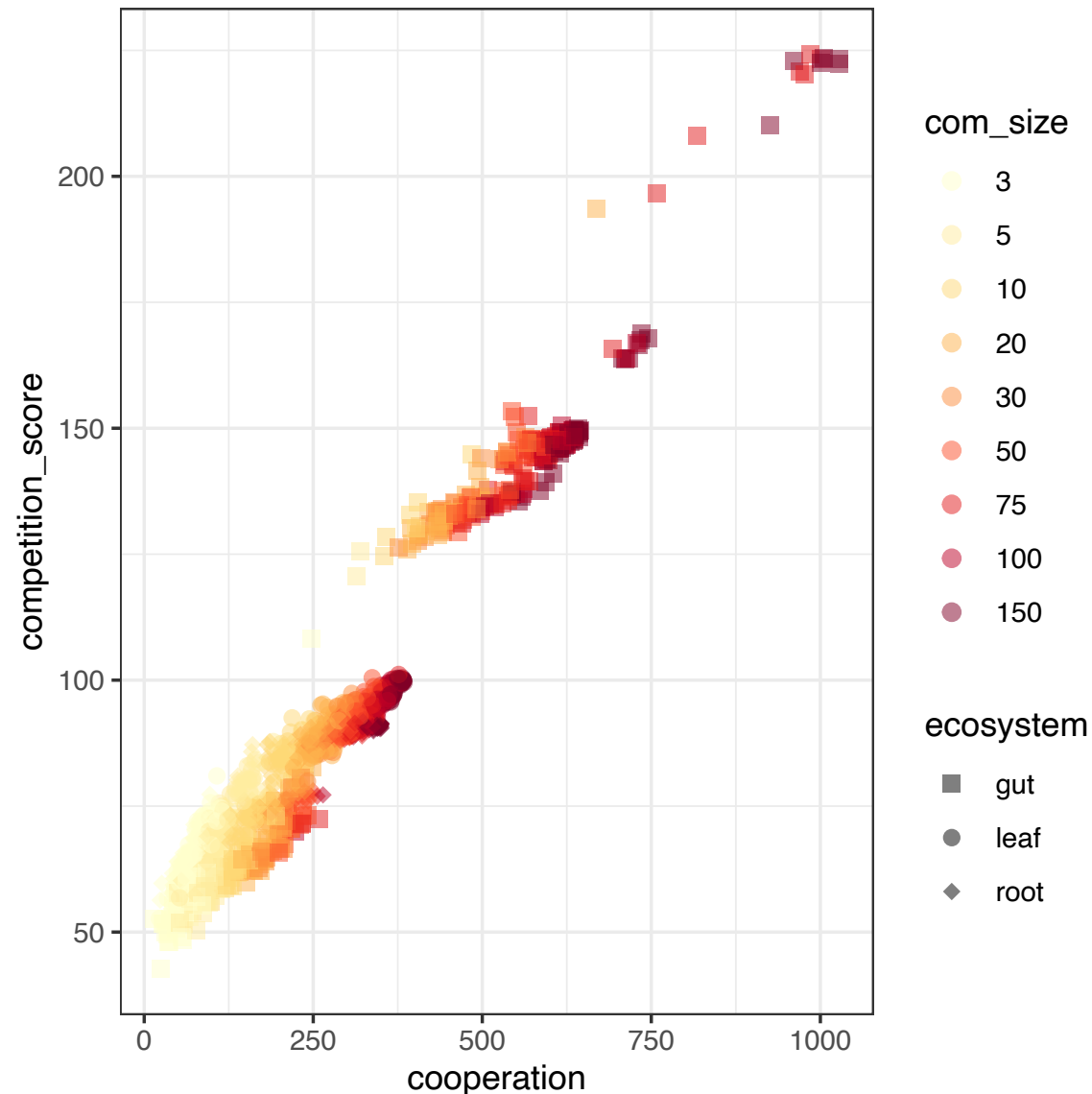
root



50 communities of size X

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*