The ecology and evolution of small bacterial communities

Sara Mitri
Department of
Fundamental Microbiology
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Microbes and their communities (naturally)

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Microbes and their communities (naturally)

Microbes provide many services:

- Oxygen production
- Food industry
- Food digestion & vitamin provision
- Nitrogen fixation
- Eliminating plant pests
- Wastewater treatment

Etc.

3

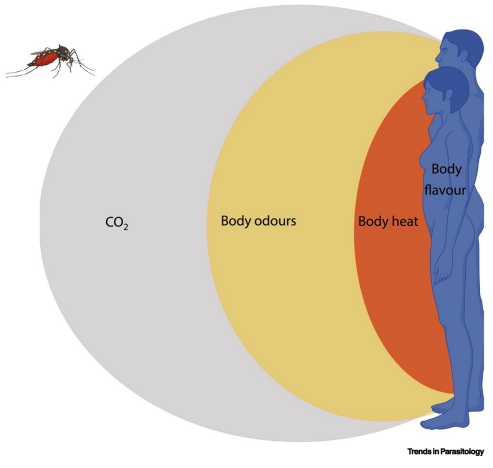
What can microbial community design make possible?

4

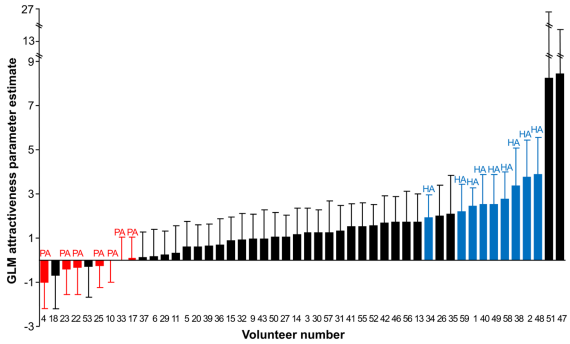
Could we turn industrial emissions into plastic?

5

Could we make probiotic skin creams to repel mosquitoes?



Lucas-Barbosa et al (2022) Tr Parasit



Verhulst et al (2011) PLoS ONE

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Why is engineering microbial ecosystems so difficult?

We don't know enough about how microbes interact!

We don't know which species are expected to live together or "coexist"

We don't know how species composition affects community function

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Lecture outline

Part IA: How do species interact?

Part IB: Can we predict how interactions change over time and space?

Part III: Can we design better communities?

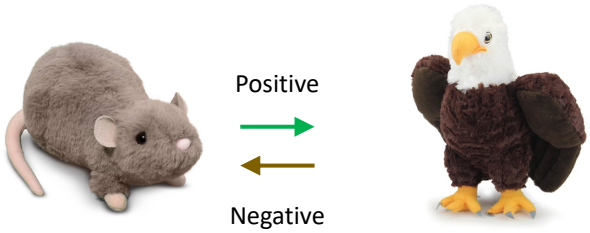
8

Part IA: How do species interact?

9

Defining “interactions”

The effect of one species on the growth and survival of another.



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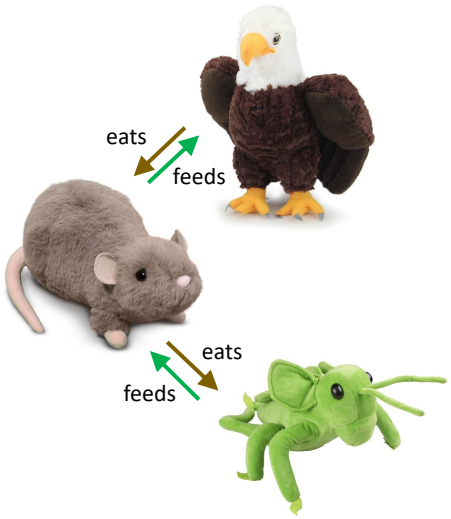
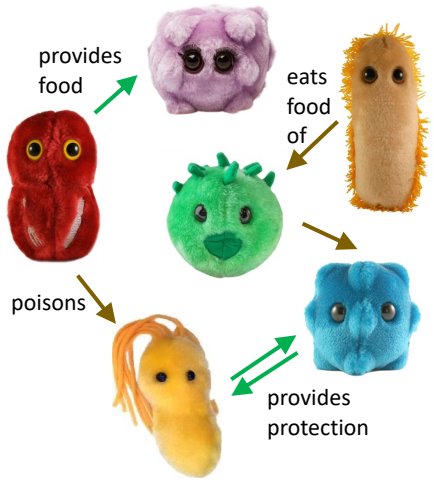
Classical view of species interactions



Microbial species interactions



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They compete!

How do microbial species interact?

They cooperate!

Current Biology
Volume 22, Issue 19, 9 October 2012, Pages 1845-1850

Report

Competition, Not Cooperation, Dominates Interactions among Culturable Microbial Species

Kevin R. Foster [1], Thomas Bell [2]

Bacterial species rarely work together

Competition is prevalent and could be harnessed as an alternative to antibiotics

JACOB D. PALMER AND KEVIN R. FOSTER

SCIENCE · 5 May 2022 · Vol 376, Issue 6593 · pp. 581-582 · DOI: 10.1126/science.abn5093

Positive interactions are common among culturable bacteria

JARED KEHE, ANTHONY ORTIZ, ANTHONY KULESA, JEFF GORE, PAUL C. BLAINEY, AND JONATHAN FRIEDMAN

SCIENCE ADVANCES · 5 Nov 2021 · Vol 7, Issue 45 · DOI: 10.1126/sciadv.abi7159

Prevalent emergence of reciprocity among cross-feeding bacteria

Samir Giri, Ghada Yousif, Shraddha Shitut, Leonardo Oña & Christian Kost

ISME Communications 2, Article number: 71 (2022) | Cite this article

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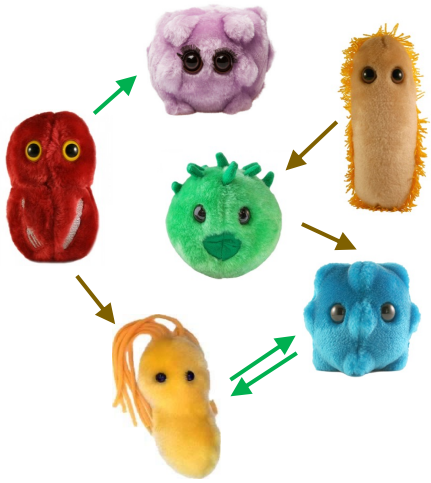
How do we find out how microbial species interact?

Synthetic microbial communities

Too simple!



Too complex!

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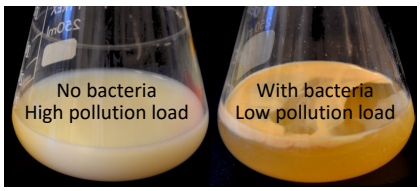
A model bacterial synthetic community

Machine oils: Metal-working fluids



Community function: Machine oil degradation

At *Agrobacterium tumefaciens*

Ms *Microbacterium saperdae*

Ct *Comamonas testosteroni*

Oa *Ochrobactrum anthropi*

Why are all four species needed to degrade machine oil?

van der Gast et al (2014) US Patent
Piccardi et al (2019) PNAS

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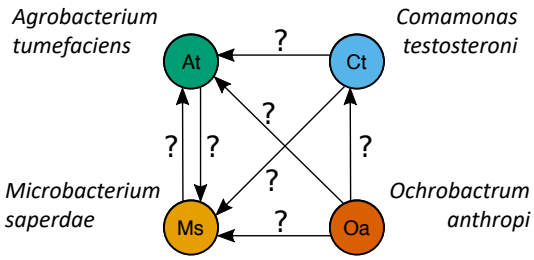
Why are all four species needed to degrade machine oil?
How do these species interact?

Philippe Piccardi



Interaction:
The effect of one species on the growth and survival of another.

15

Why are all four species needed to degrade machine oil?
How do these species interact?

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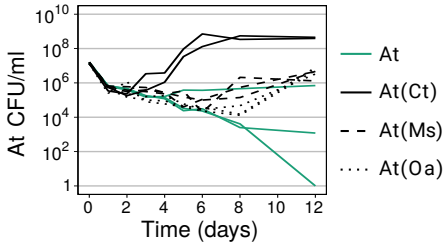
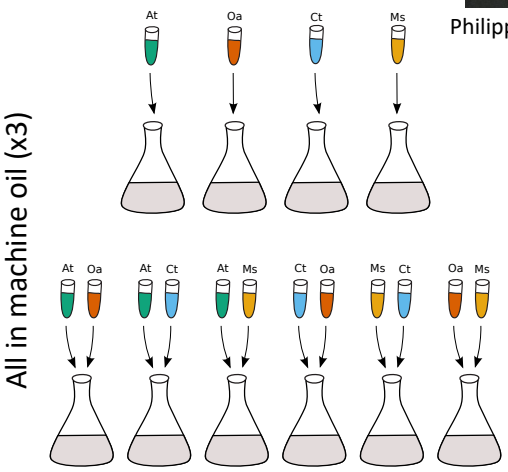


Compare their population size over time when alone versus with a partner



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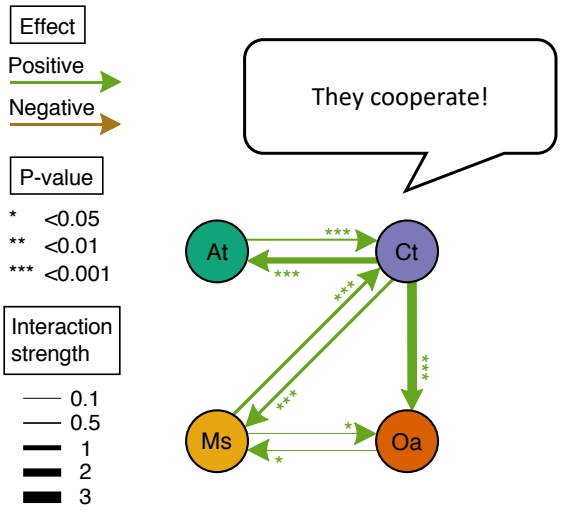

Piccardi, Vessman & Mitri (2019) PNAS

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Stress Gradient Hypothesis (Bertness & Callaway, 1994)

Harsh environments promote positive interactions (in plants)

Machine oils

Can this explain interactions between microbes living in harsh machine oils?

Björn Vessman

Hammarlund & Harcombe (2019) PNAS

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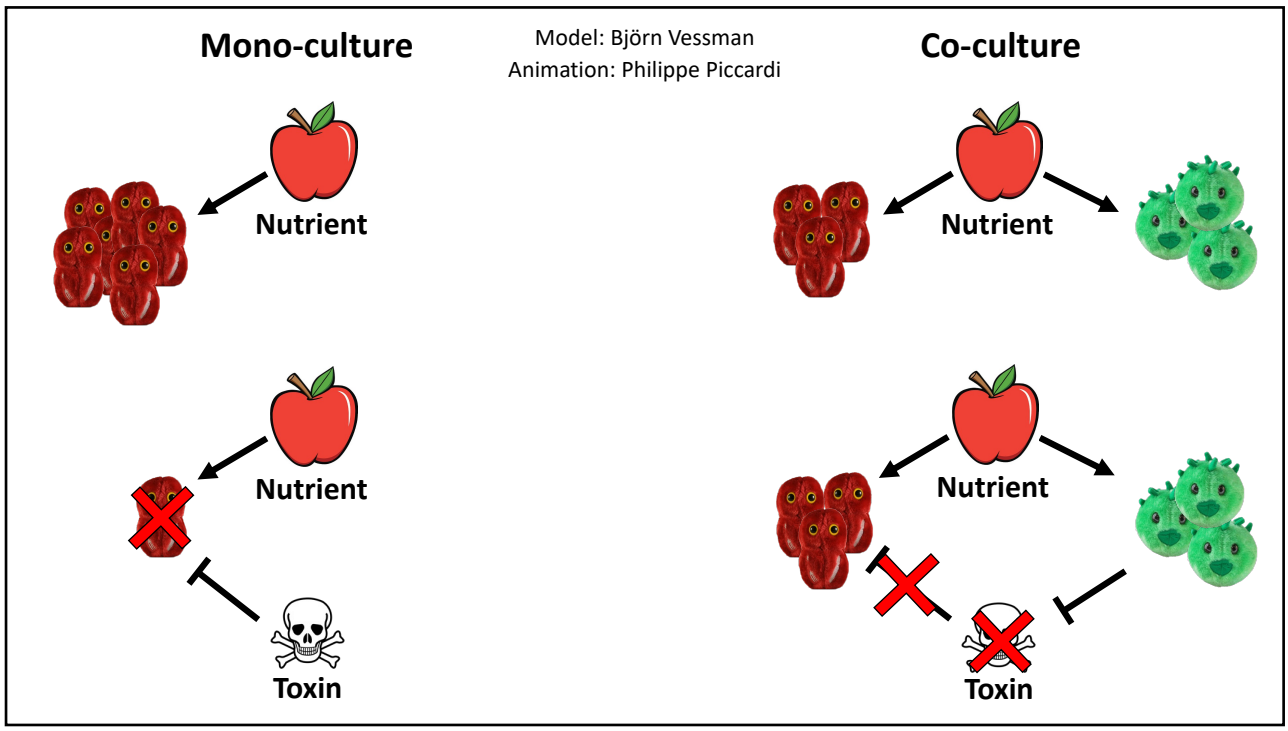

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Model equations

$$\frac{dS_i}{dt} = ((1-f_i)\rho_i(C_N) - \mu_i(C_T))S_i$$

$$\frac{dC_N}{dt} = -\sum_{i=1}^{n} \frac{1}{Y_i}\rho_i(C_N)S_i$$

$$\frac{dC_T}{dt} = -C_T \sum_{i=1}^{n}(f_i\delta_i\rho_i(C_N) + \kappa_i)S_i$$

$$\rho_i(C_N) = r_{\max,i}\frac{C_N}{C_N + K_N}$$

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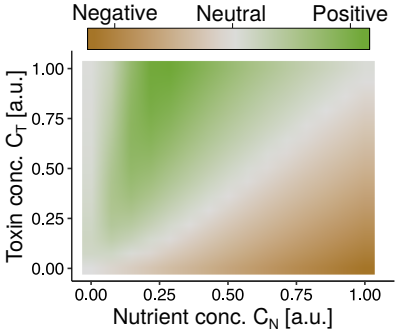
Interactions depend on nutrient and toxin concentrations



Piccardi, Vessman & Mitri (2019) PNAS

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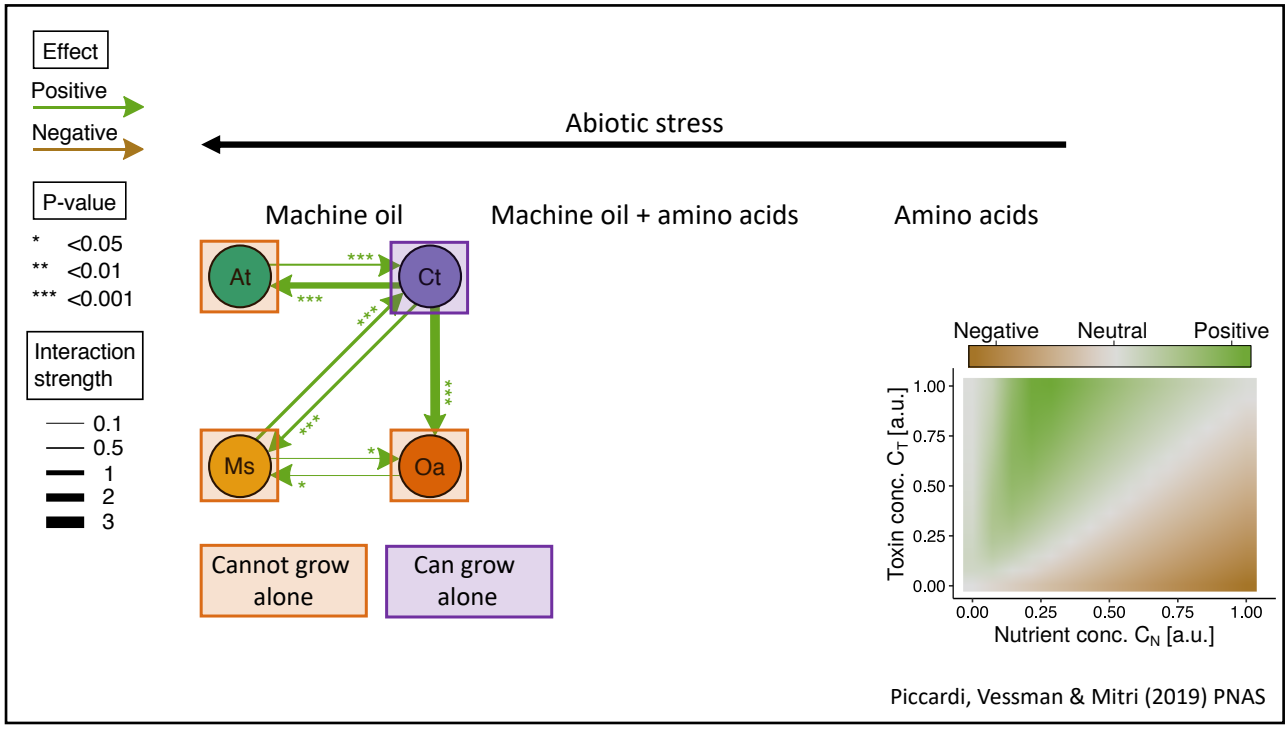

Piccardi, Vessman & Mitri (2019) PNAS

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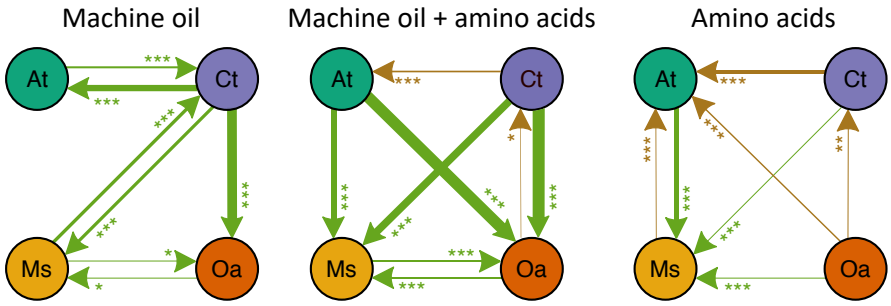
In a harsh environment, species that can grow facilitate those that cannot
This is in line with the Stress Gradient Hypothesis (SGH)



Piccardi, Vessman & Mitri (2019) PNAS

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How do microbial species interact?

They cooperate!

It depends!

Current Biology

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ISME Communications 2, Article number: 71 (2022) | Cite this article

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Toxicity favors positive interactions.

This is because many species cannot grow.
And when a species cannot grow, it is likely to be facilitated by another species that can.

Changing the environment can change interaction sign.

Piccardi, Vessman & Mitri (2019) PNAS
Di Martino*, Picot* & Mitri (2024) PLOS Biol

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Lecture outline

Part IA: How do species interact?

Part IB: Can we predict how interactions change over time and space?

Part III: Can we design better communities?

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Part II: Can we predict how interactions change over time and space?

Oliver Meacock

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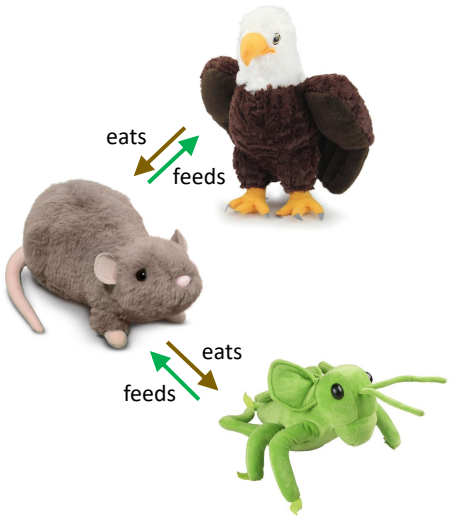
Classical view of species interactions



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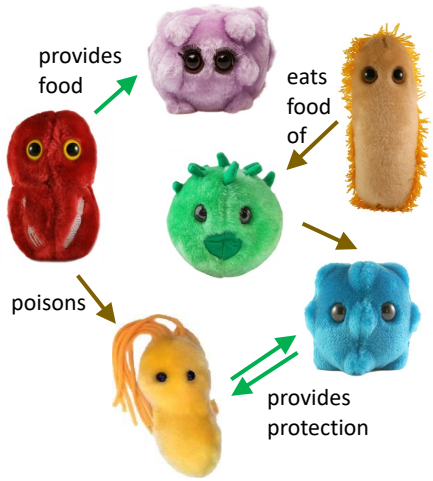

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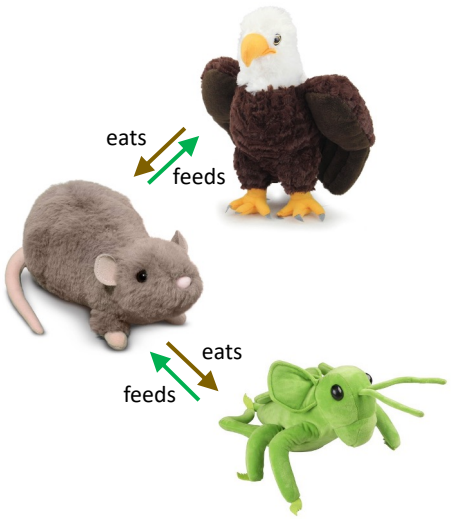
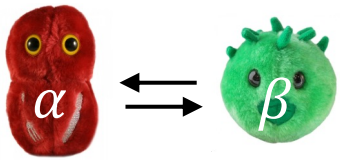
What mathematical framework is appropriate for microbial interactions?



Lotka-Volterra



$$\frac{1}{x_\alpha}\frac{dx_\alpha}{dt} = \mu_\alpha + \sum_\beta a_{\alpha\beta}\, x_\beta$$

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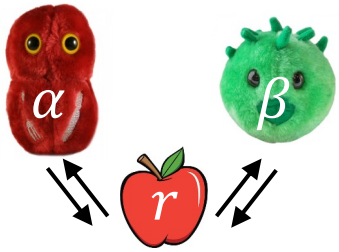
What mathematical framework is appropriate for capturing interactions?

Consumer-Resource



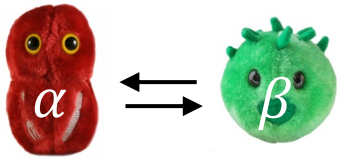
$$\frac{1}{x_\alpha}\frac{dx_\alpha}{dt} = g_\alpha(\boldsymbol{r}(t))$$

"sensitivity function"

$$\frac{d\boldsymbol{r}}{dt} = \sum_\beta x_\beta \boldsymbol{f}_\beta(\boldsymbol{r}) + \boldsymbol{\sigma}$$

"impact function"

Lotka-Volterra



$$\frac{1}{x_\alpha}\frac{dx_\alpha}{dt} = \mu_\alpha + \sum_\beta a_{\alpha\beta}\, x_\beta$$

Interaction matrix

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Interactions depend on nutrient and toxin concentrations

$$\frac{dS_i}{dt} = ((1-f_i)\rho_i(C_N) - \mu_i(C_T))S_i$$

$$\frac{dC_N}{dt} = -\sum_{i=1}^{n}\frac{1}{Y_i}\rho_i(C_N)S_i$$

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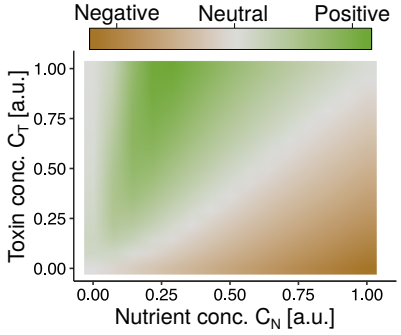
$$\rho_i(C_N) = r_{\max,i}\frac{C_N}{C_N + K_N}$$

$$\mu_i(C_T) = m_{\max,i}\frac{C_T}{C_T + K_T}$$

Can such context-dependency be captured by the gLV?



Piccardi, Vessman & Mitri (2019) PNAS

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Interactions in the gLV framework are an integral

Oliver Meacock

Generalised Lotka-Volterra

$$\frac{1}{x_\alpha}\frac{dx_\alpha}{dt} = \mu_\alpha + \sum_\beta a_{\alpha\beta}\, x_\beta$$

Population-weighted interaction

Consumer-resource (Closed systems)

$$\frac{1}{x_\alpha}\frac{dx_\alpha}{dt} = g_\alpha(\boldsymbol{r}(0)) + \sum_\beta \int_0^t a'_{\alpha\beta}(\boldsymbol{r}(\tau))\, x_\beta(\tau)\, d\tau$$

Per-capita growth rate

Basal growth rate

$$a'_{\alpha\beta}(\boldsymbol{r}(t)) = \nabla g_\alpha(\boldsymbol{r}(t)) \cdot \boldsymbol{f}_\beta(\boldsymbol{r}(t))$$

'Instantaneous interaction'

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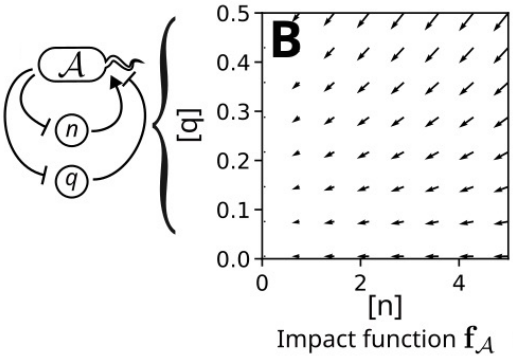
Decomposing instantaneous interactions

Effect of species A on the distribution of resources



Impact function $\mathbf{f}_\mathcal{A}$

Meacock & Mitri (2024) Ecol Lett

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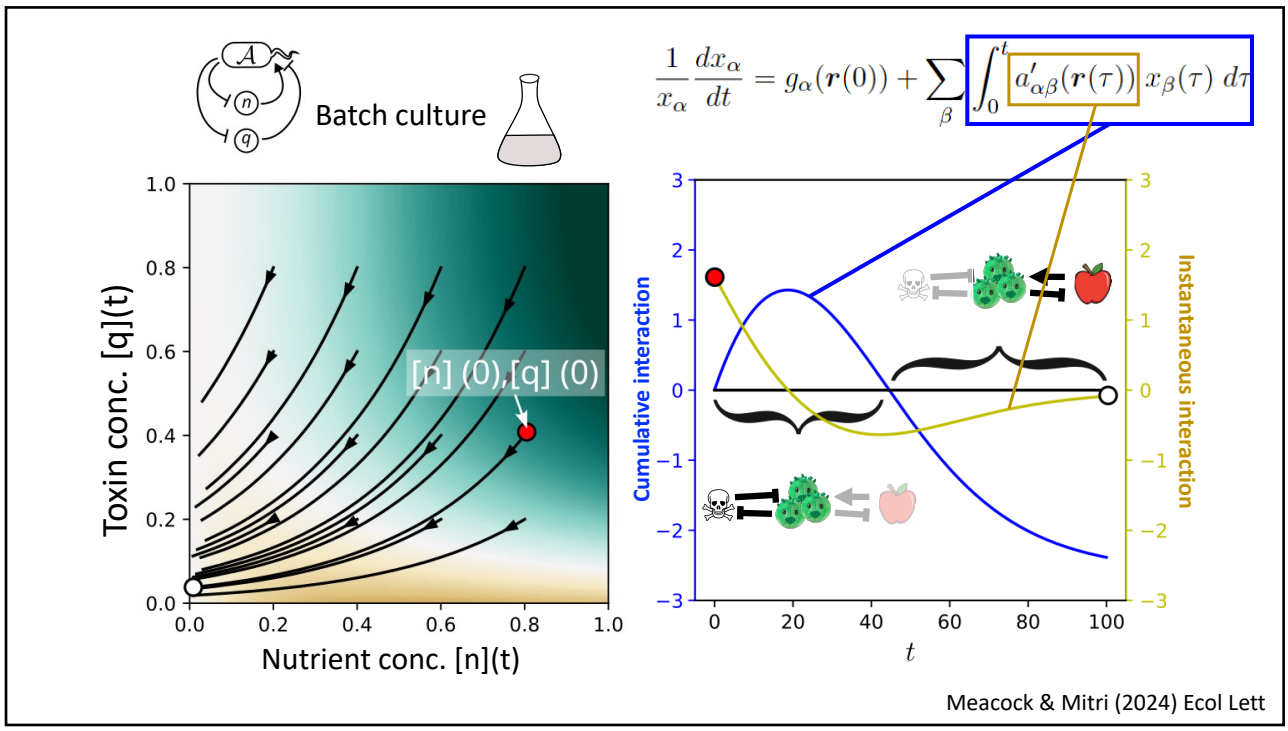

Meacock & Mitri (2024) Ecol Lett

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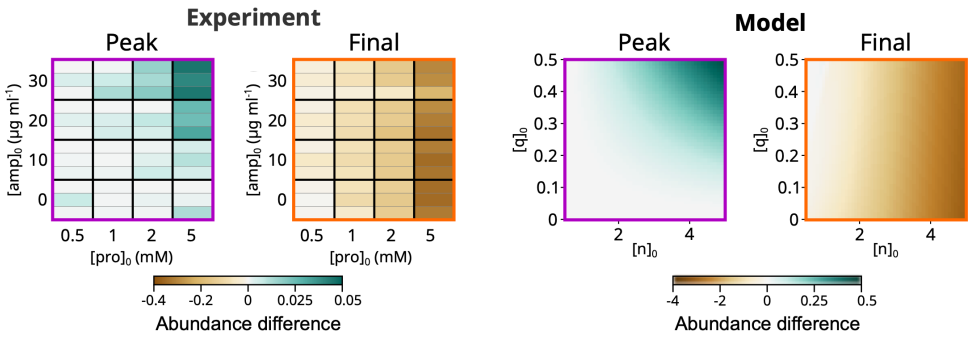
Applying the framework to predict interactions in the lab



Meacock & Mitri (2024) Ecol Lett

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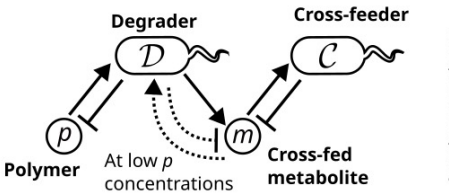
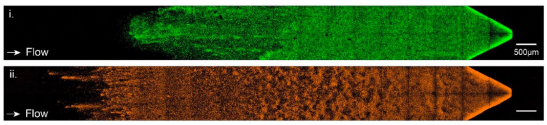
Applying the framework to two more published experiments



1. Batch culture experiments
Daniels et al (2023) ISMEJ

2. Spatial (microfluidic) experiments
Wong et al (2023) PNAS



Meacock & Mitri (2024) Ecol Lett

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Interactions are constantly changing over time and space

This framework can *predict* how interactions will change if we know the impact and sensitivity functions

gLV assumes that the environment is at steady-state (more appropriate for chemostats)

Meacock & Mitri (2024) Ecol Lett
Picot, Shibasaki et al (2023) Curr Opin Microbiol

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Lecture outline

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Part III: Can we design better communities?

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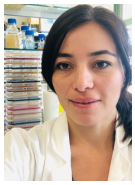
Part III: Can we design better communities?


Flora Arias-Sánchez


Björn Vessman


Pablo Guridi


Afra Salazar

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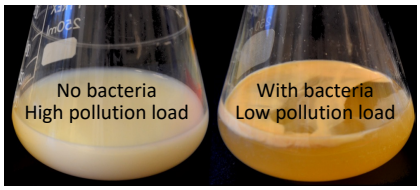
What combination of species gives us the best function?

Machine oils: Metal-working fluids



Community function: Machine oil degradation

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Ms *Microbacterium saperdae*

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Oa *Ochrobactrum anthropi*

van der Gast et al (2014) US Patent

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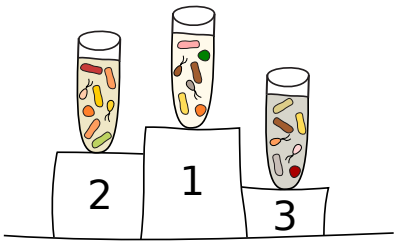
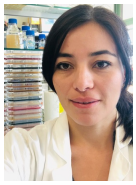
Artificially selecting microbial communities: If we can breed dogs, why not microbiomes?

Flor I. Arias-Sánchez, Björn Vessman, Sara Mitri

Published: August 30, 2019 • https://doi.org/10.1371/journal.pbio.3000356



Swenson et al (2000, 2000), Blouin et al (2015), Panke-Buisse et al (2015, 2017), Wright et al (2019), Arora et al (2019), Raynaud et al (2019), Jochum et al (2019), Xie et al (2019), Doulcier et al (2020), Chang et al (2020, 2021), Mueller et al (2021), Jacquiod et al (2021), Fraboul et al (2022)



Flora Arias-Sánchez

Björn Vessman

Pablo Guridi

Vessman*, Guridi* et al. (bioRxiv)

Arias-Sánchez et al. (2024) Nature Comm

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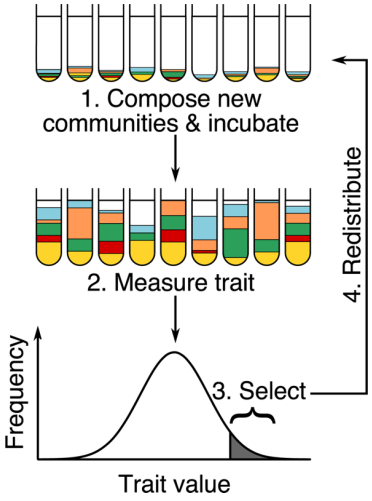

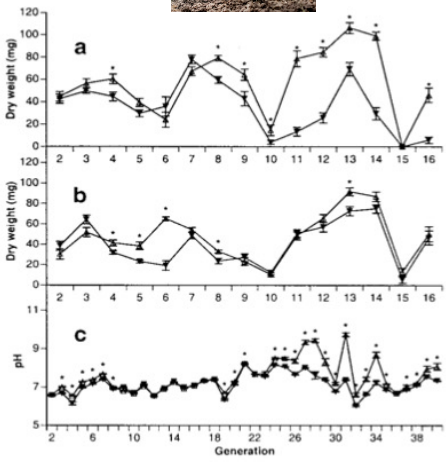

Swenson et al (2000)

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What is the problem?

It's difficult to maintain variability between communities

Ecological dynamics lower heritability

Selection acts at the individual level
(a microbial community is **not an evolutionary individual**)

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How many evolutionary individuals do you see?

Afra Salazar

Evolutionary individuals are the entities that undergo evolution by natural selection as a single unit

Salazar and Mitri (2025)

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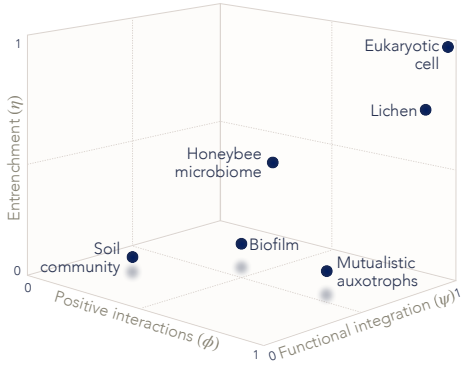
Can a microbial community be an evolutionary individual?



Evolutionary ~~individuals are~~ the ~~entities that~~ undergo evolution by natural selection as a single unit

individuality is **capacity** of an entity to

Salazar and Mitri (2025)

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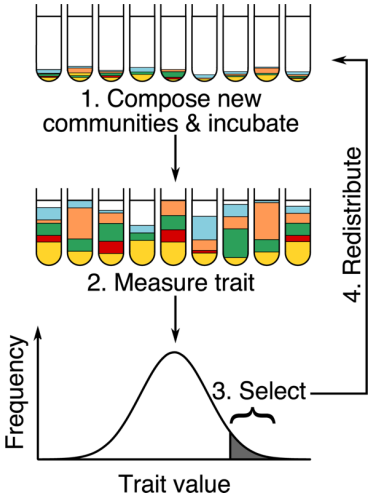
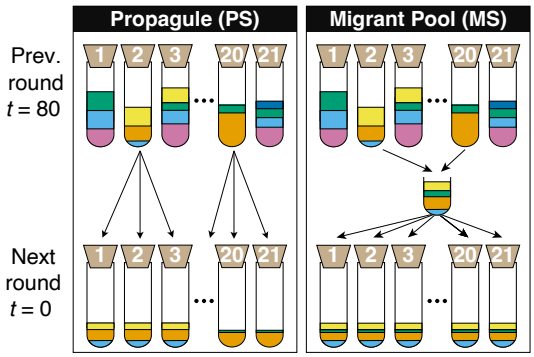


The classical redistribution step



It's difficult to maintain variability between communities

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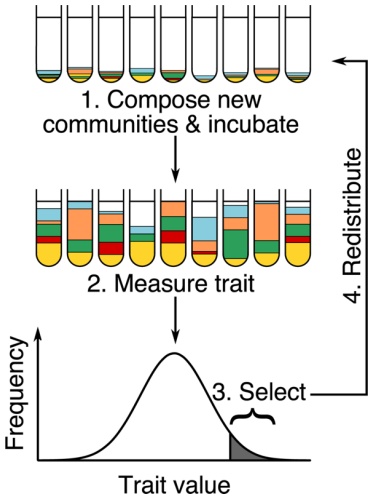
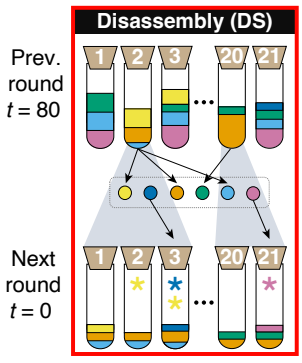


We came up with a redistribution step inspired by genetic algorithms



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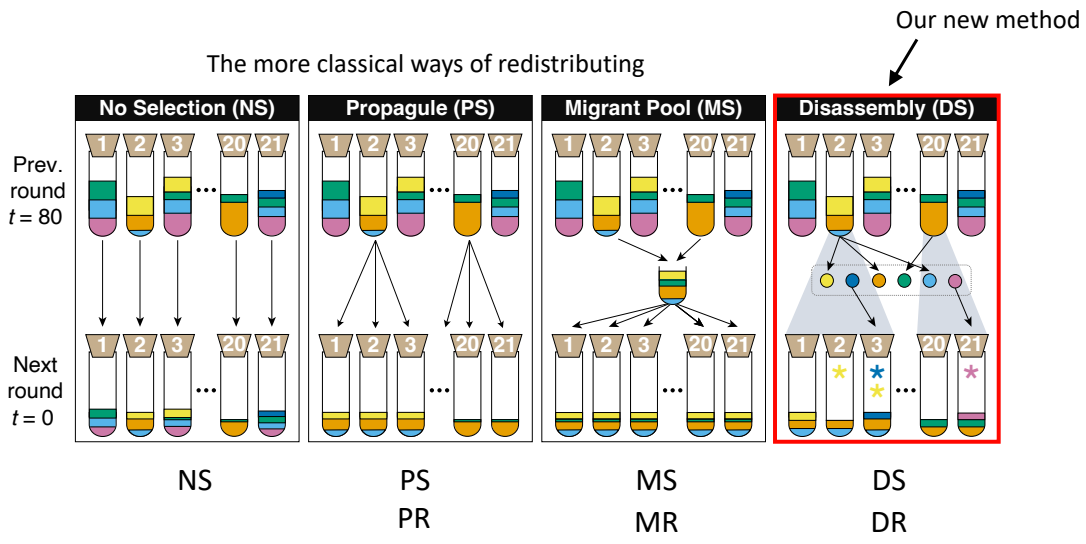

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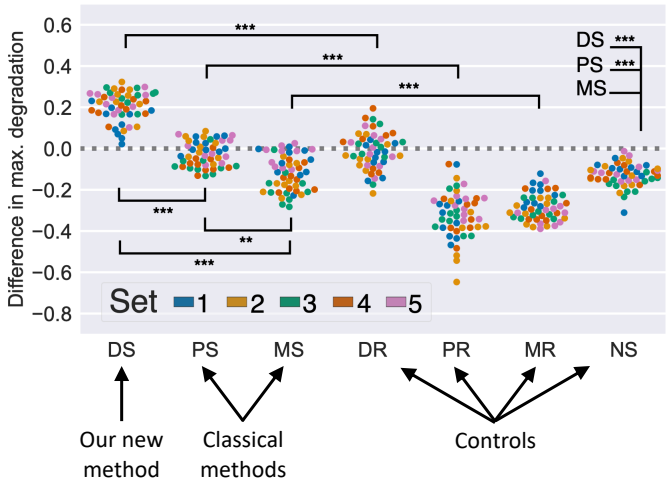
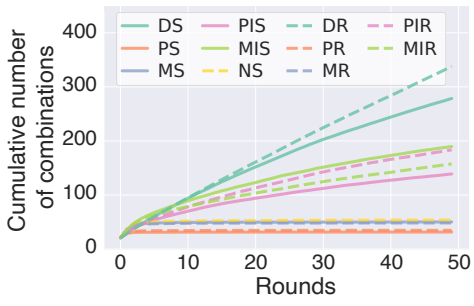
Theoretically, our new method (DS) should select for increased degradation





Vessman*, Guridi* et al. (biorxiv)

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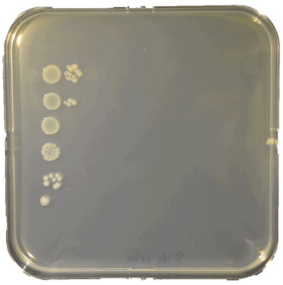
Björn Vessman

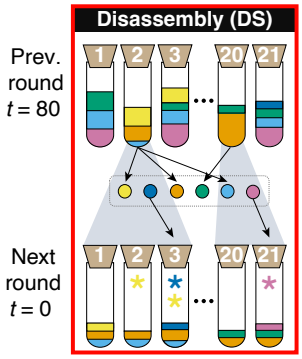
"Disassembly selection": disassemble winning communities and shuffle their members

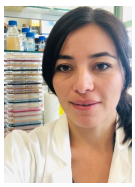
Designed selective media to separate 11 species isolated from machine oil



Selective media

Performed 18 rounds of disassembly selection (DS) and disassembly random (DR)





Flora Arias-Sánchez

Alice Wallef

Géraldine Alberti

Arias-Sánchez et al. (2024) Nature Comm

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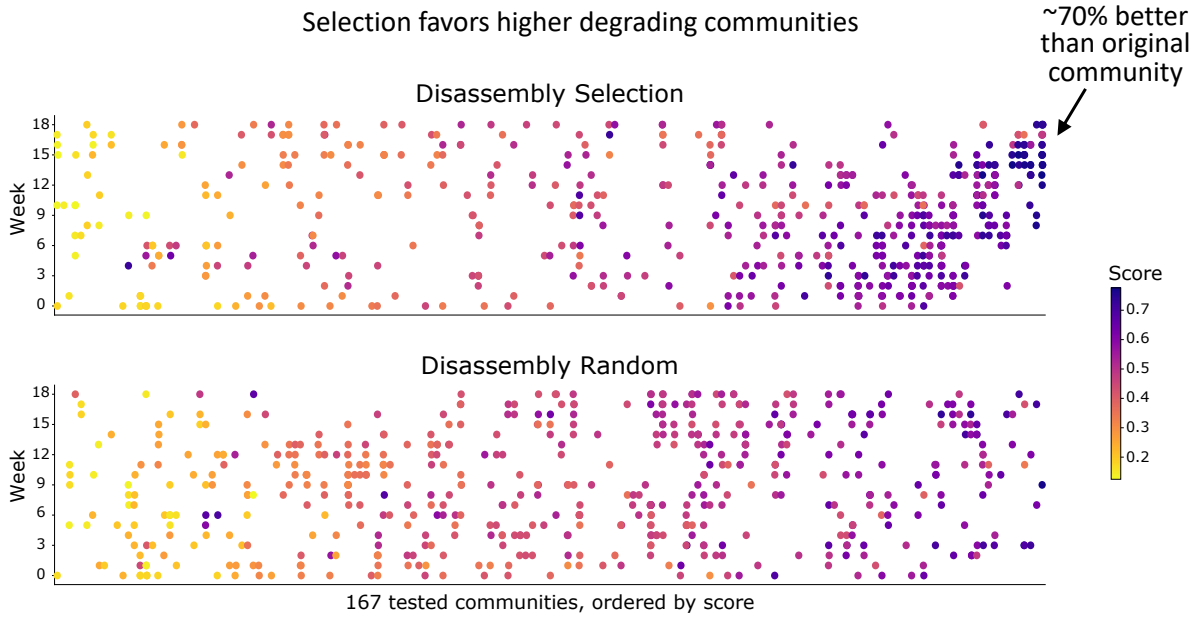
Selection favors higher degrading communities



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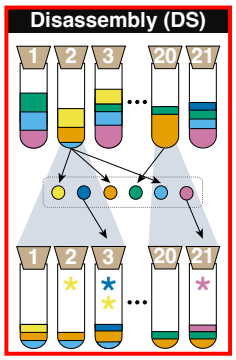

What is the problem?

It's difficult to maintain variability between communities

Ecological dynamics lower heritability

Selection acts at the individual level
(a microbial community is **not an evolutionary individual**)

We were hoping to select for increased cooperation

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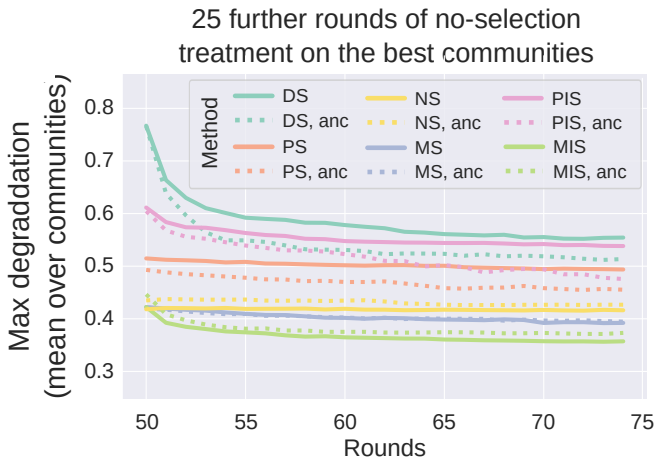
Communities were not stable over time (simulated and experimental)



Vessman*, Guridi* et al. (biorxiv)

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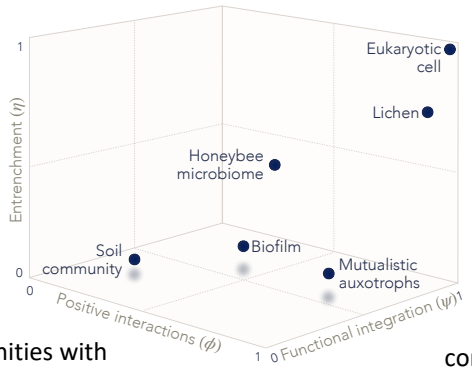
Did selected communities have high evolutionary individuality?

Afra Salazar

Selected communities had low entrenchment. When selective pressure was removed, community function collapsed.



Communities with positive interactions were favored but did not increase their positive interactions.

There was some compelementarity but communities evolved to lose their function.

Salazar & Mitri (2025) Curr Opin Micobiol

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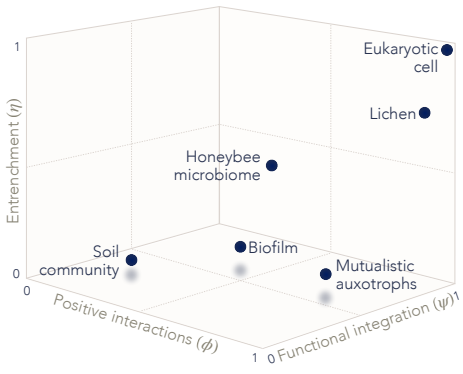
“Disassembly” 2.0

Afra Salazar



Individuality first, selection second

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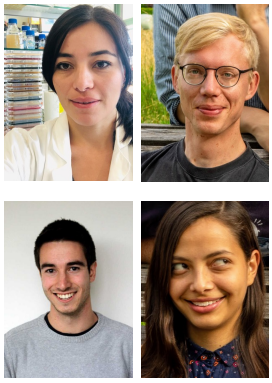

Selection operates at several levels simultaneously making it difficult to select at the community level.

We developed a method to improve community function.

We can do even better if communities had higher individuality before we applied selection.

Vessman*, Guridi* et al. (biorxiv)
Arias-Sánchez et al. (2024) Nature Comm
Salazar & Mitri (2025) Curr Opin Micobiol

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Could we turn industrial emissions into plastic?

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What I hope you will remember

1. Synthetic microbial communities can be useful model systems
2. Interactions are context-dependent
3. Models help us predict how interactions will change over time and space
4. One can use principles from multi-level selection to engineer microbial communities
5. Eco-evolutionary models can be very useful ☺

There are still many challenges and open questions ahead!

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Acknowledgements

Current lab members
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