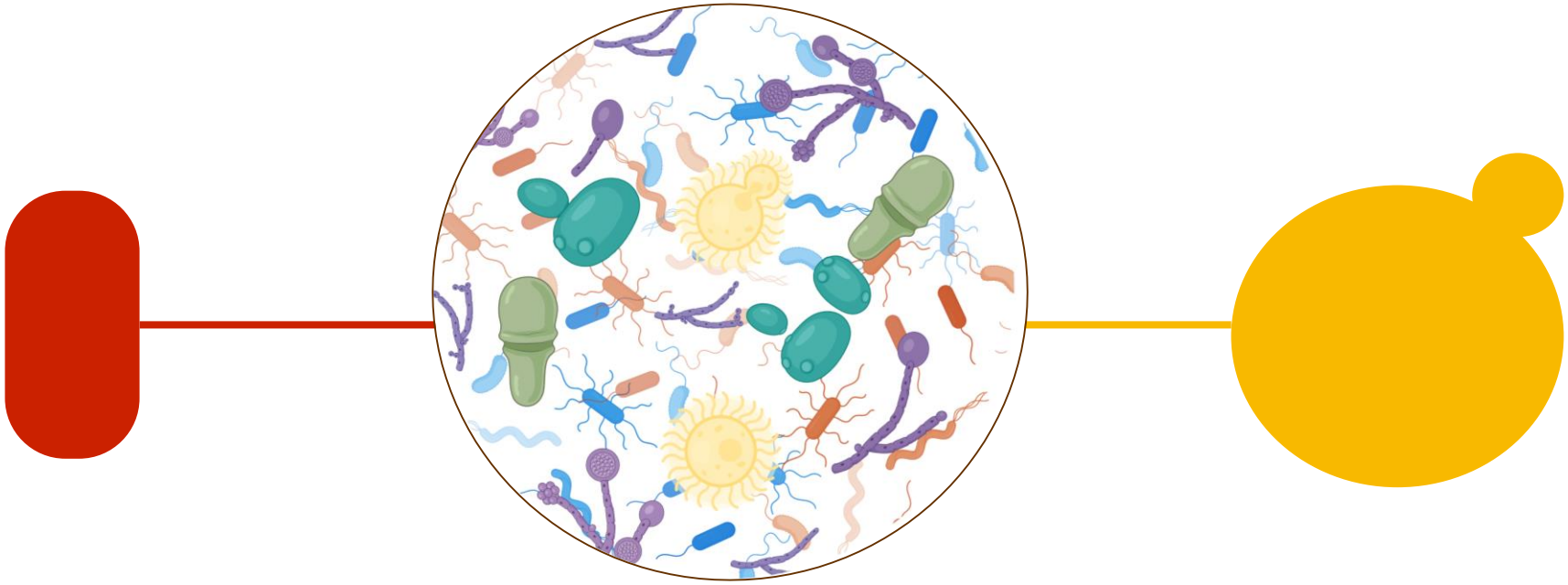
Tuning Interdomain Conjugation Toward *in situ* Population Modification in Yeast



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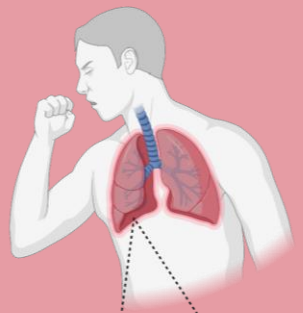
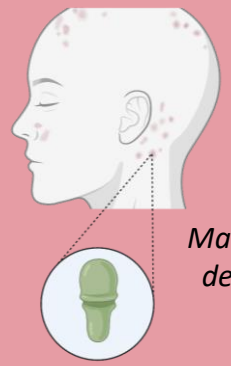
12 / 09 / 2023

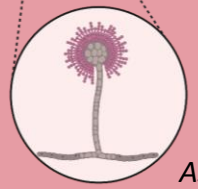
International Conference MICROBIOME ENGINEERING

Human pathogens



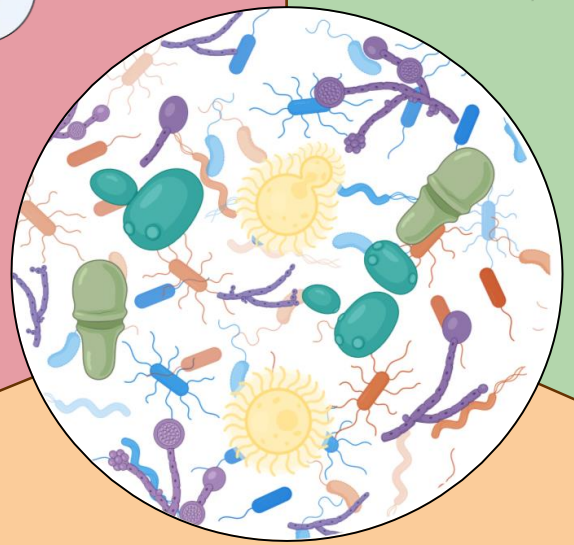


Malassezia dermatis

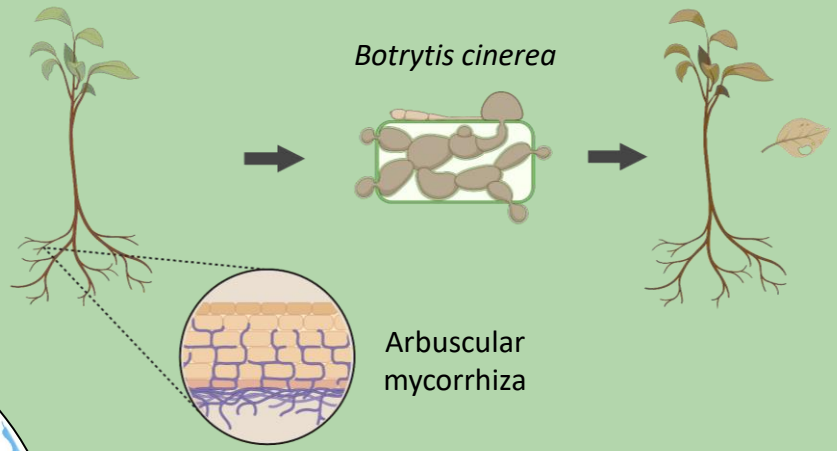


Aspergillus fumigatus

Candida albicans

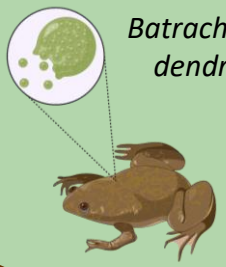


Environmental factors

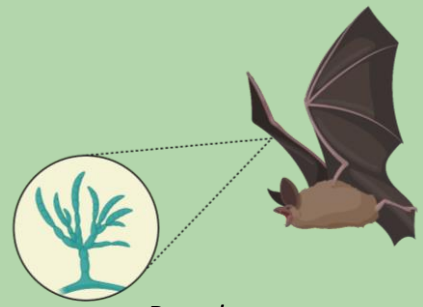


Botrytis cinerea

Arbuscular mycorrhiza



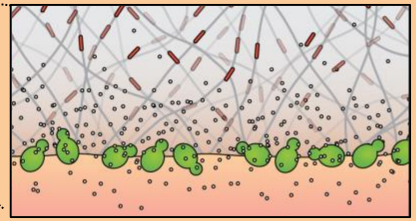
Batrachochytrium dendrobatidis



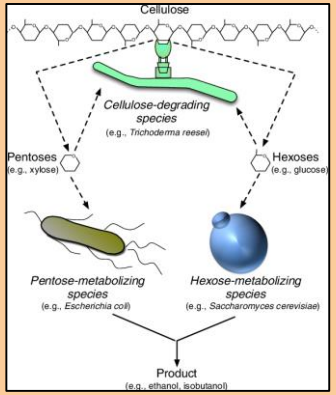
Pseudogymnoascus destructans

Production

Kombucha



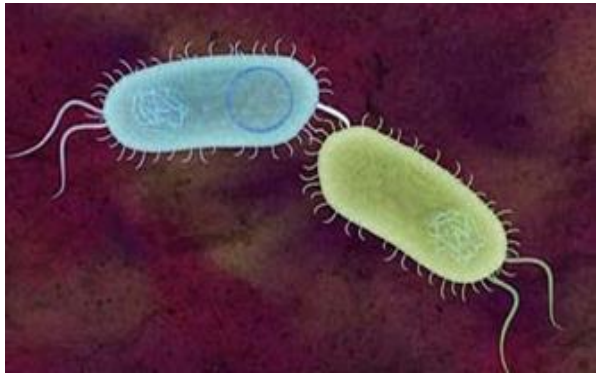
Gilbert et. al. 2019



Zomorrodi et. al. 2016

Image CC BY-SA 3.0, Michael Garten

Bacterial conjugation



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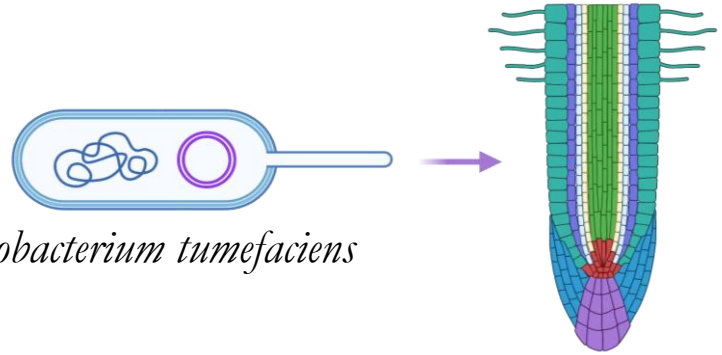
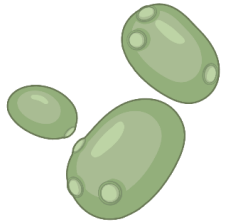
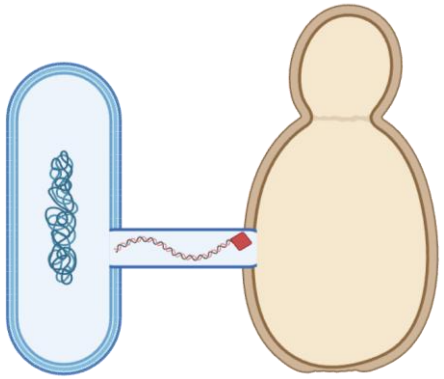


Agrobacterium tumefaciens



Yeast genera

Saccharomyces
Schizosaccharomyces
Kluyveromyces
Pichia
Pachysolen
Metschnikowia
Candida



E. coli
donor

S. cerevisiae
recipient

The problem with conjugation:

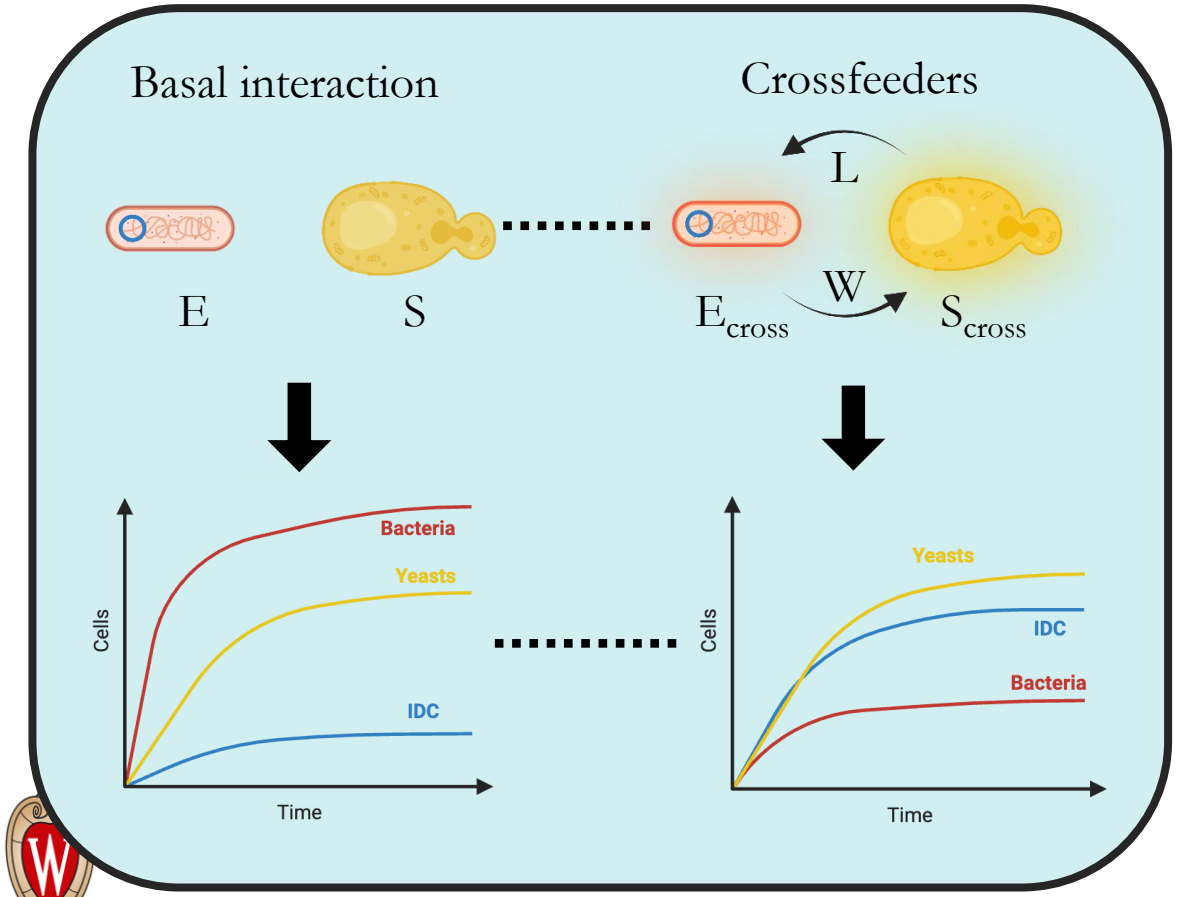
…it requires cell contact

How do we **increase** or **control** interdomain conjugation (IDC)?

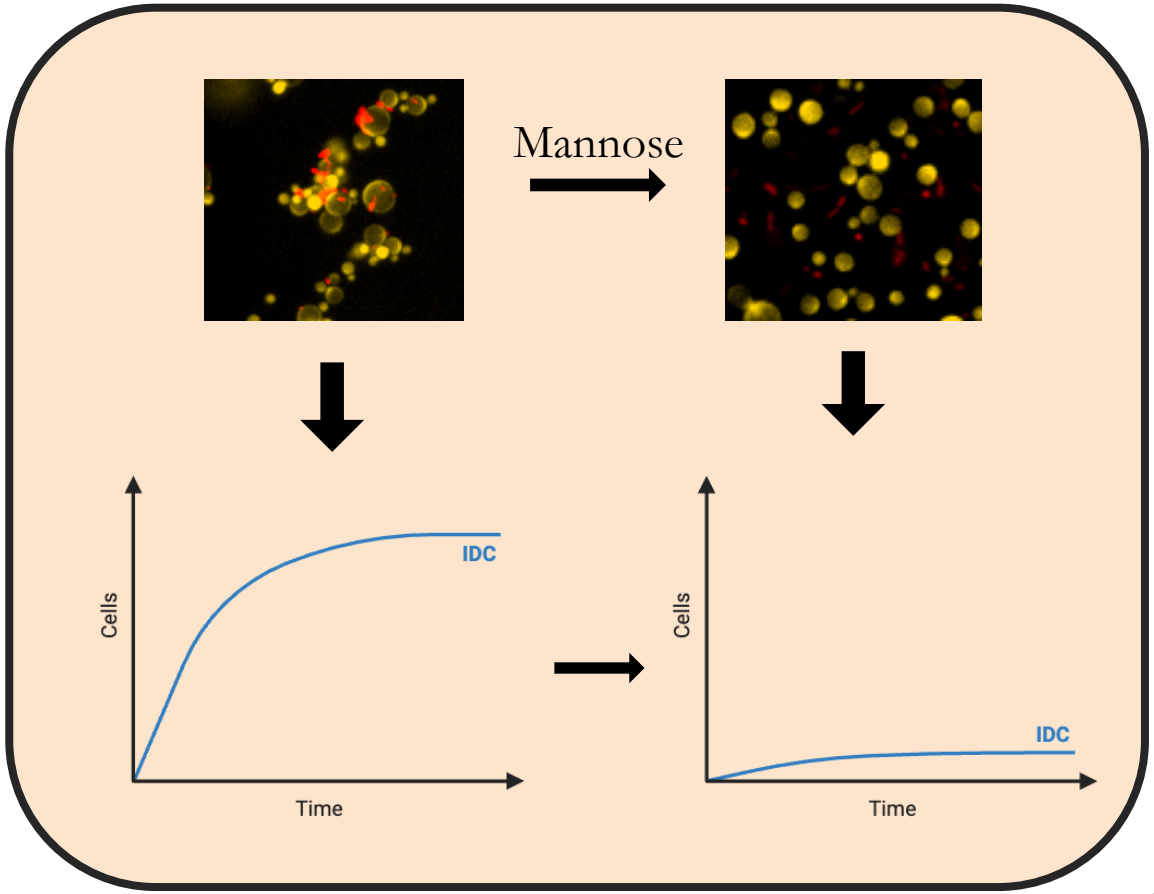
1. DNAtube, "Genetic Material Exchange in Bacterial Conjugation"

Knobs for control: population ratios and adhesion

Targeted mutations to find optimal growth conditions for IDC



Disruption of cell adhesion to interrupt IDC



Knobs for control: population ratios and adhesion

Targeted mutations to find optimal growth conditions for IDC

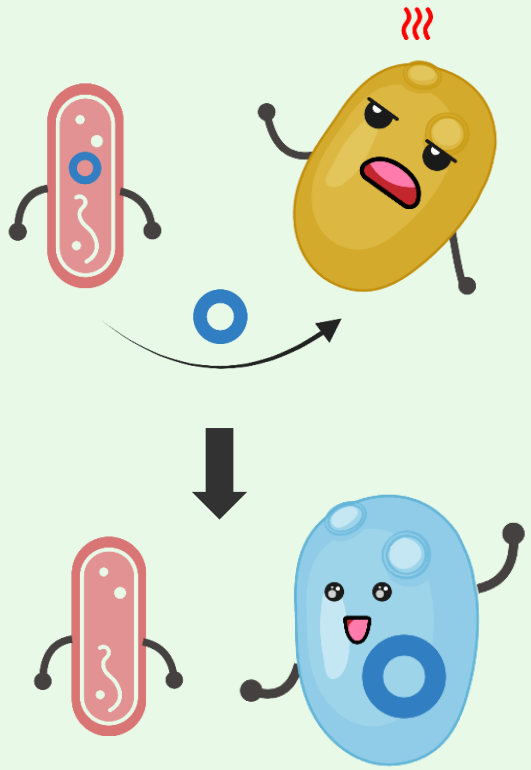
The **lower** the long-term donor-to-recipient ratio, the **higher** the net IDC

Disruption of cell adhesion to interrupt IDC

Adherent (clumped) cells result in ≥10x higher IDC, which can be disrupted

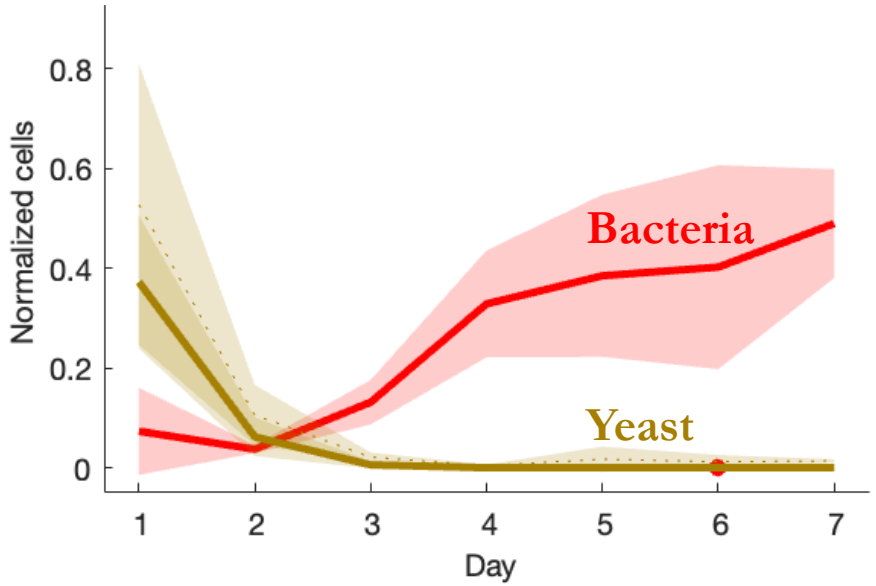
Can we use IDC to rescue a recipient population?

Rescue assay:
Make a sick population healthy by conjugating an essential gene

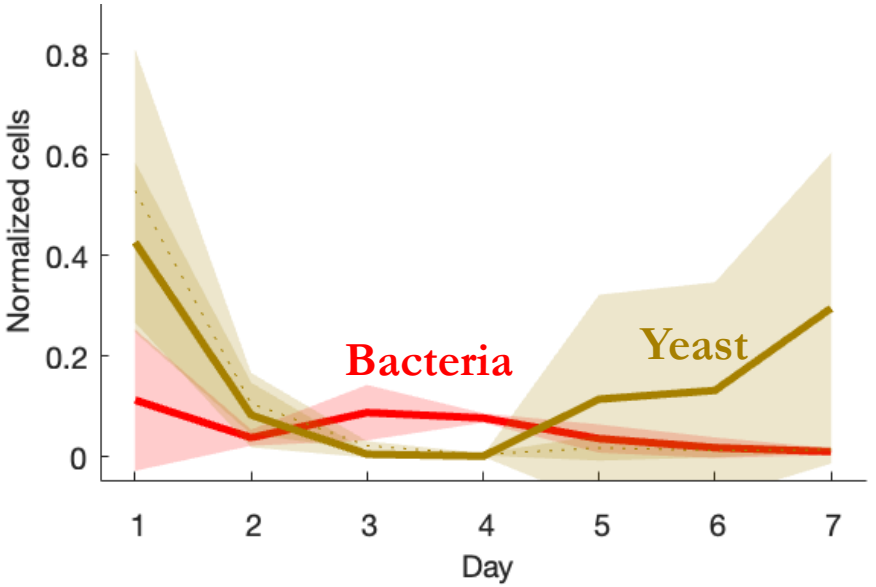


Unmodified donor (no tuning)

Mutant donor (tuned growth)



No rescue



Rescue

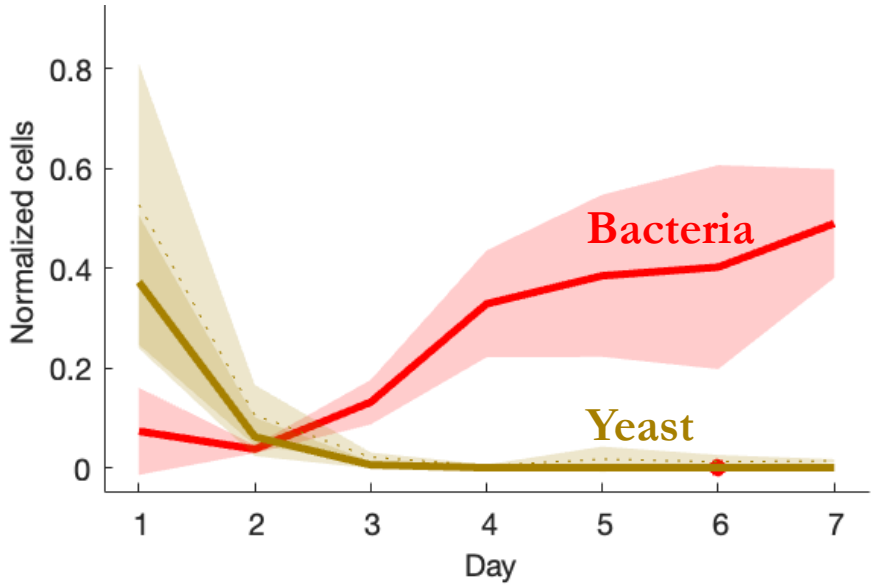
Can we use IDC to rescue a recipient population?

IDC can rescue a recipient population

IF

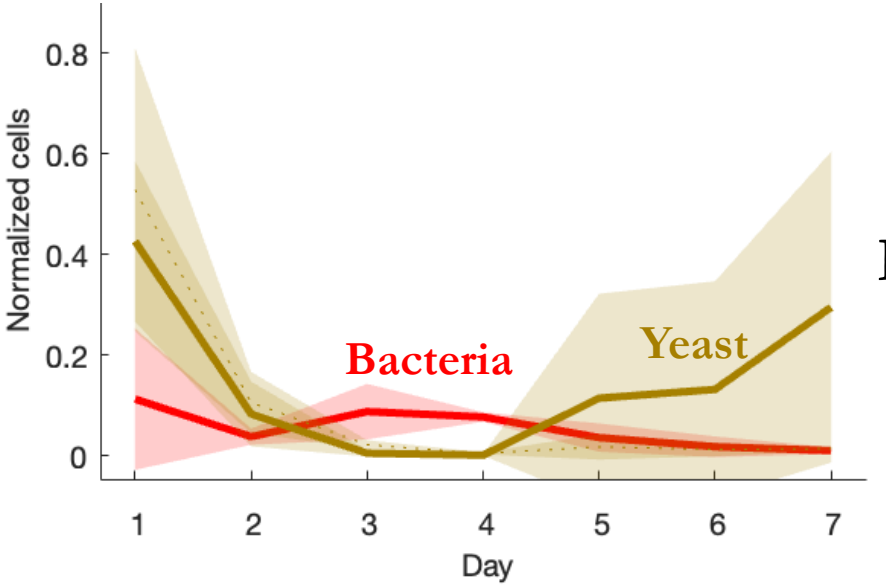
we tune populations

Unmodified donor
(no tuning)



No rescue

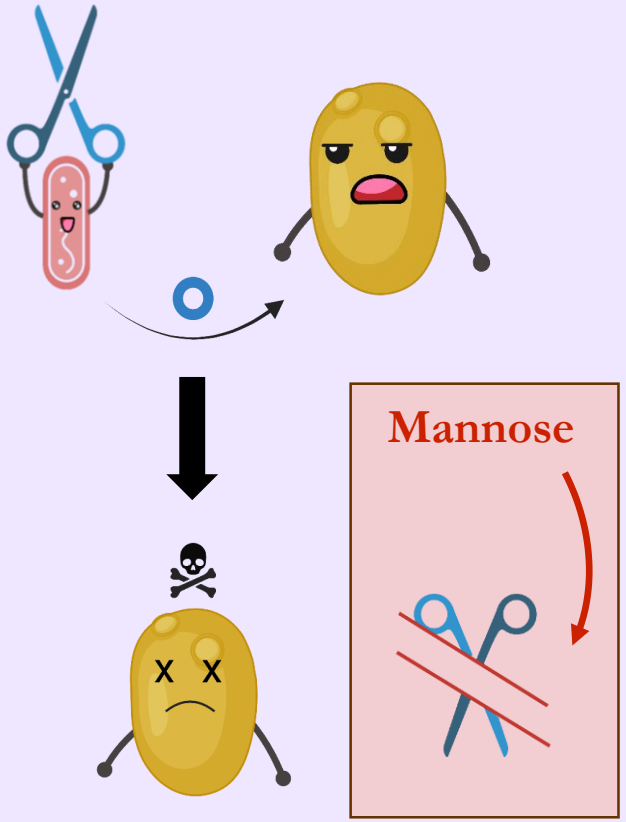
Mutant donor
(tuned growth)

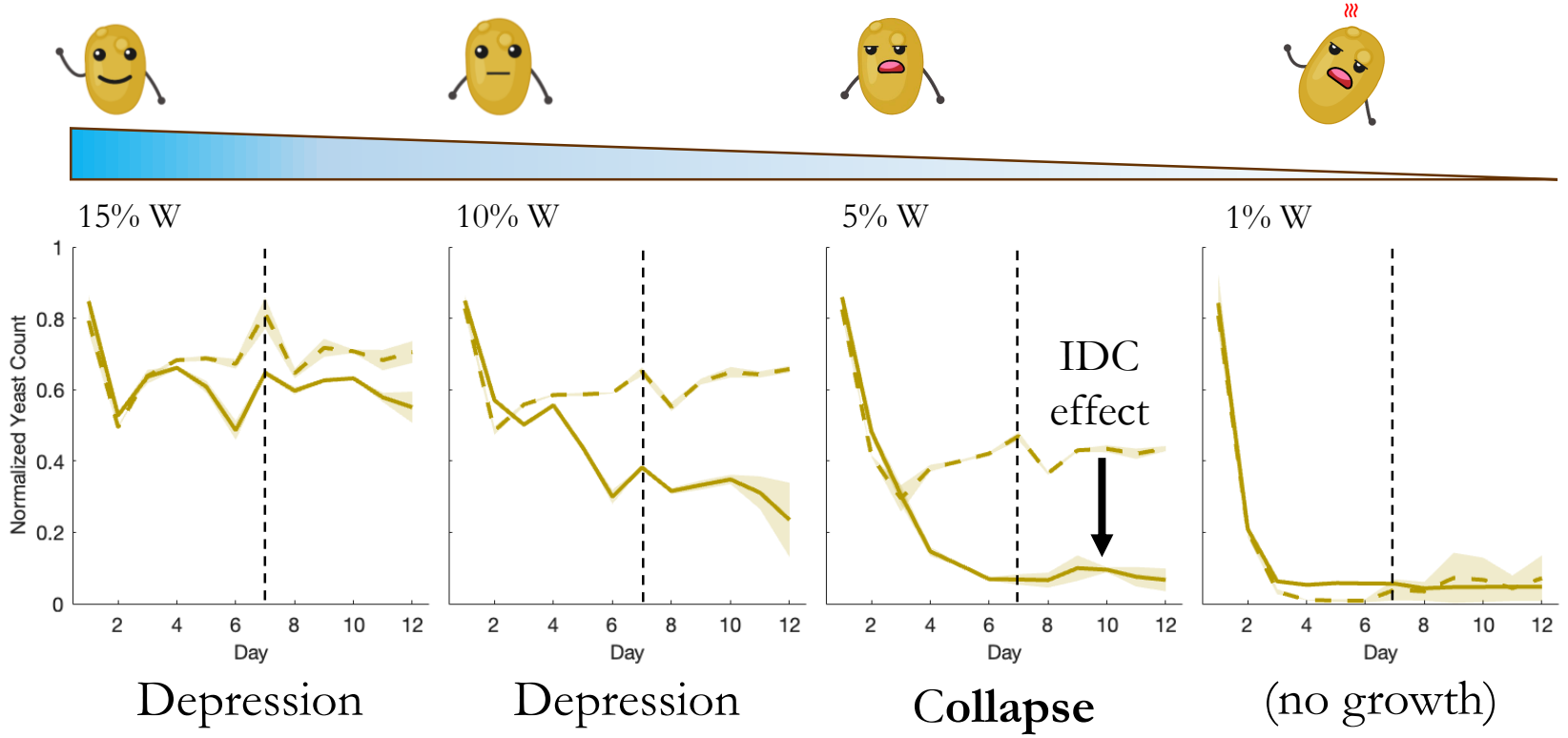


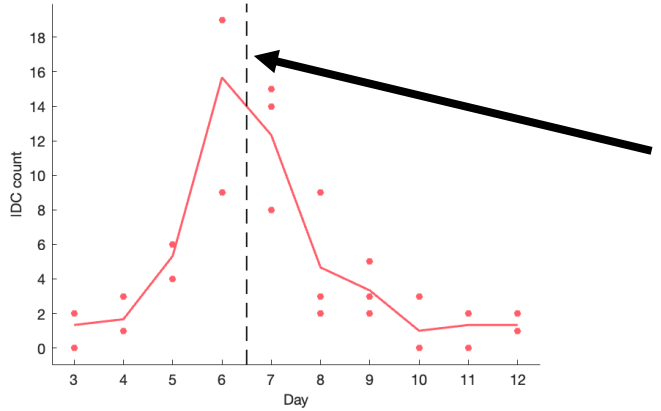
Rescue

Can we use IDC to kill a recipient population?

IDC-mediated CRISPR:
Depress or collapse recipients by cutting essential gene





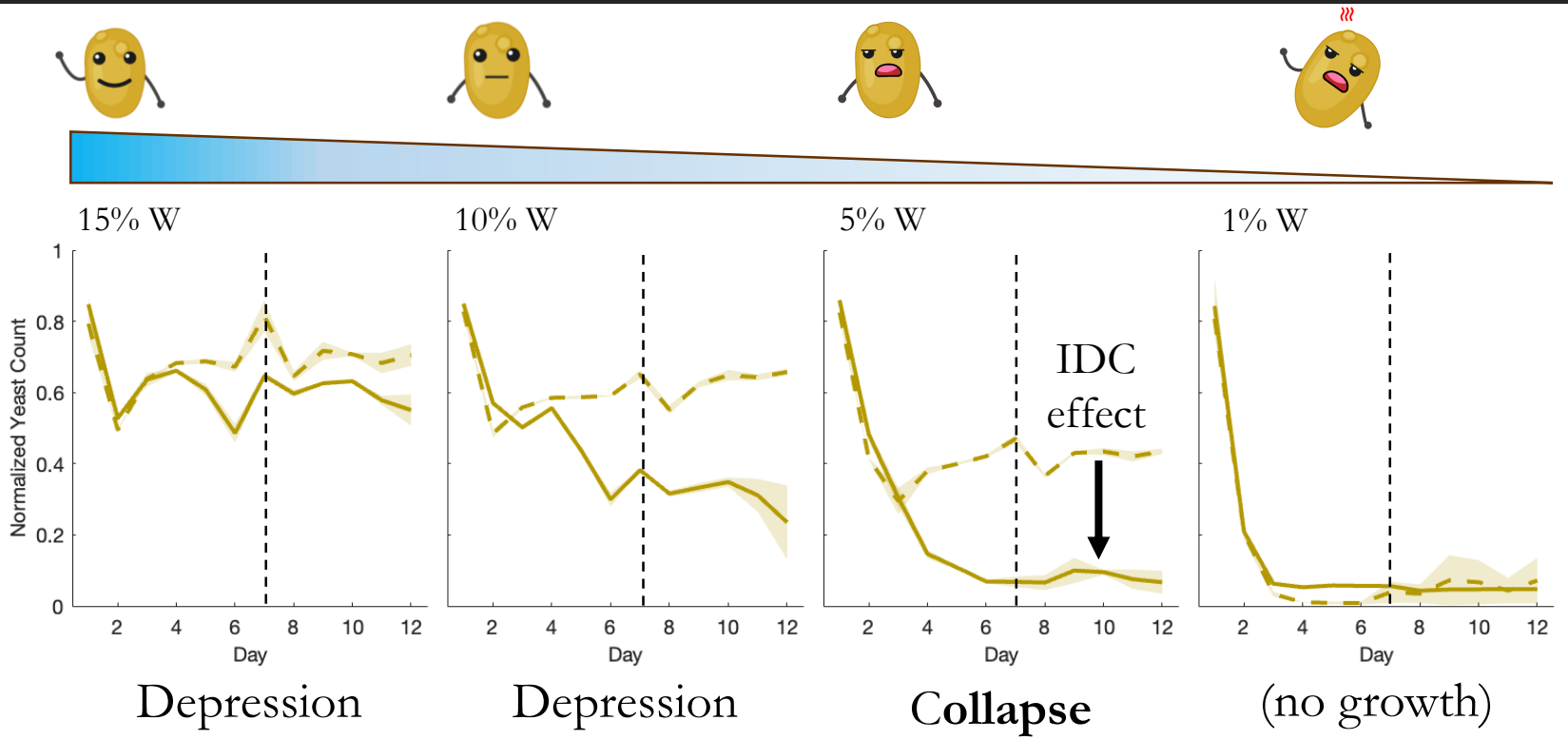


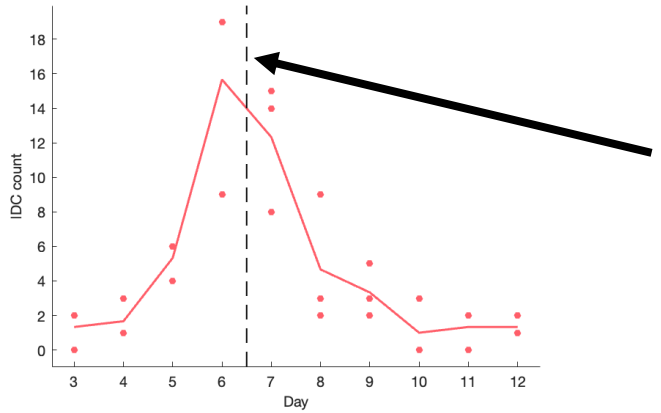
Mannose added, clumps disrupted, **IDC tapers off**

Can we use IDC to kill a recipient population?

IDC can depress or collapse recipient populations

We can interrupt IDC function by disrupting cell clumps





Mannose added, clumps disrupted, **IDC tapers off**

Acknowledgements

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- **Megan McClean**
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- Ryan Cochrane
- Maximilian Soltysiak

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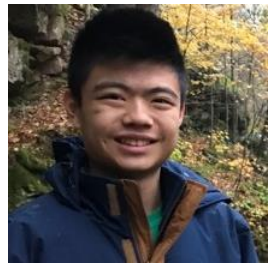
- Samuel Moss



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Find out more at the poster session!