

Stochastic acquisition of the gut microbiome in *Drosophila*

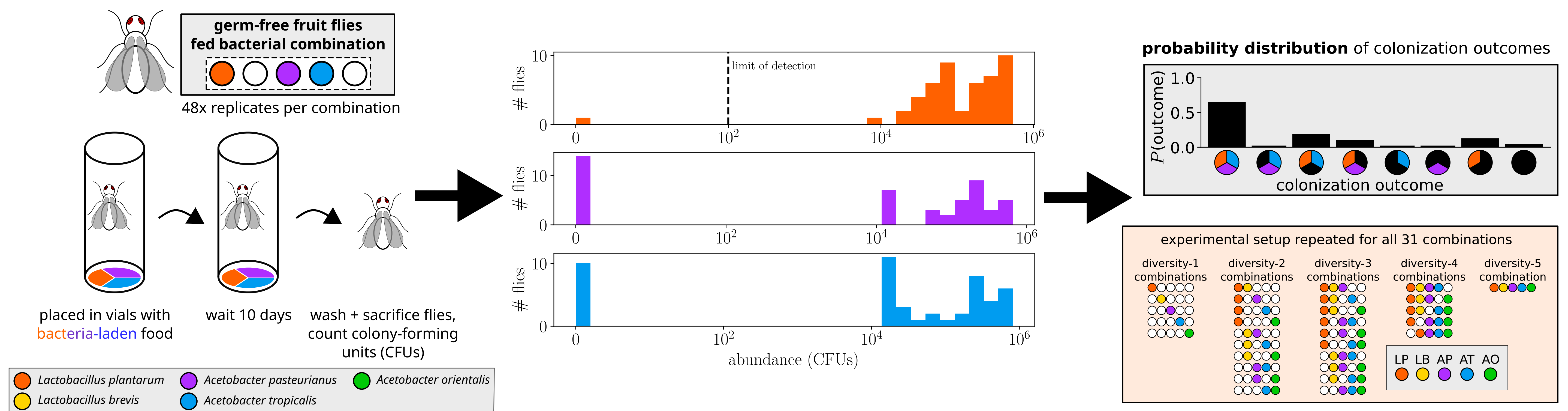
Banting and PIMS
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Experimental
overview

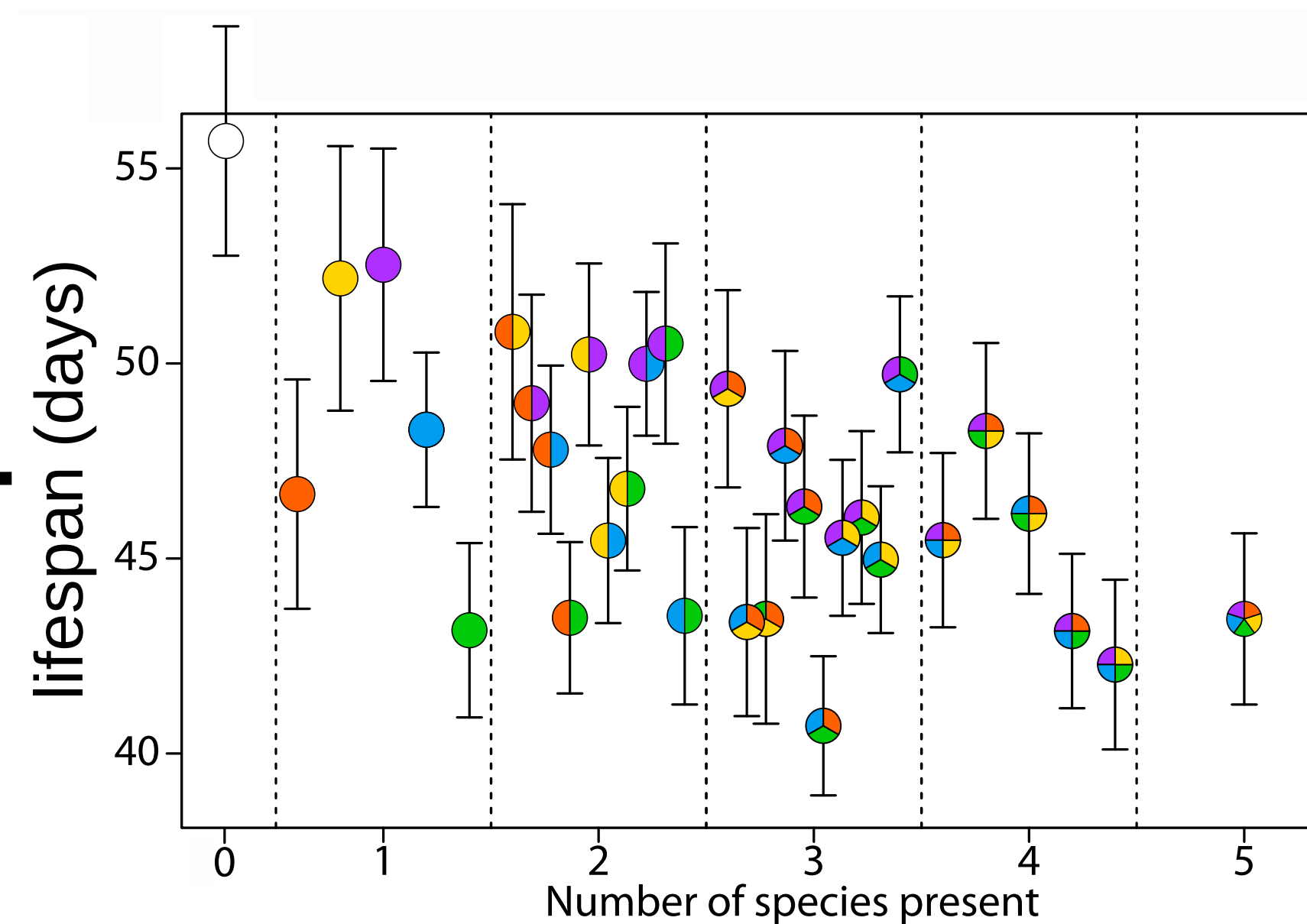


Motivation

Microbiome composition affects human health¹

- commensal microbes train immune system
- imbalanced microbiome associated w/ obesity, Crohn's disease, type-2 diabetes
- in *Drosophila*, microbiome composition causally affects fly lifespan and fecundity²

The human microbiome is as unique as a fingerprint, but **how was this variability established?**
We demonstrate that this variability is at least partially driven by **stochastic microbiome assembly**.



Microbiome-based medicine shows promise for many human diseases³

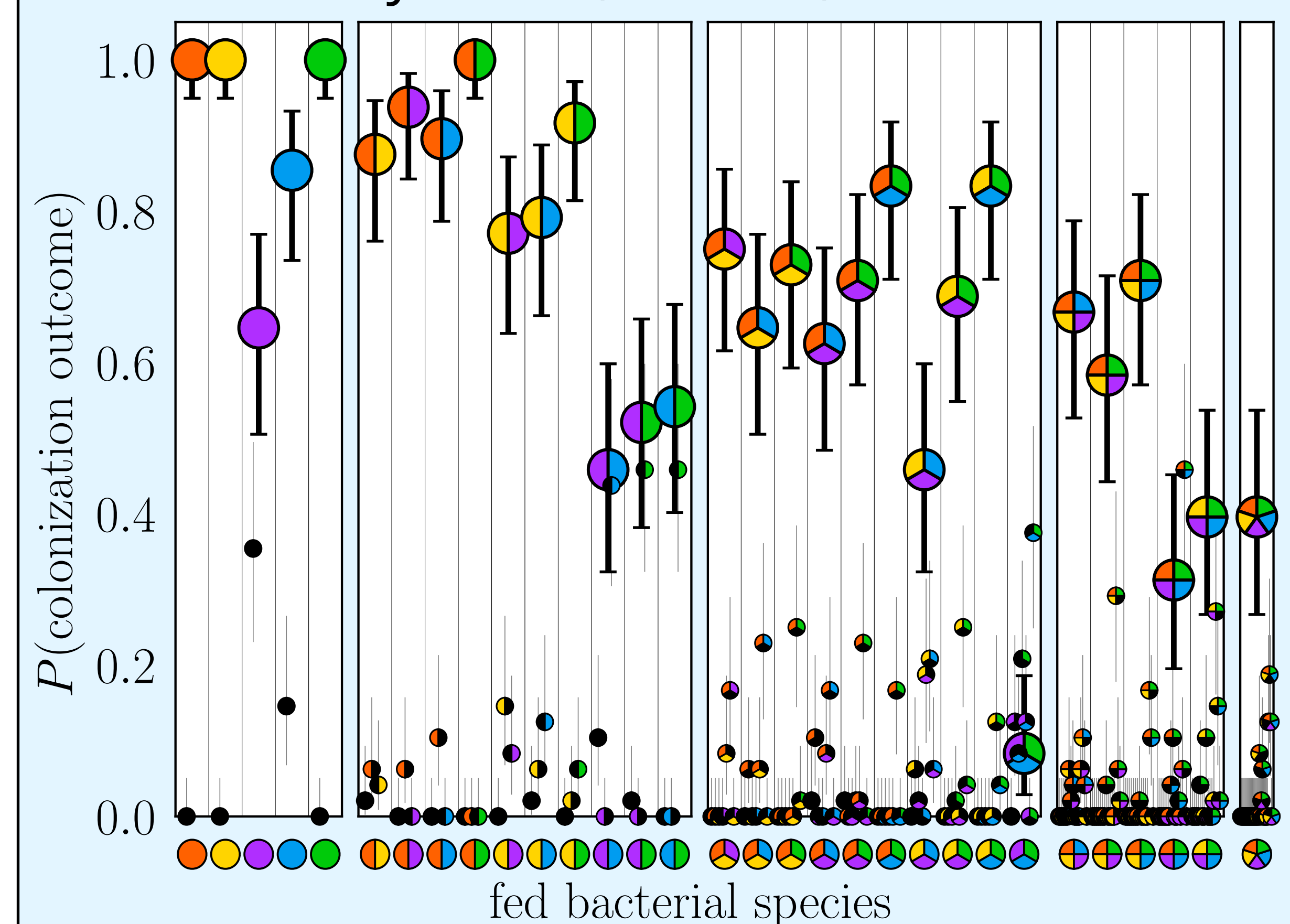
- fecal microbiota transplantation (FMT) relies on successfully engrafting a set of "healthy" microbes into a sick person's gut
- FMT treats *C. difficile* infection, ulcerative colitis; can even improve immunotherapy outcomes

Stochastic microbiome assembly underpins FMT treatments.

Our research helps answer the clinical question: "Which microbes in an FMT will stick in a patient's gut?"

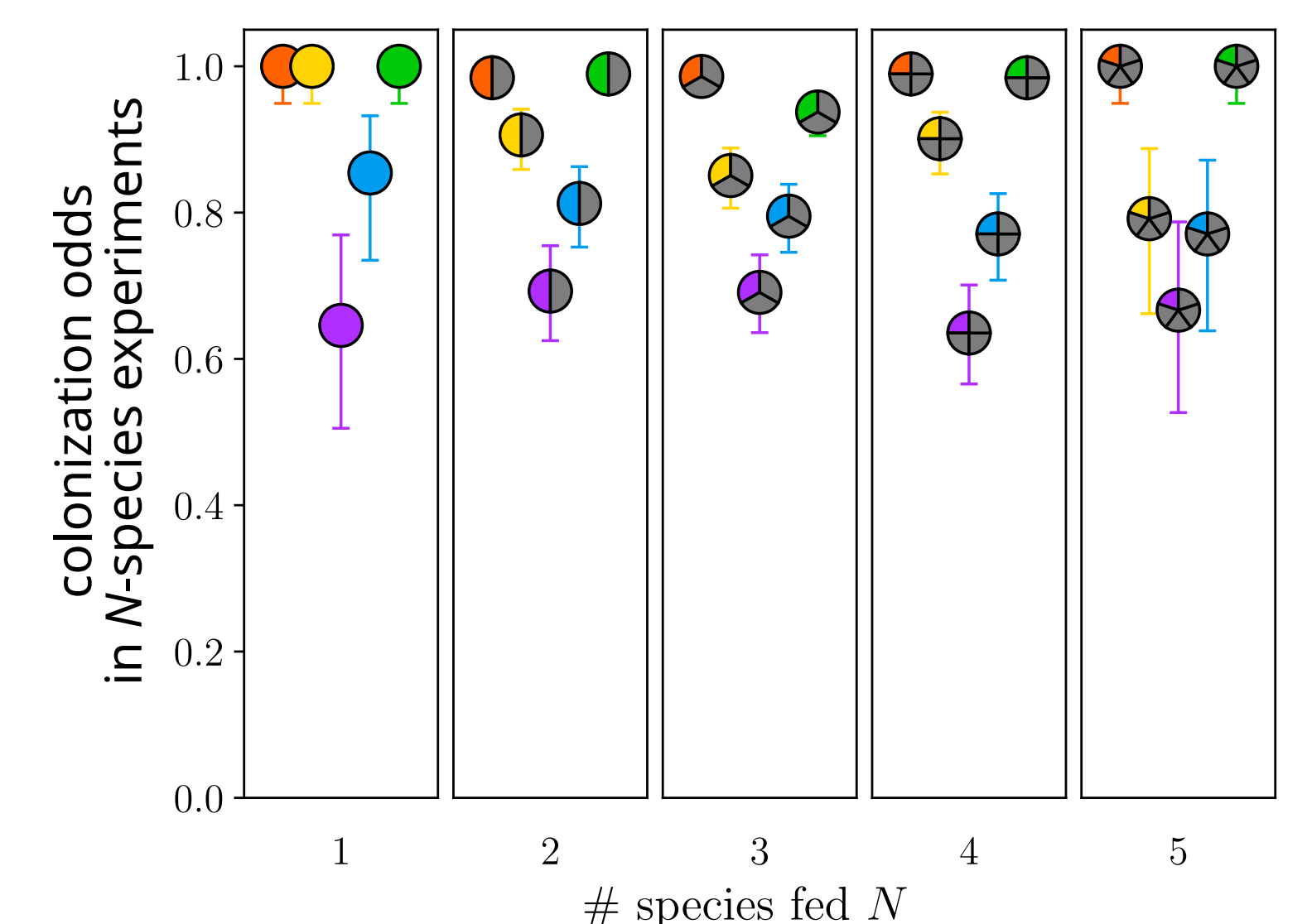
Empirical findings

Variability in colonization outcomes even in flies identically reared, housed, and fed



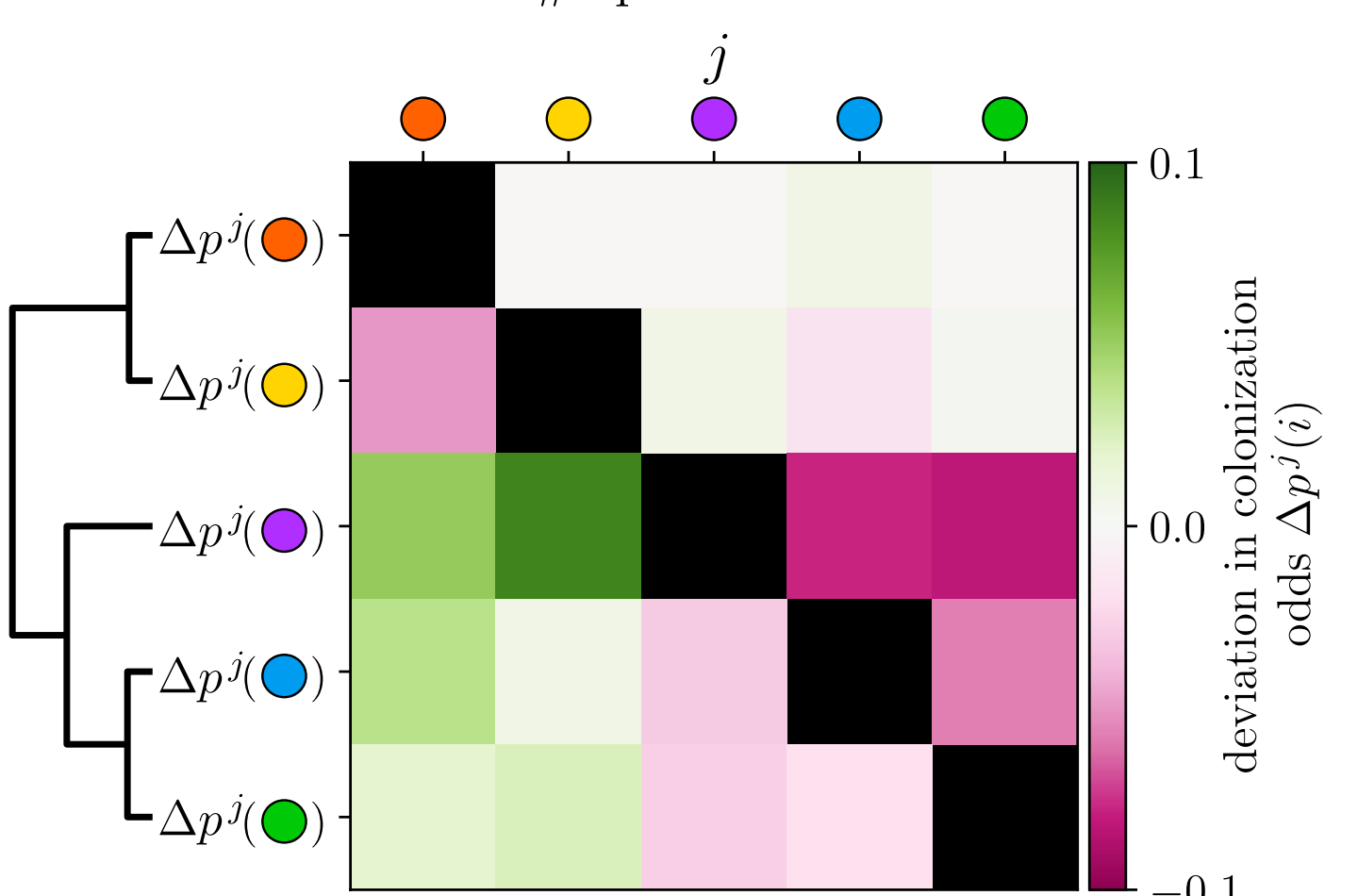
Colonization odds are species- and diversity-dependent

- some bacterial species (orange and green) are strong colonizers; others (purple) are weak
- single-species experiments are insufficient to capture colonization ability of bacterial species
- useful to know which species in an FMT are strong colonizers (likely to stick) versus weak



Colonization odds depend on context

- colonization odds of *Acetobacter* species (purple, blue, green) are higher when fed with *Lactobacillus* species (orange, yellow), and are lower when fed with other *Acetobacter* species
- inference of interactions between species based on presence/absence patterns
- useful to know which species in an FMT facilitate versus inhibit another species' colonization



Modeling
results

Model the probability of each colonization outcome w/ independent marginal probs

e.g. fed bacterial combination $\equiv S$

$$P(\text{outcome}) = p(\text{orange}) * p(\text{purple}) * [1 - p(\text{orange})]$$

in general for $R \subseteq S$,

$$P(i \in R \text{ colonize}) = \prod_{i \in R} p_i \prod_{j \in S \setminus R} (1 - p_j)$$

for marginal probabilities p_i

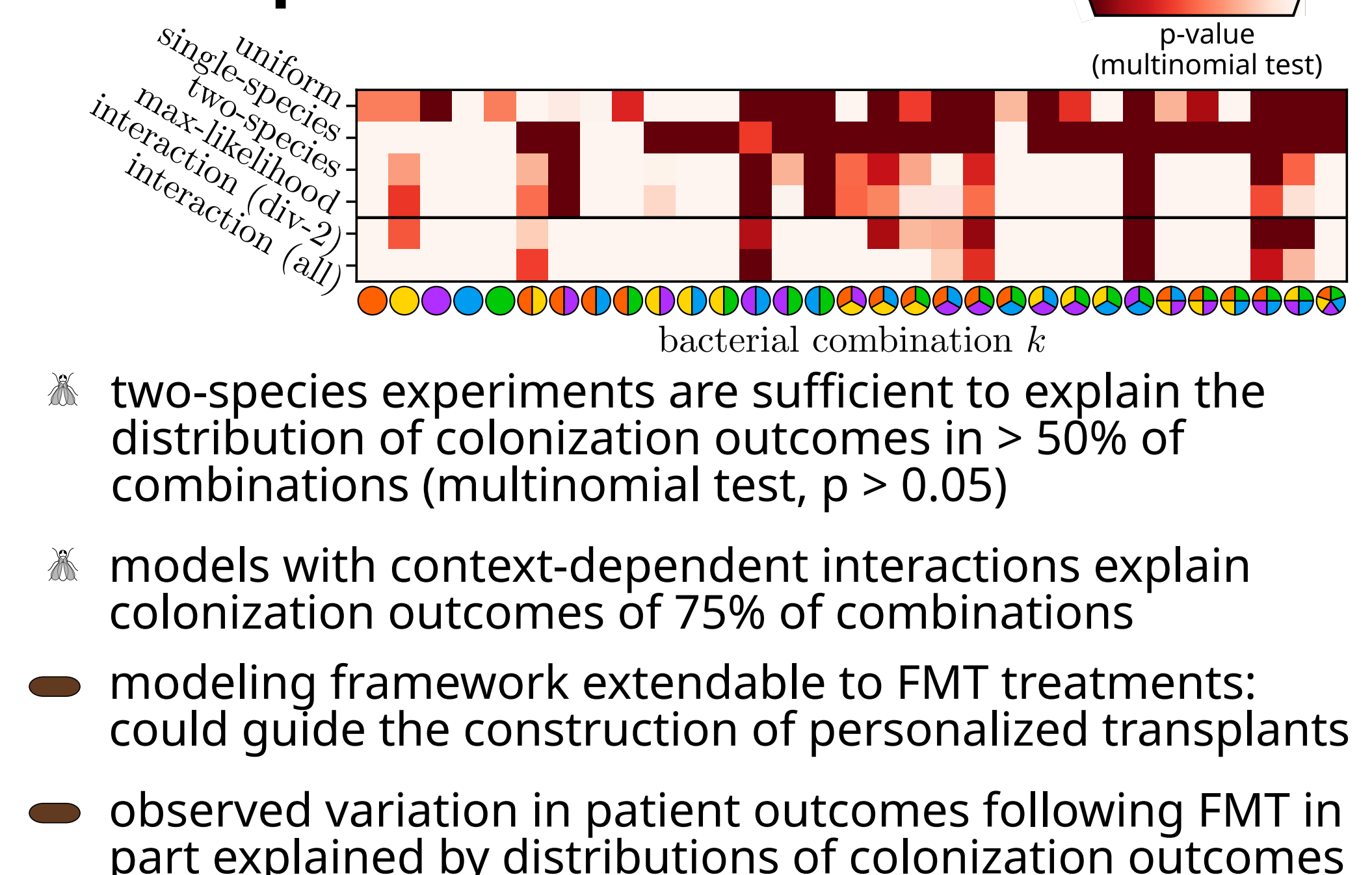
Colonization models w/ fixed marginal probabilities

model	fit to combs	# combs explained
uniform	diversity-1	10/31
single-species	diversity-1	8/31
two-species	diversity-2	18/31
max-likelihood	all	20/31

Colonization model w/ context-specific marginal probabilities

interaction	all	# combs explained
interaction	all	24/31

Model performances



References

Poster adapted from Jones et al., *PNAS* 2022
[1] Gilbert et al., *Nat. Med.* 2018; [2] Gould et al., *PNAS* 2018; [3] Kim and Gluck, *Clin. Endosc.* 2019