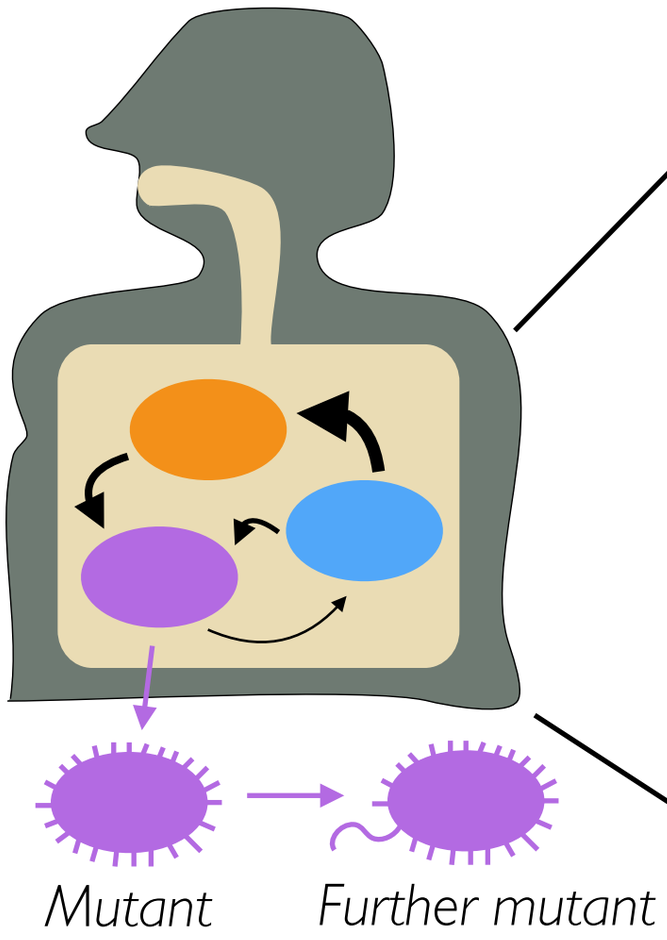
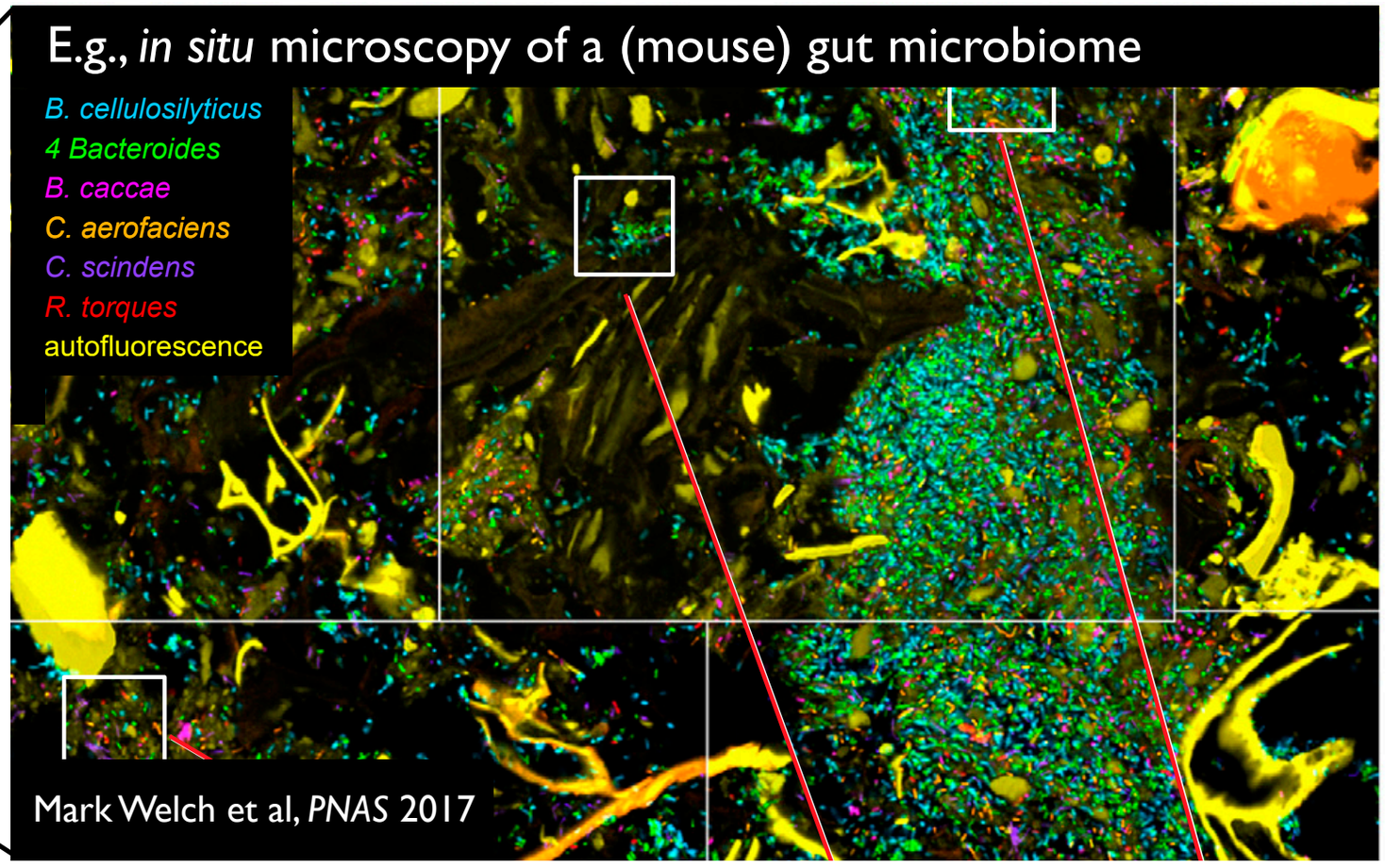
Evolutionary dynamics of commensal gut bacteria within and across hosts

Benjamin Good
Assistant Professor of Applied Physics
Stanford University

Bridging Population and Quantitative Genetics 7/6/22
Kavli Institute for Theoretical Physics

Understanding the *collective behavior* of microbial communities



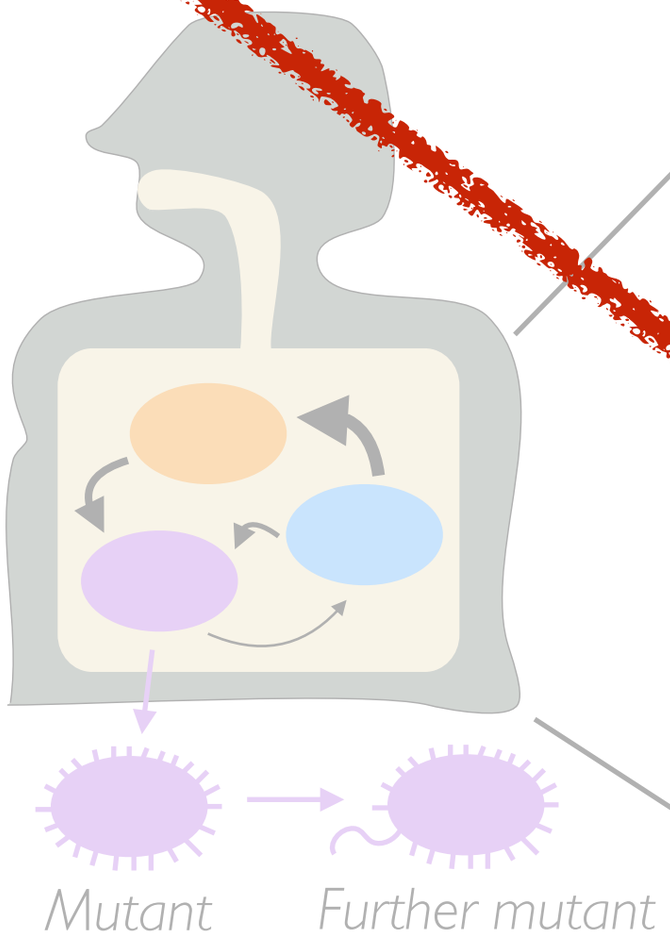


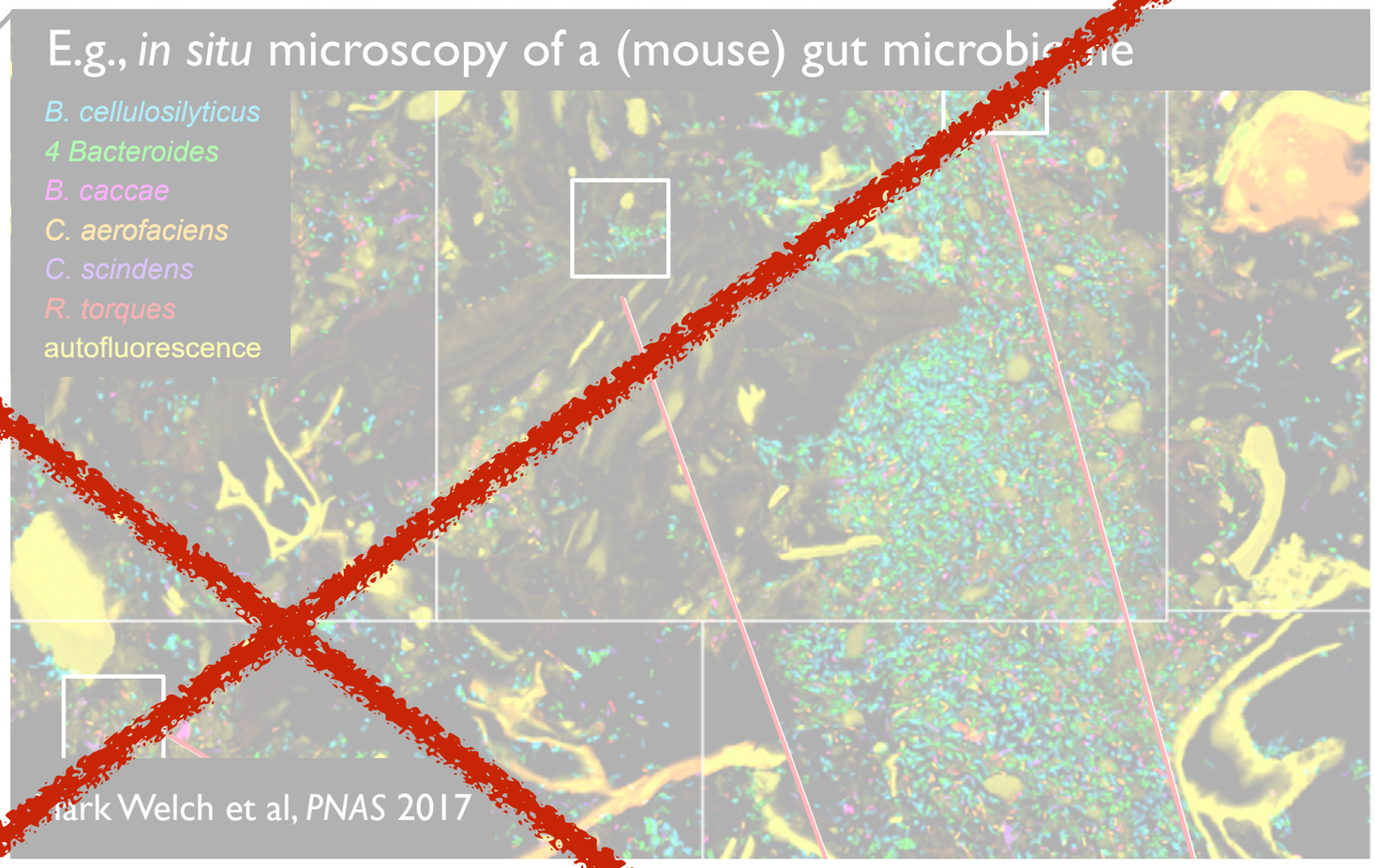
Challenges:

1. Structure & function emerge from many interacting parts ***(ecology)***
2. Residents can potentially evolve over time ***(evolution)***

(**pathogens, lab expt's:** Δt ~ years, months, days)

Understanding the *collective behavior* of microbial communities





Challenges:

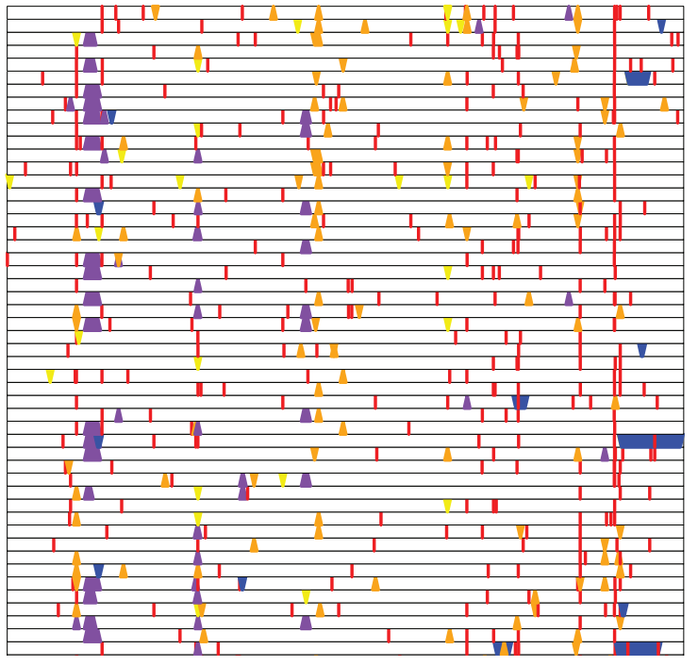
1. Structure & function emerge from many interacting parts ***(ecology)***

2. Residents can potentially evolve over time ***(evolution)***

(**pathogens, lab expt's:** Δt ~ years, months, days)

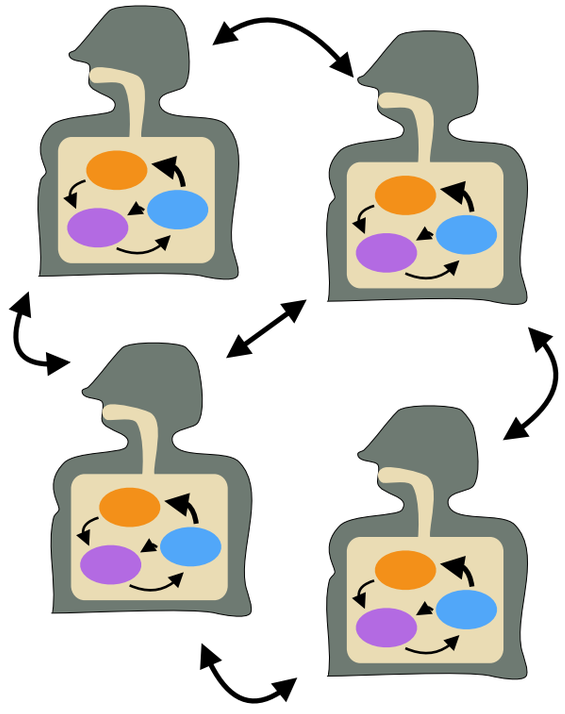
Gut microbiome as a model system for studying evolution

Experimental evolution

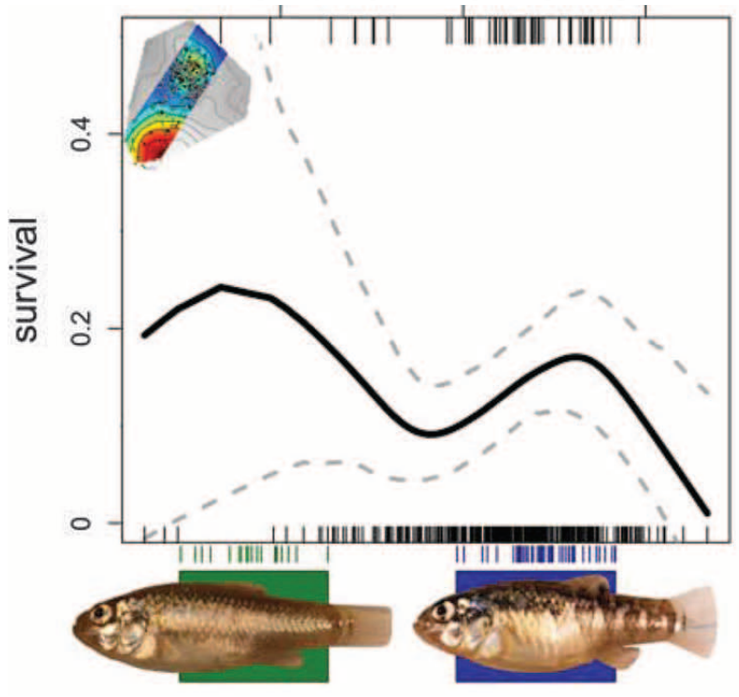


Tenaillon et al (2012)

Commensal gut bacteria



Natural variation



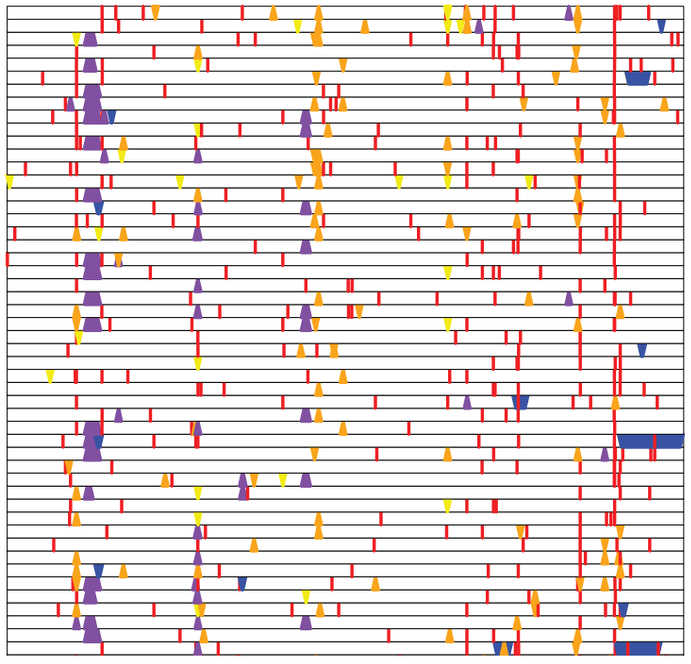
Martin & Wainright (2013)

← greater control

greater realism →

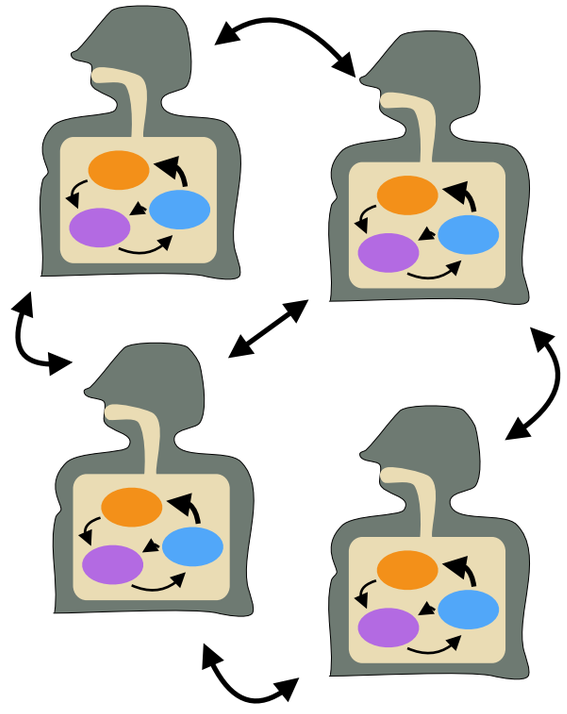
Gut microbiome as a model system for studying evolution

Experimental evolution

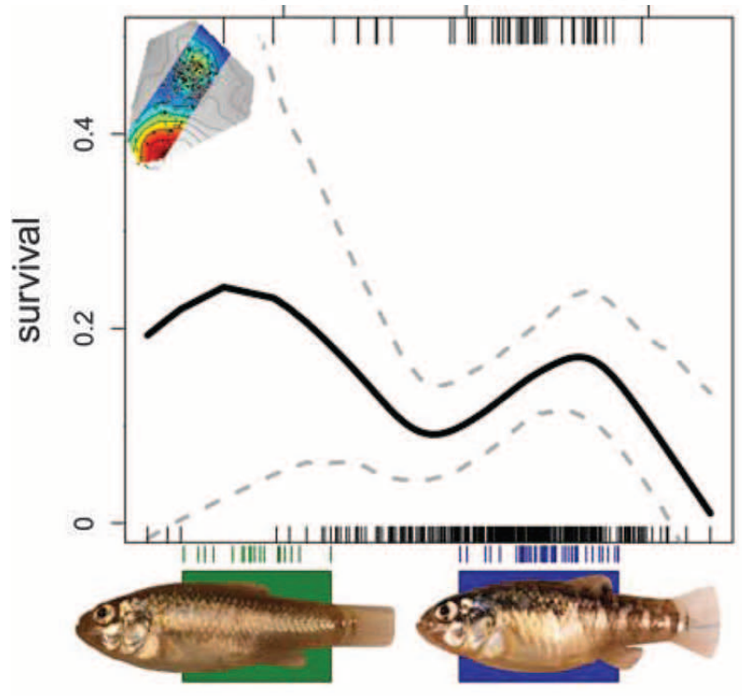


Tenaillon et al (2012)

Commensal gut bacteria



Natural variation



Martin & Wainright (2013)

←greater control

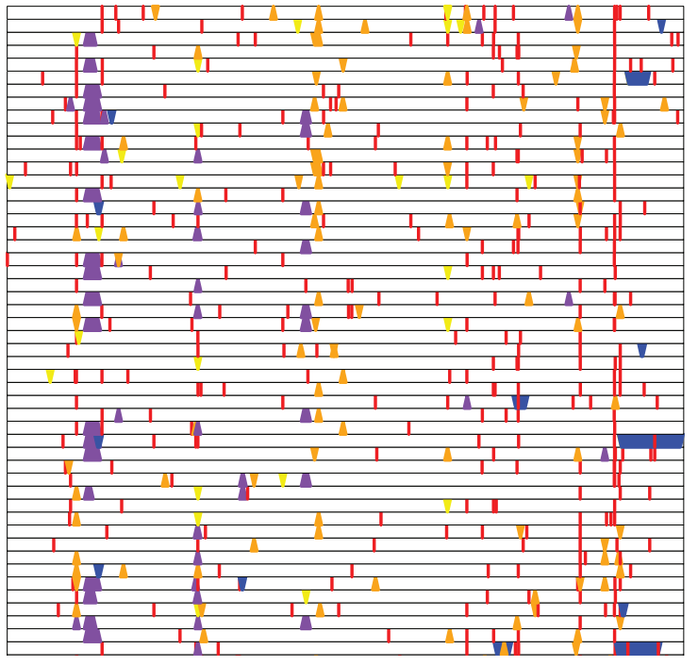
greater realism→

Advantages: **1.** Hosts = semi-isolated, complex ecosystems

>10^{12} cells, ~100 species

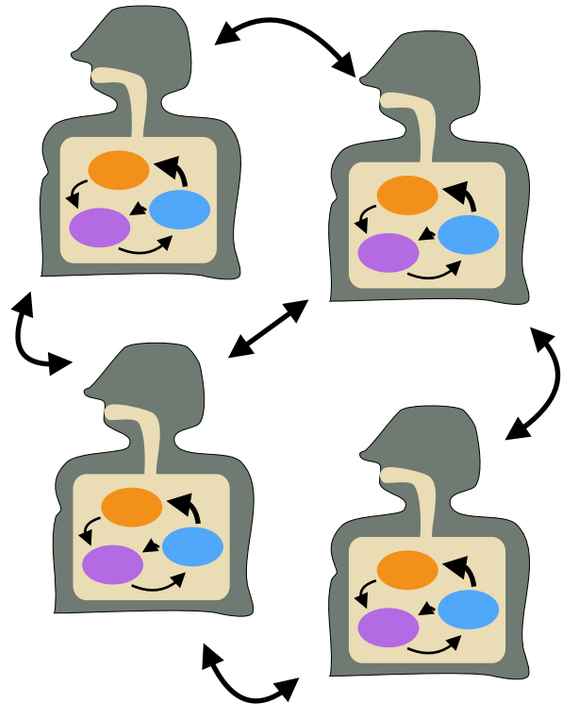
Gut microbiome as a model system for studying evolution

Experimental evolution

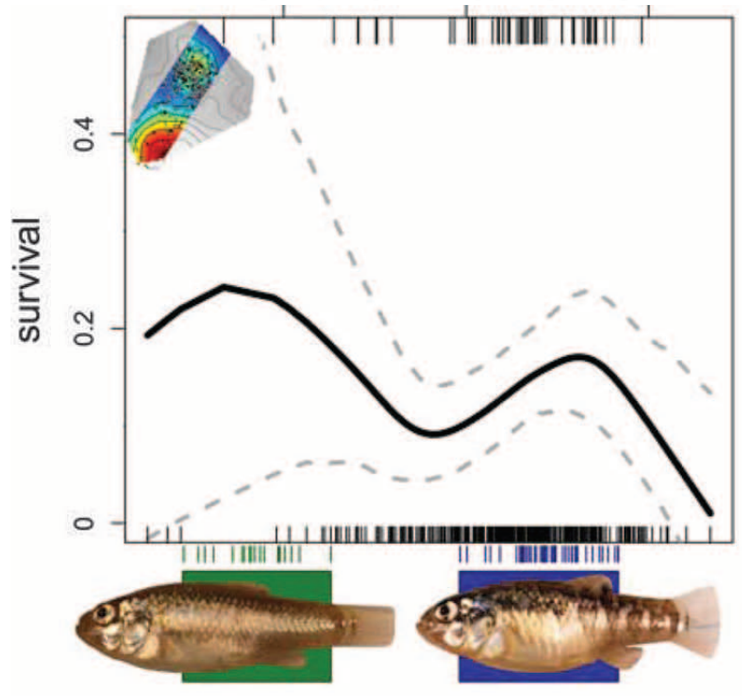


Tenaillon et al (2012)

Commensal gut bacteria



Natural variation



Martin & Wainright (2013)

← greater control

greater realism →

Advantages: **1.** Hosts = semi-isolated, complex ecosystems

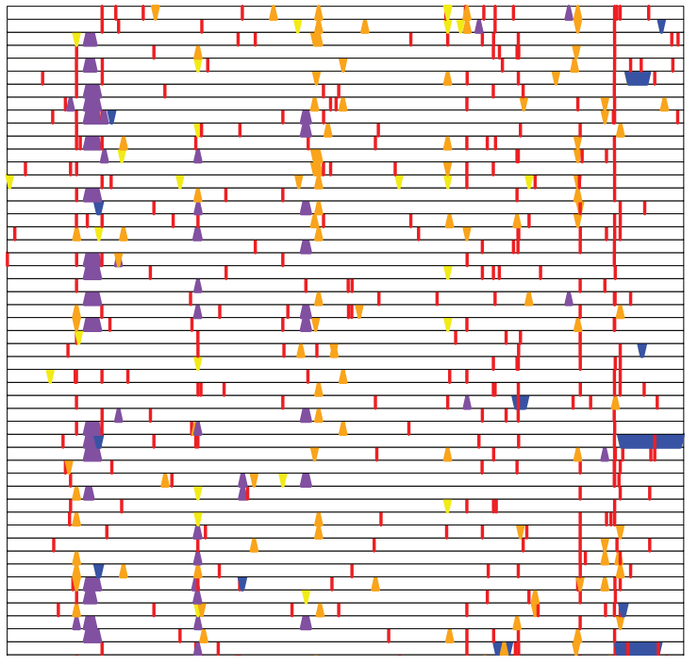
>10^{12} cells, ~100 species

2. Non-destructive sampling (feces)

~1-10 gens/day

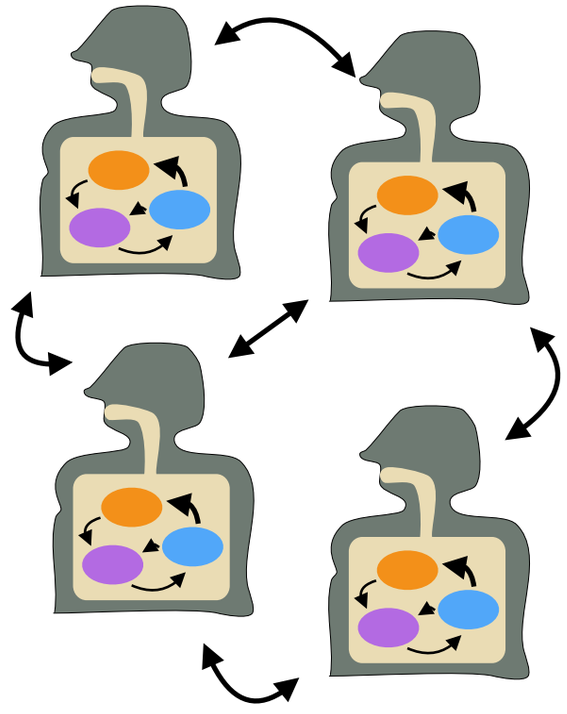
Gut microbiome as a model system for studying evolution

Experimental evolution

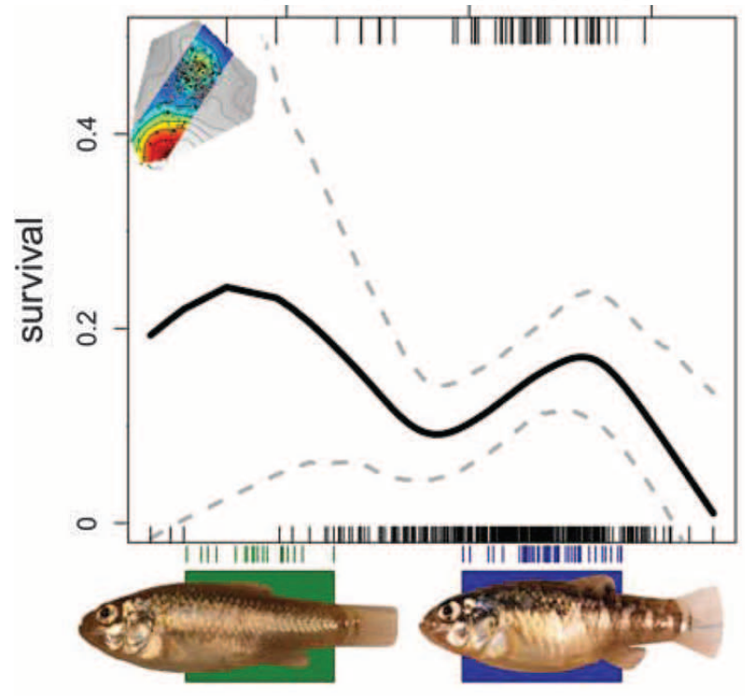


Tenaillon et al (2012)

Commensal gut bacteria



Natural variation



Martin & Wainright (2013)

← greater control

greater realism →

Advantages: **1.** Hosts = semi-isolated, complex ecosystems

>10^{12} cells, ~100 species

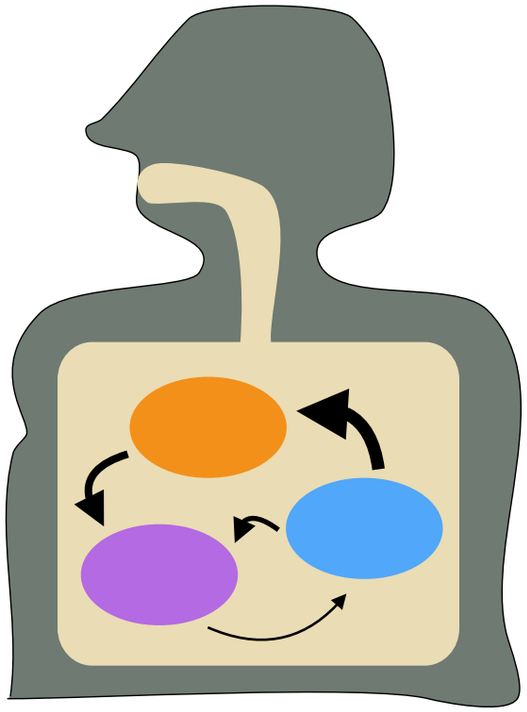
2. Non-destructive sampling (feces)

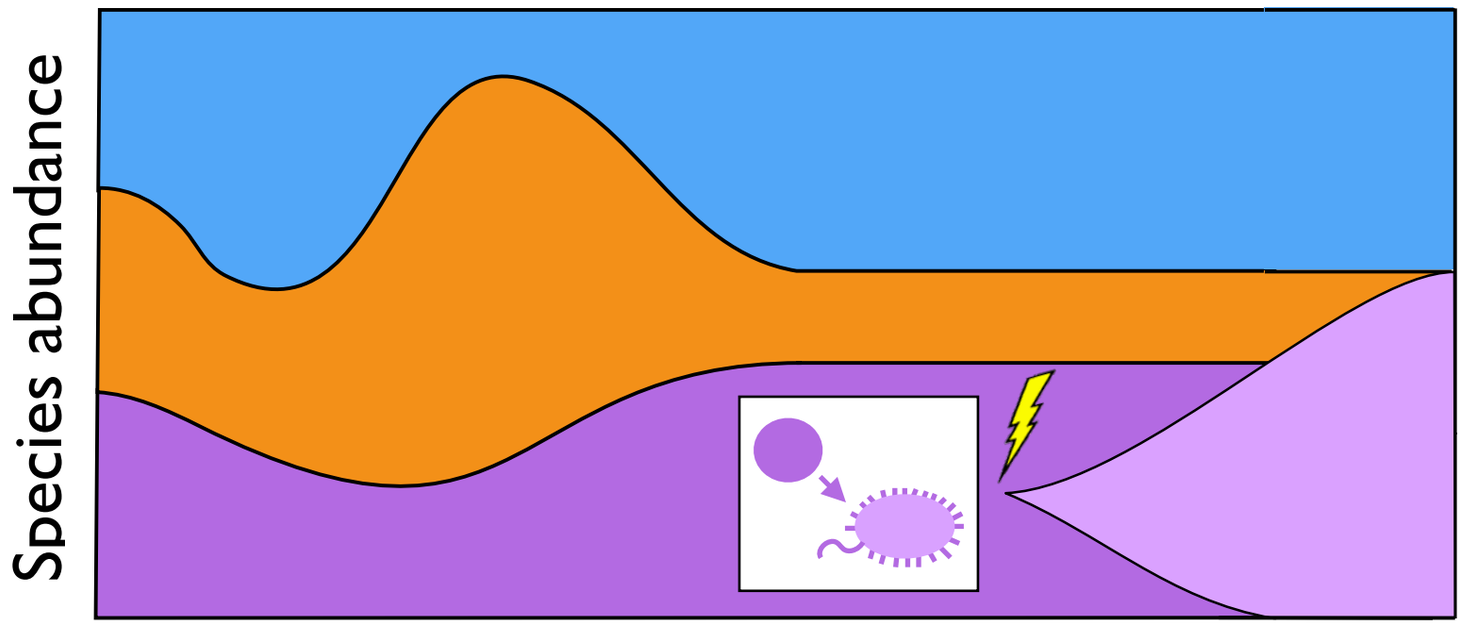
~1-10 gens/day

3. Biomedical applications

>> genomic resources

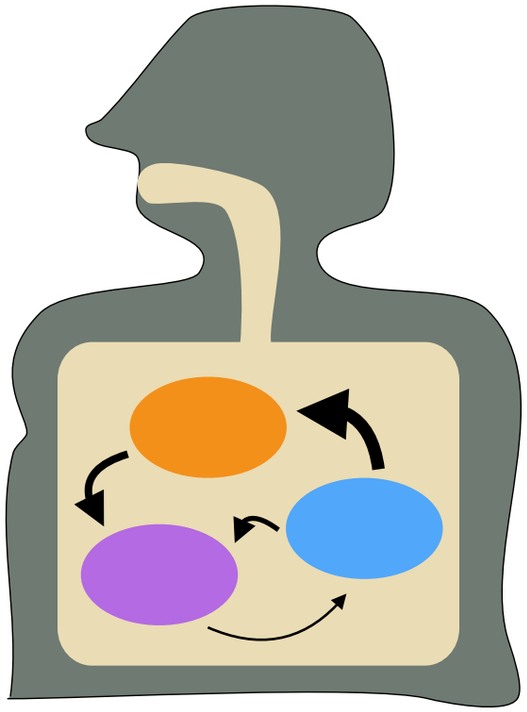
Is short-term evolution important in the gut microbiome?

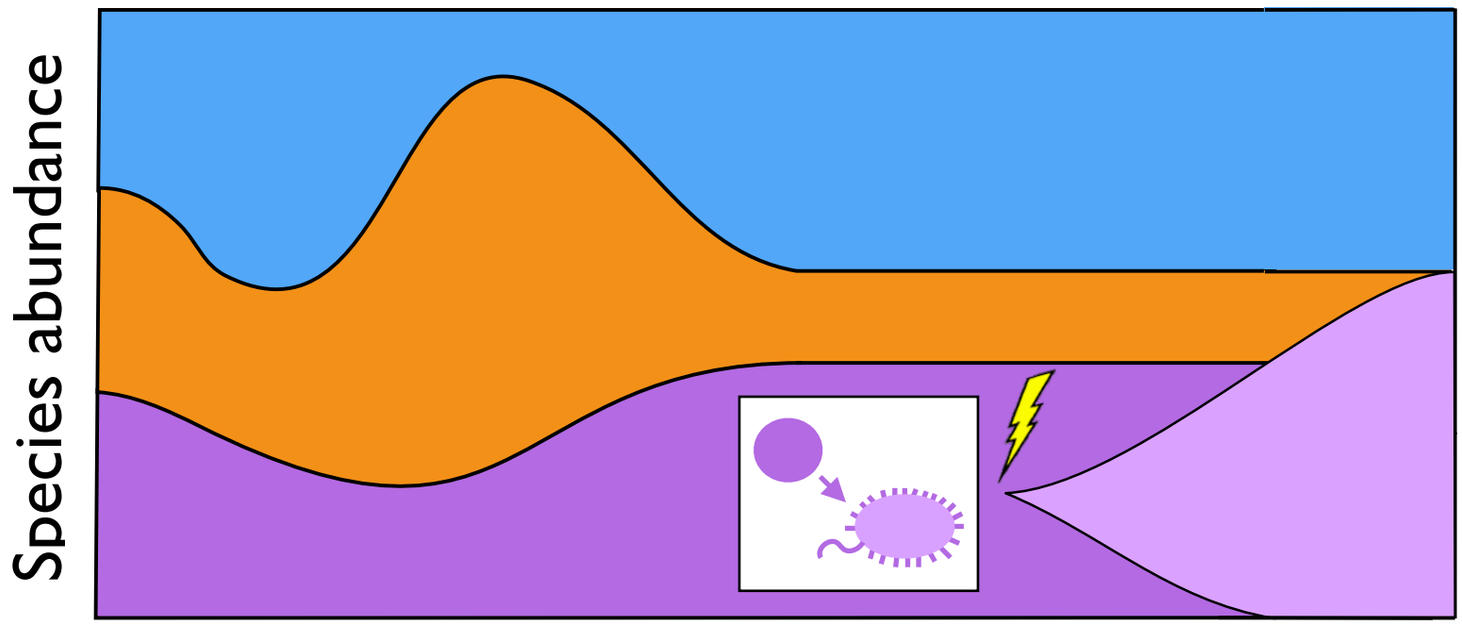




Problem: little empirical data. **Many basic questions still not known.**

Is short-term evolution important in the gut microbiome?

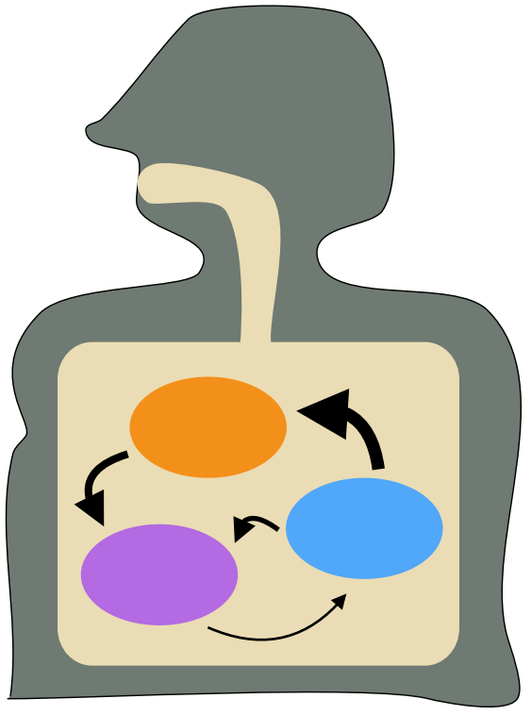


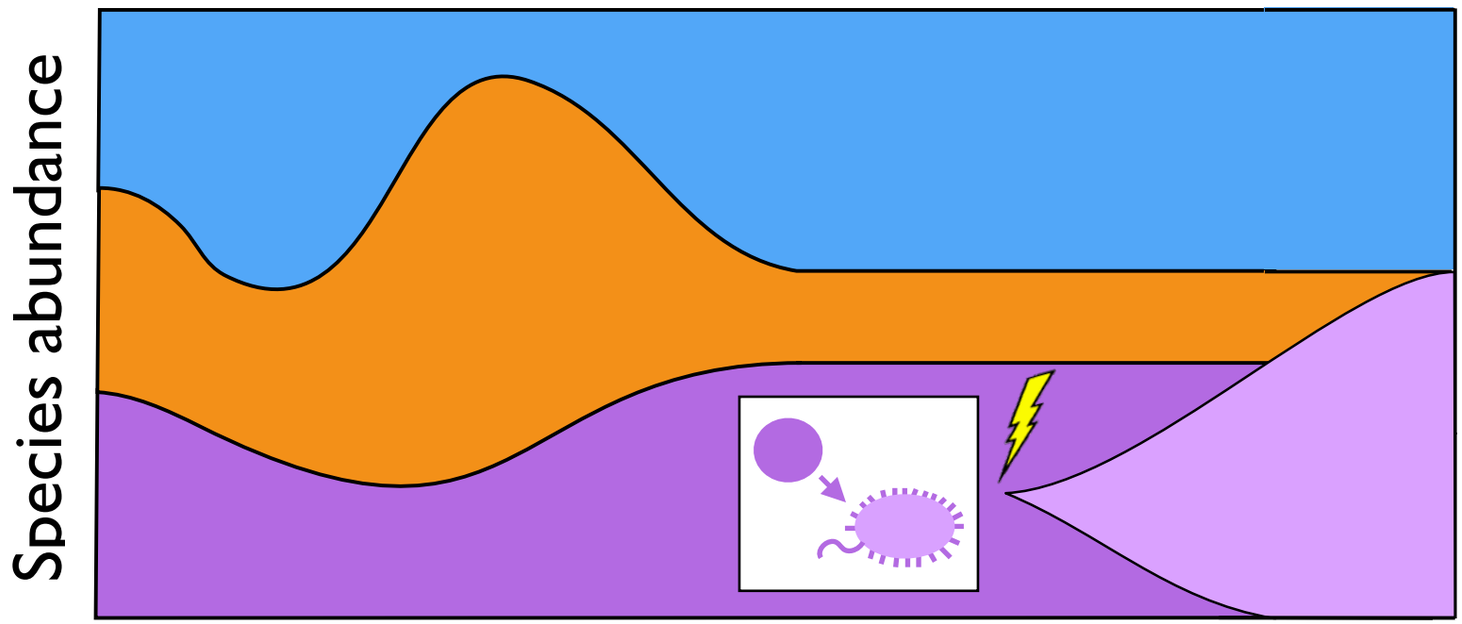


Problem: little empirical data. **Many basic questions still not known.**

- What are relevant timescales for within-host evolution? Does it happen at all?

Is short-term evolution important in the gut microbiome?

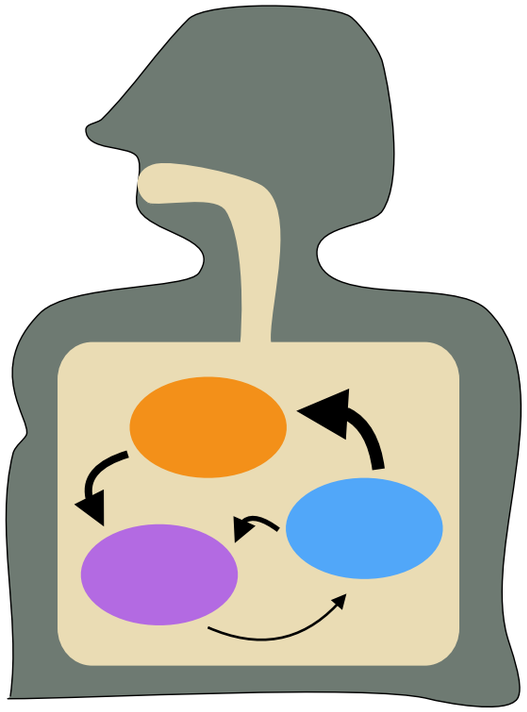


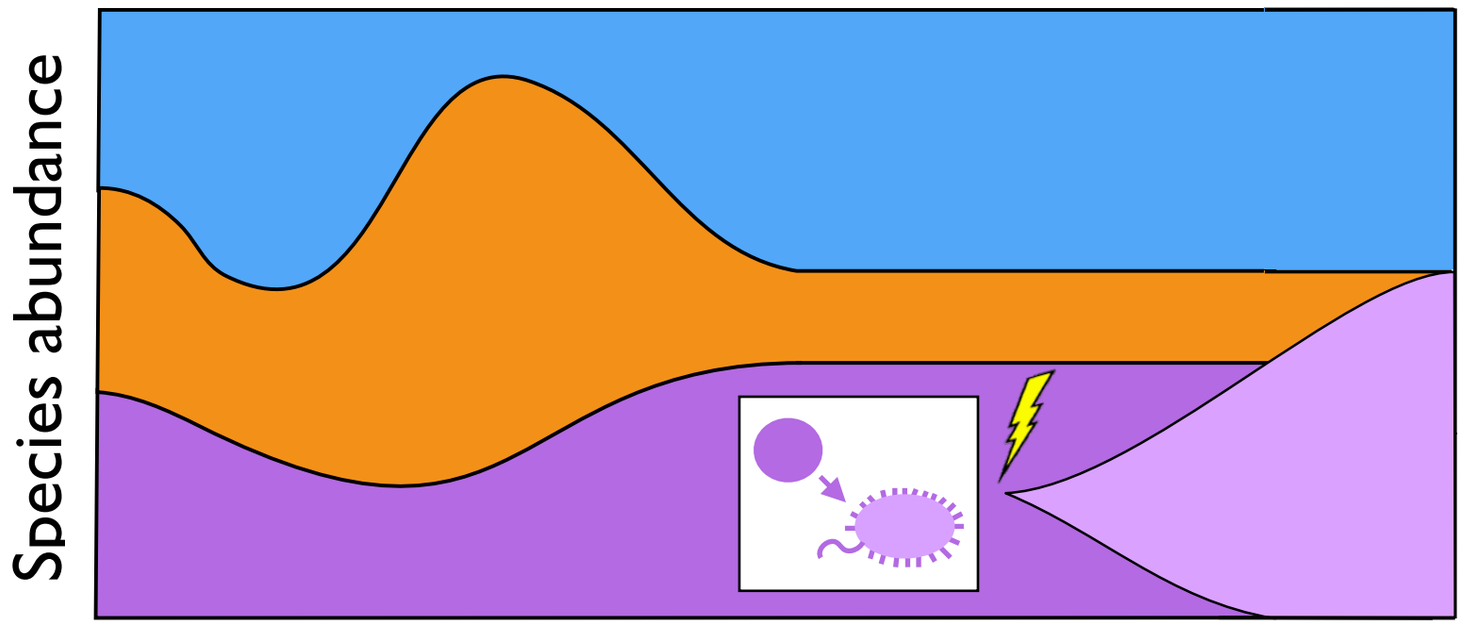


Problem: little empirical data. **Many basic questions still not known.**

- What are relevant timescales for within-host evolution? Does it happen at all?
- What do population genetics of this process look like?

Is short-term evolution important in the gut microbiome?

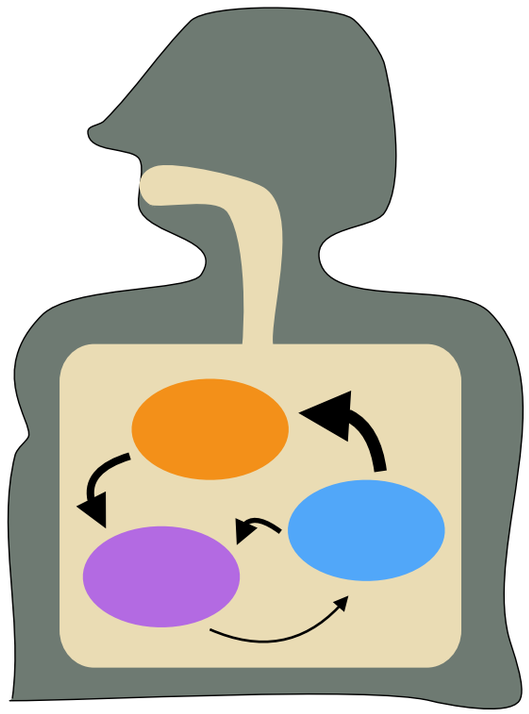


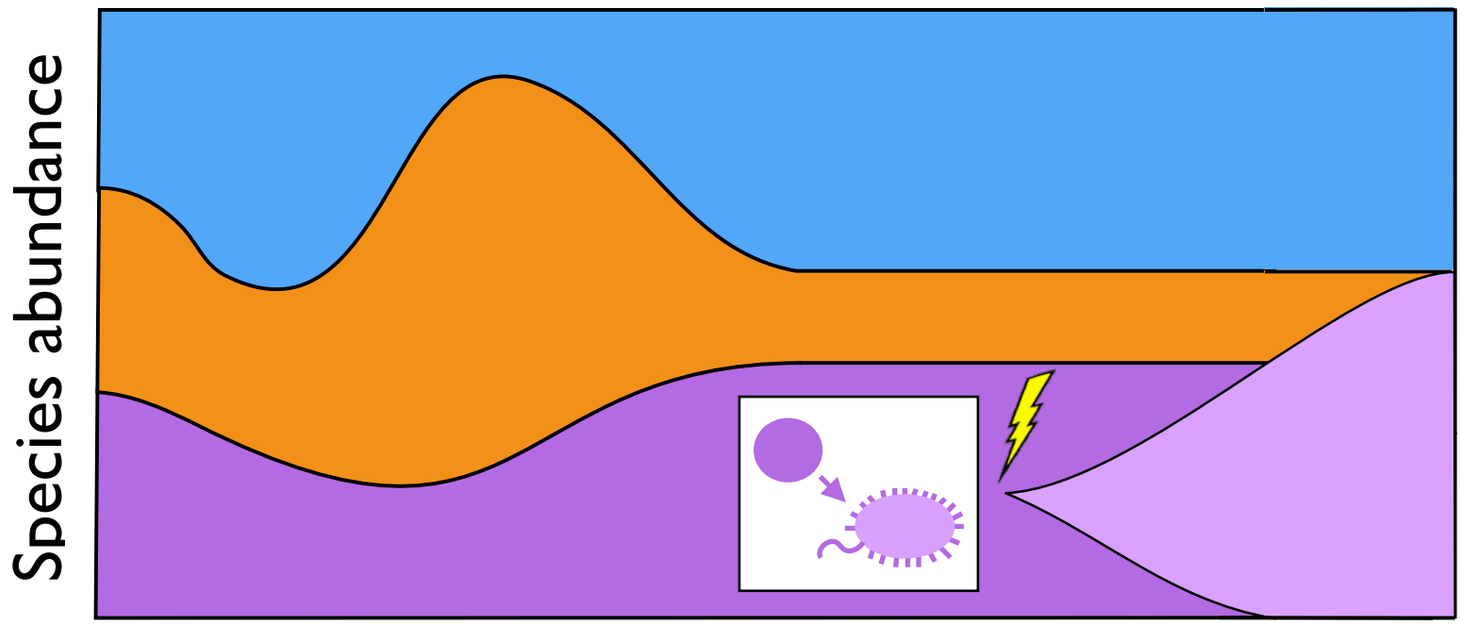


Problem: little empirical data. **Many basic questions still not known.**

- What are relevant timescales for within-host evolution? Does it happen at all?
- What do population genetics of this process look like?
    - Genetic structure of typical resident population?

Is short-term evolution important in the gut microbiome?

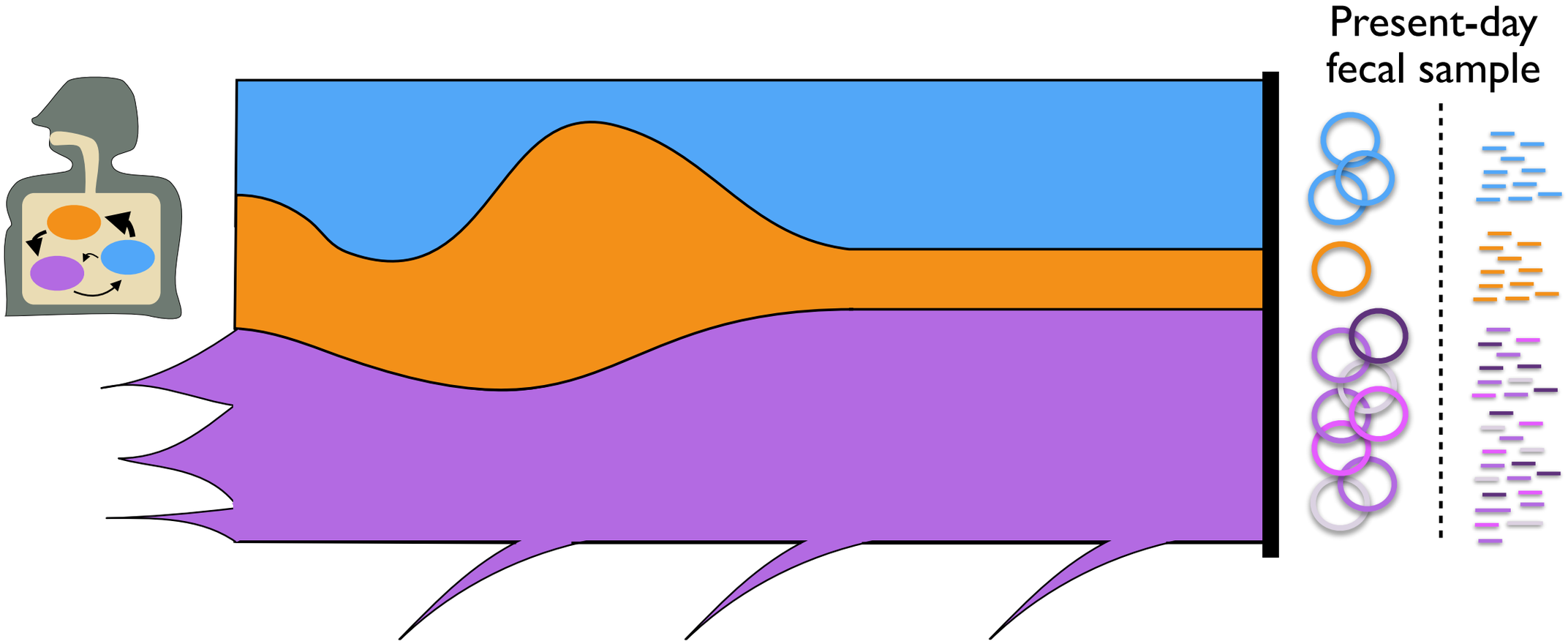




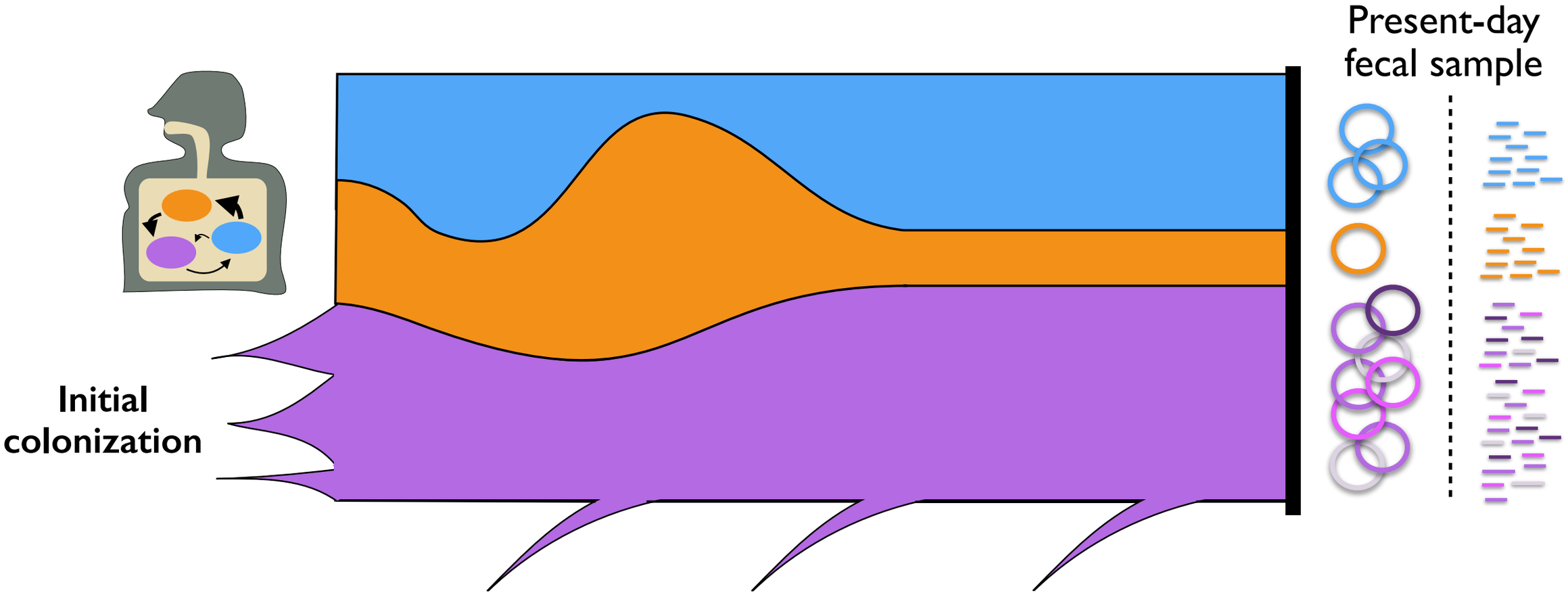
Problem: little empirical data. **Many basic questions still not known.**

- What are relevant timescales for within-host evolution? Does it happen at all?
- What do population genetics of this process look like?
    - Genetic structure of typical resident population?
    - How important are genetic drift, horizontal gene transfer, immigration?

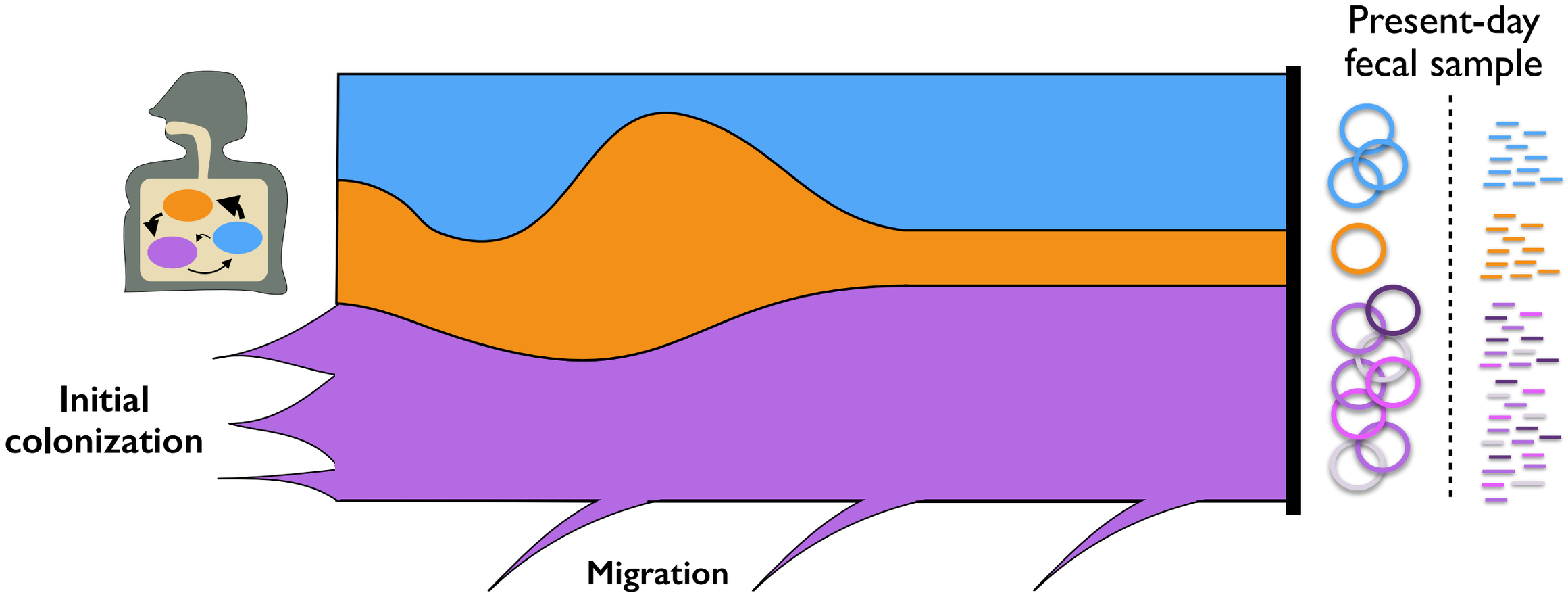
Measuring evolutionary dynamics in shotgun metagenomes



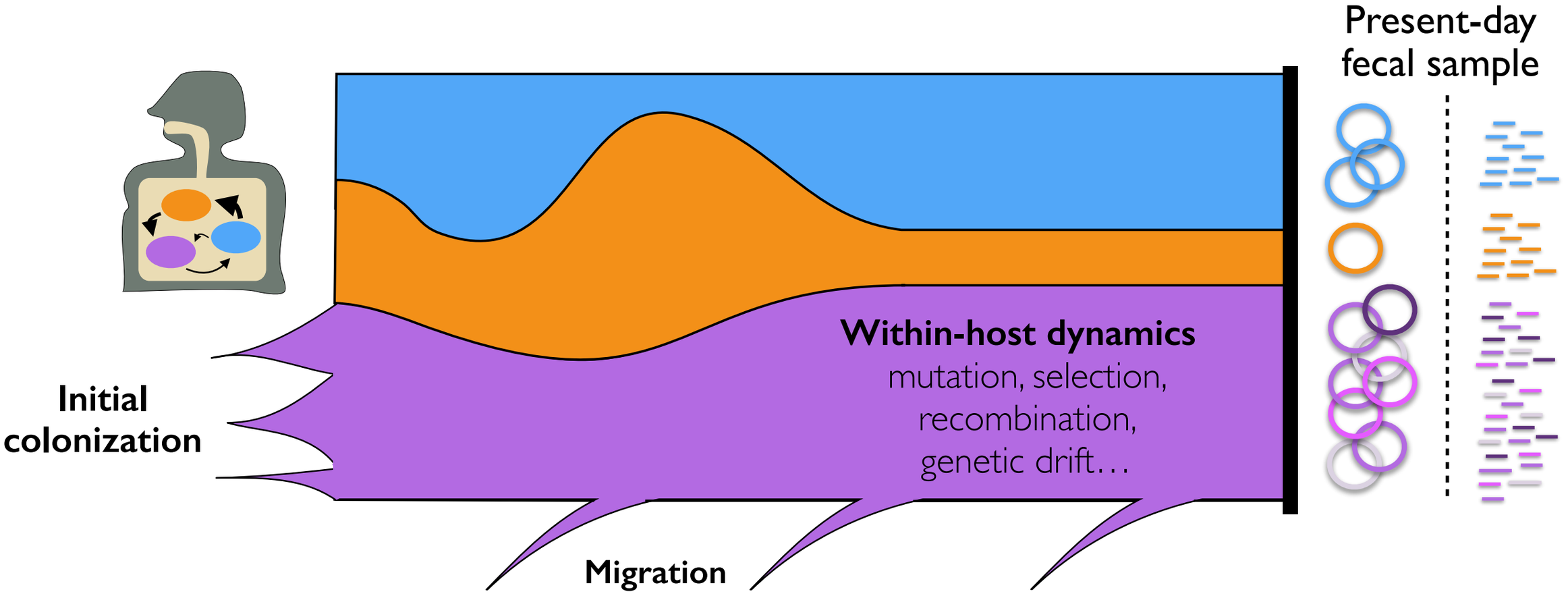
Measuring evolutionary dynamics in shotgun metagenomes



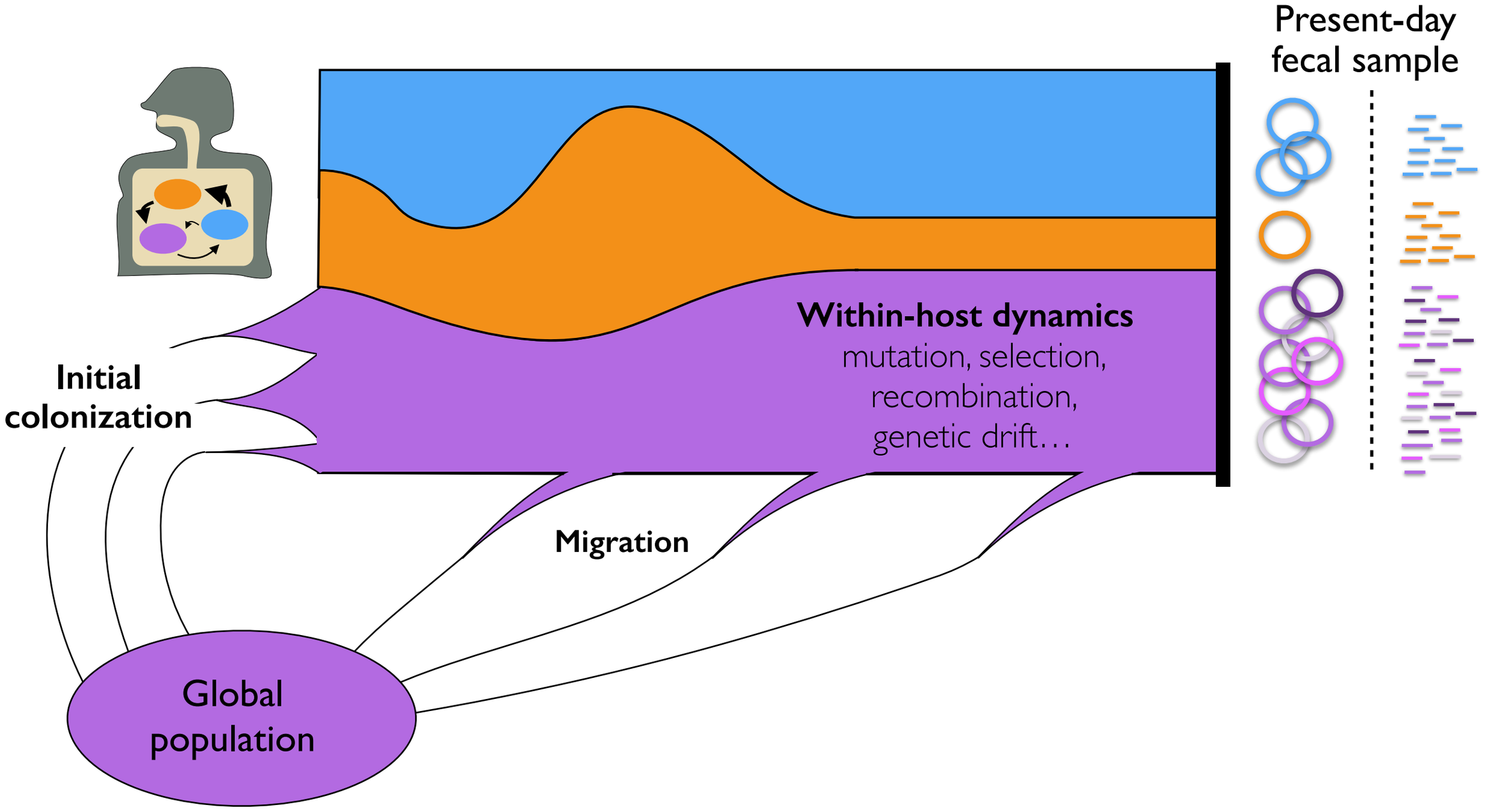
Measuring evolutionary dynamics in shotgun metagenomes



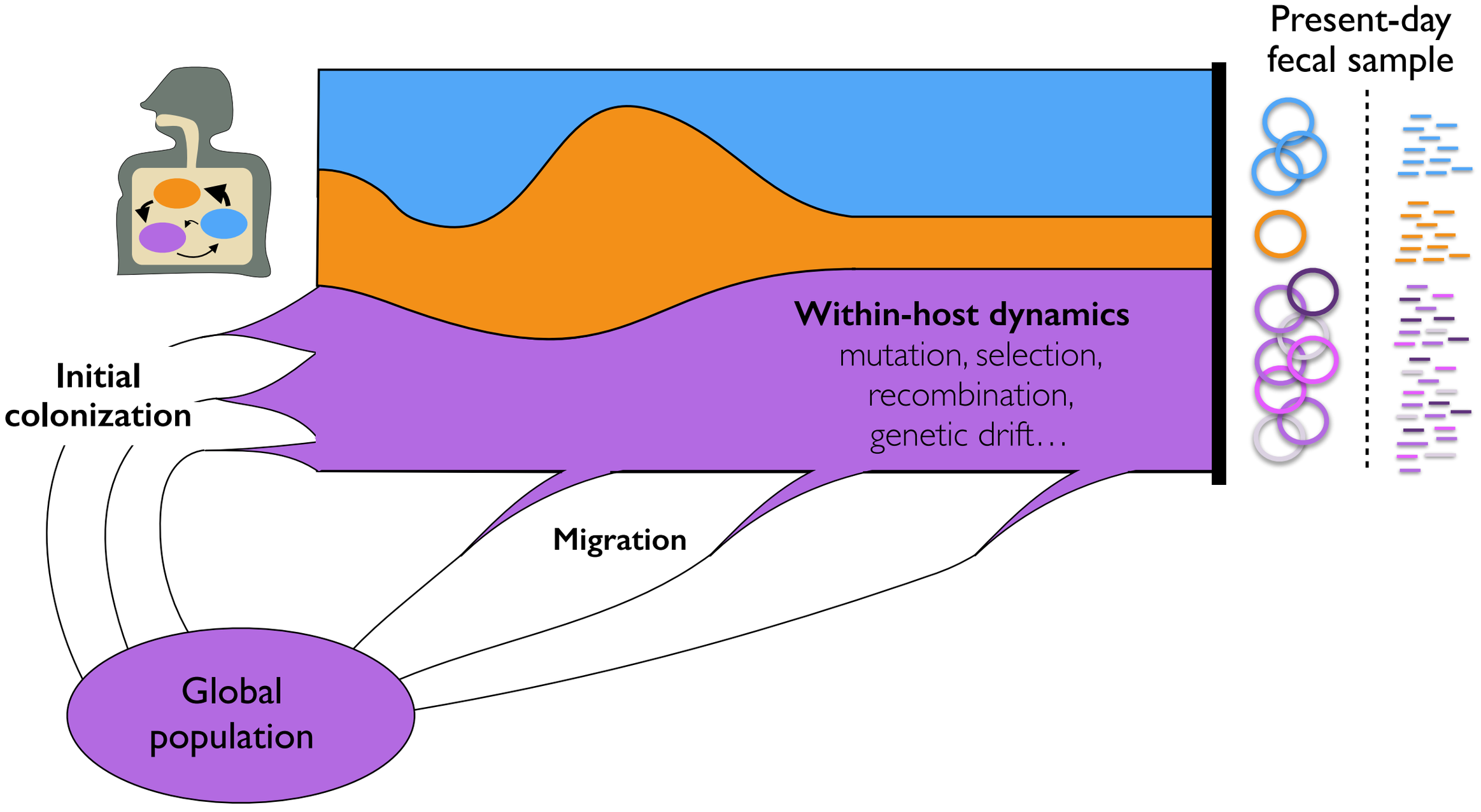
Measuring evolutionary dynamics in shotgun metagenomes



Measuring evolutionary dynamics in shotgun metagenomes

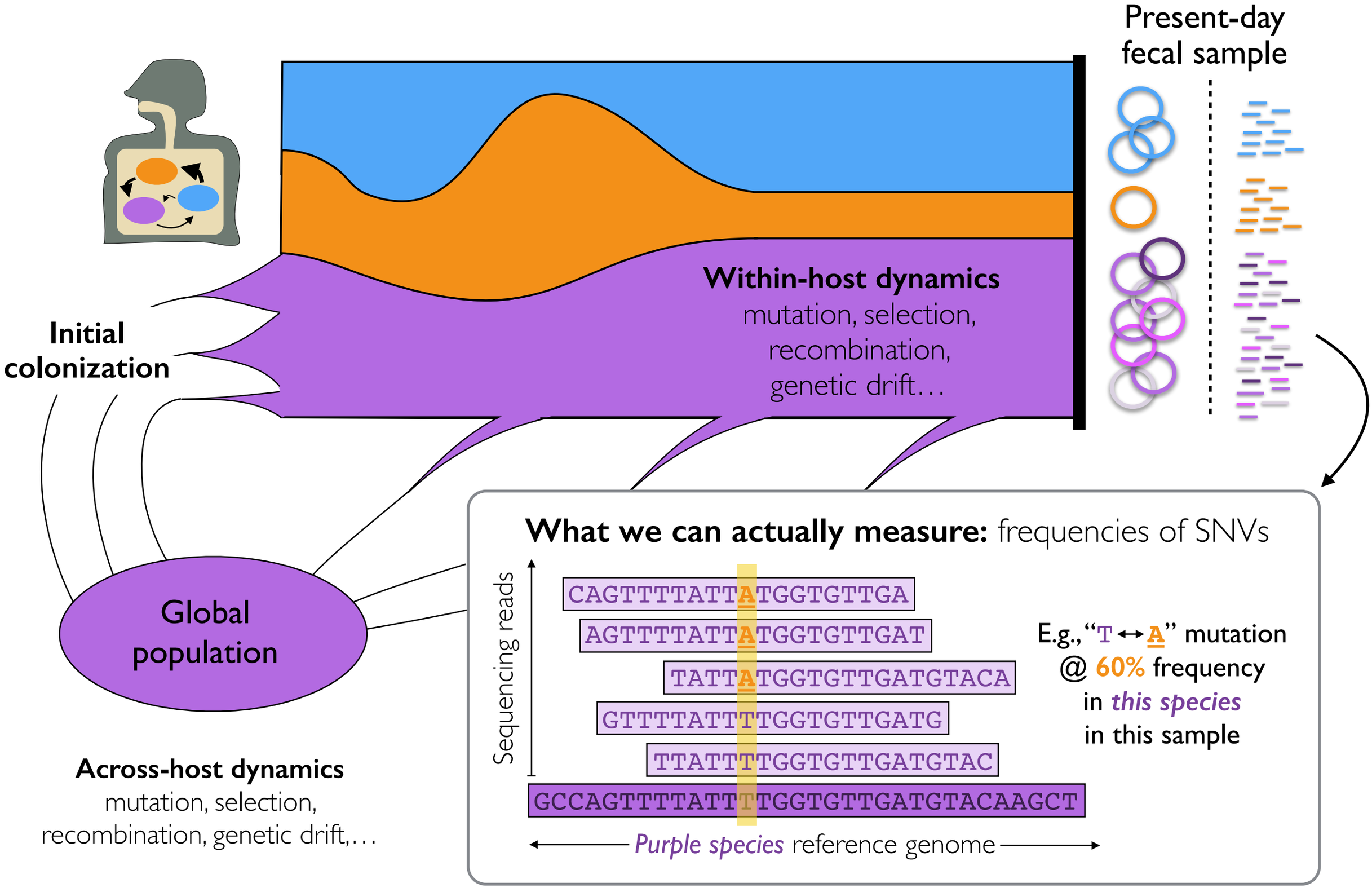


Measuring evolutionary dynamics in shotgun metagenomes

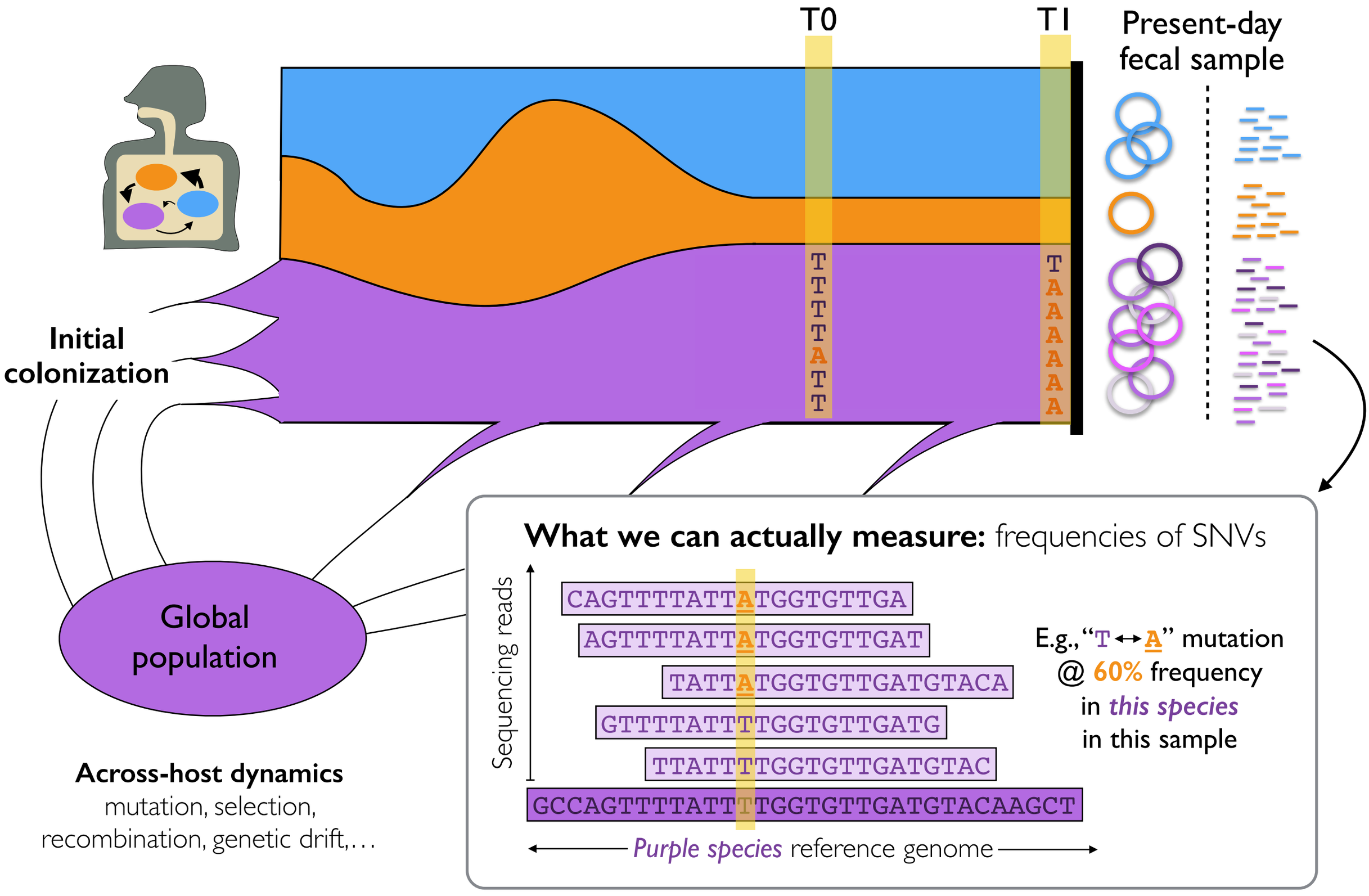


Across-host dynamics
mutation, selection,
recombination, genetic drift,…

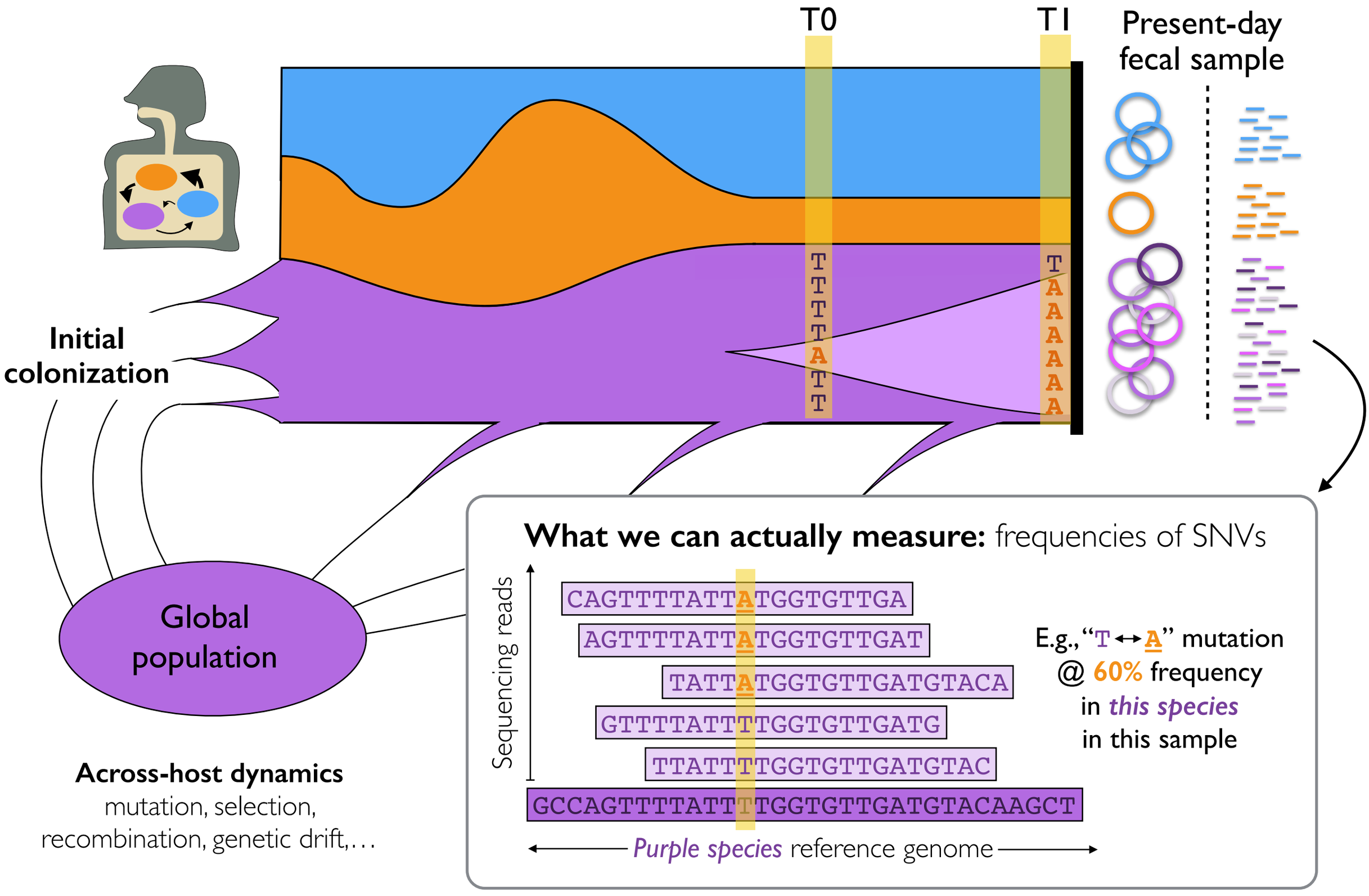
Measuring evolutionary dynamics in shotgun metagenomes



Measuring evolutionary dynamics in shotgun metagenomes

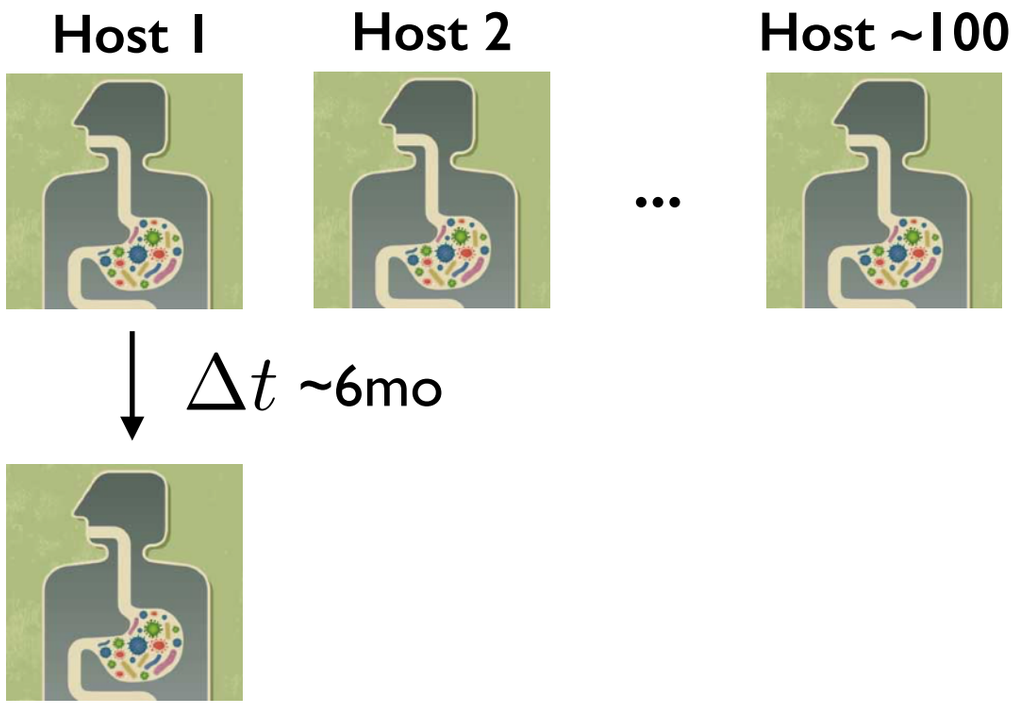


Measuring evolutionary dynamics in shotgun metagenomes



First pass: what can we learn from a large healthy cohort?

Samples: NIH Human Microbiome Project



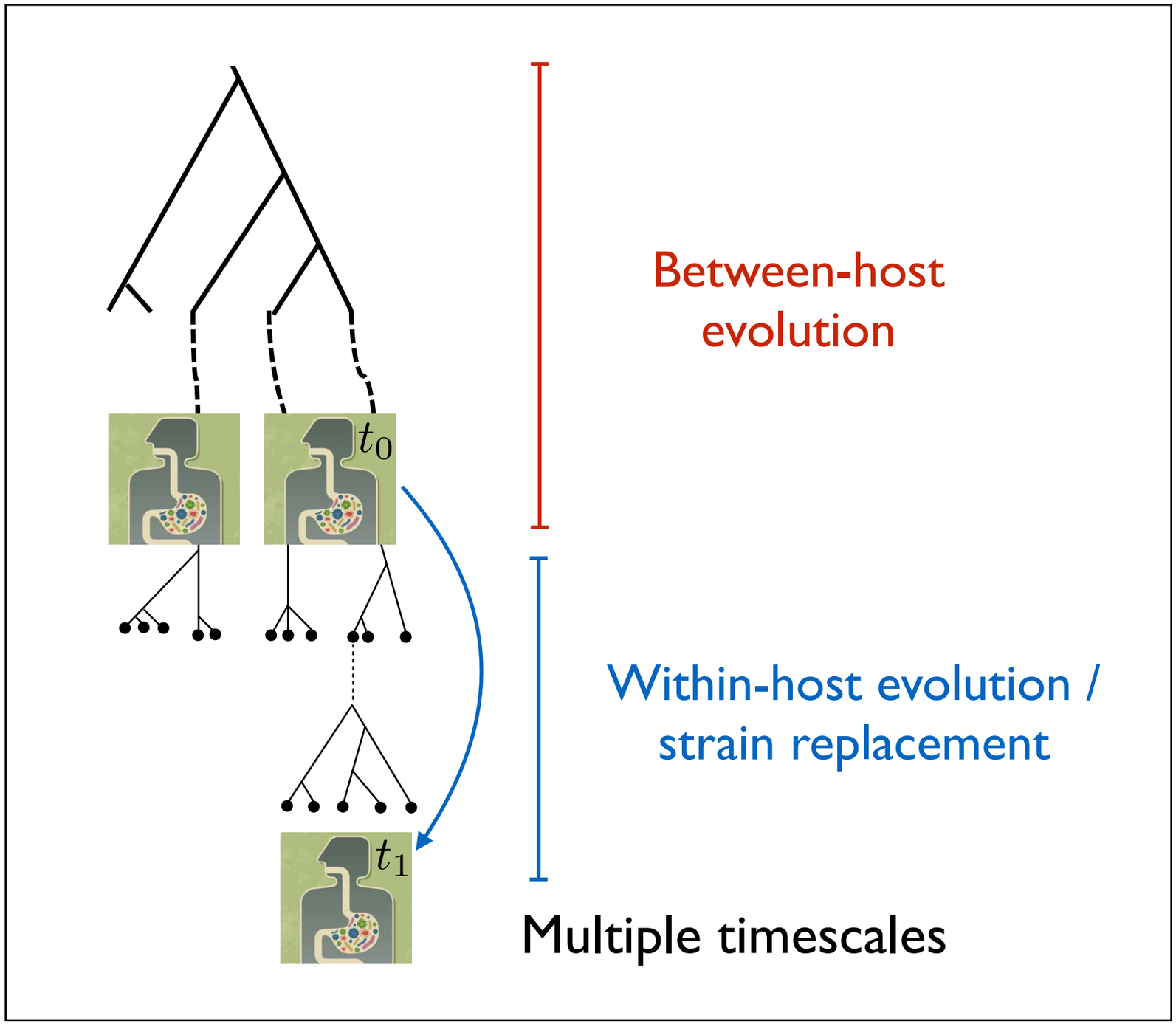
joint work with

*** Nandita Garud**
(UCLA)

K. Pollard
(UCSF)

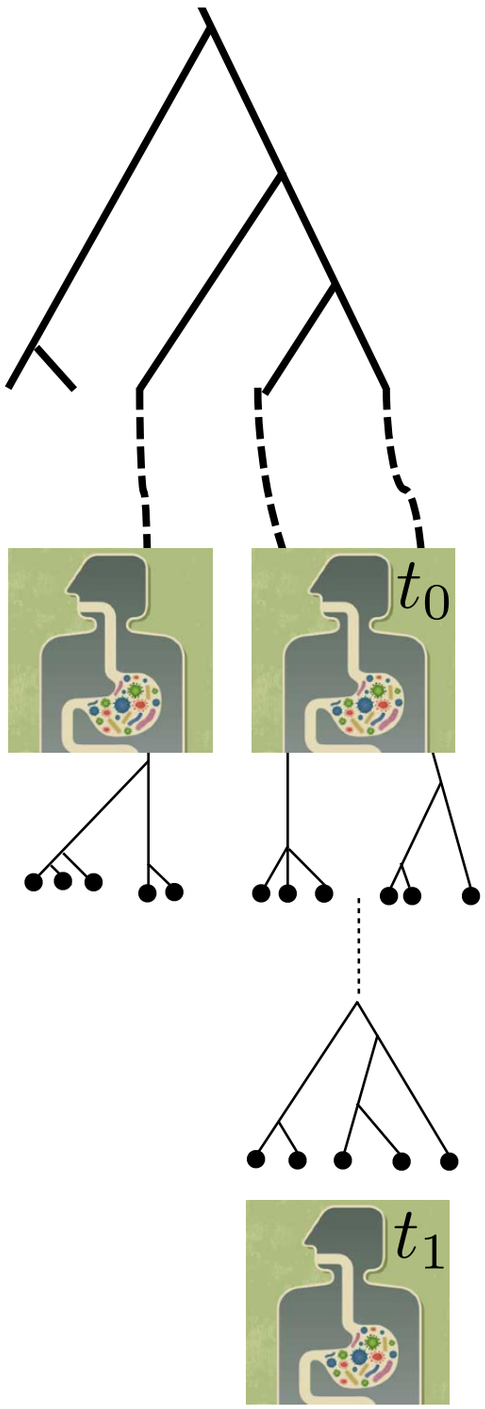
O. Hallatschek
(UC Berkeley)

First pass: what can we learn from a large healthy cohort?



(~40 bacterial species)

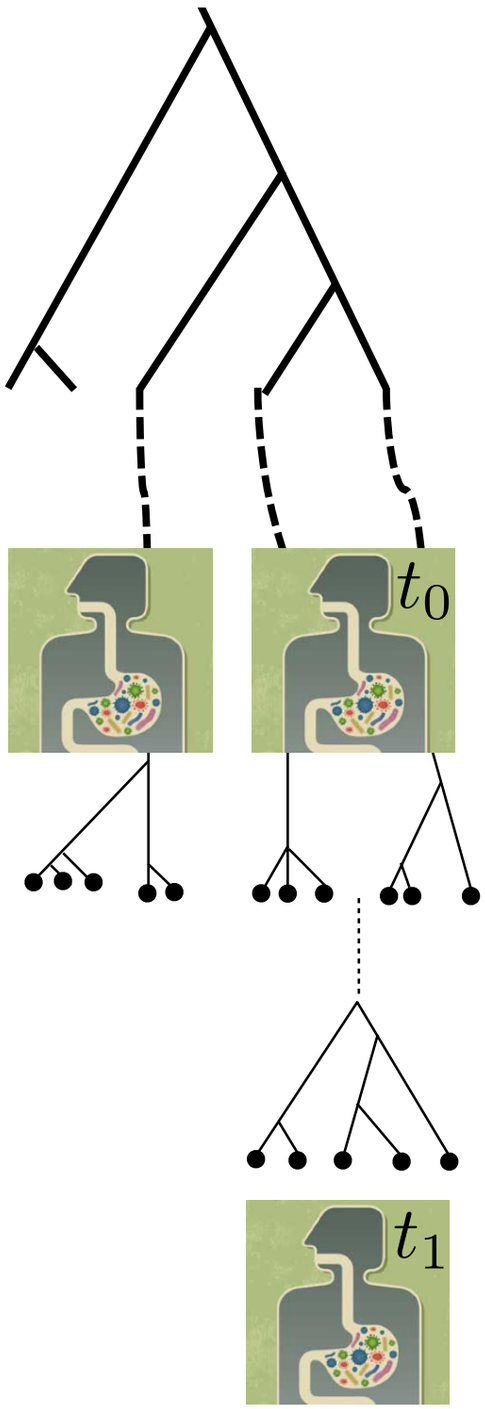
Applications to HMP cohort: general trends across ~40 species



Across-host timescales (~Tc)

- Genetic diversity is "old" ($T_c \sim 10^3 - 10^4$ SNVs/Mb)

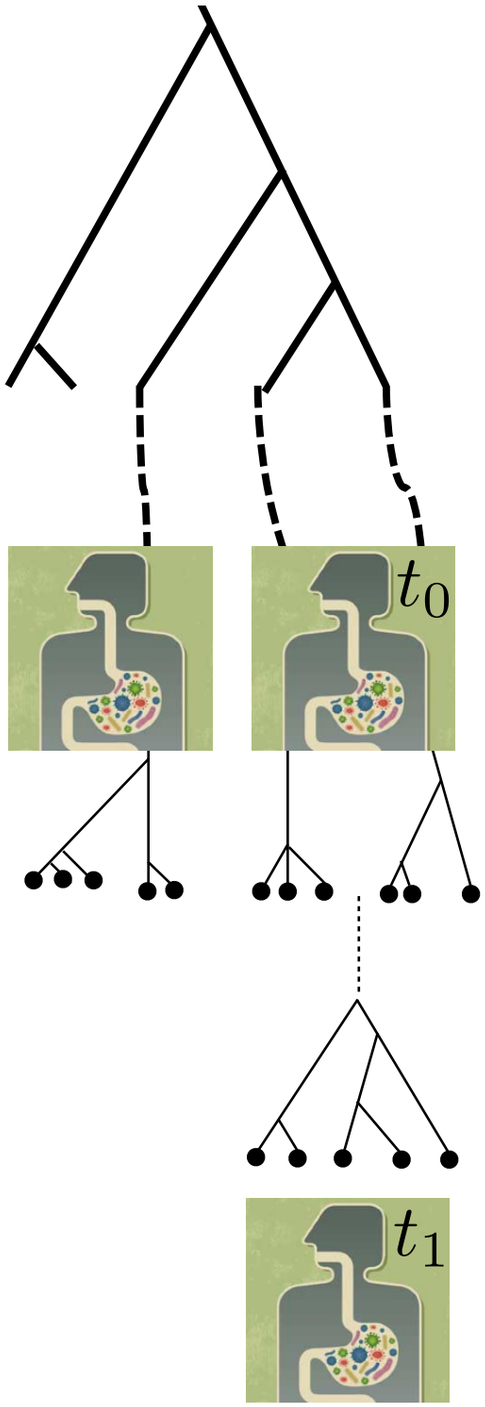
Applications to HMP cohort: general trends across ~40 species



Across-host timescales (~Tc)

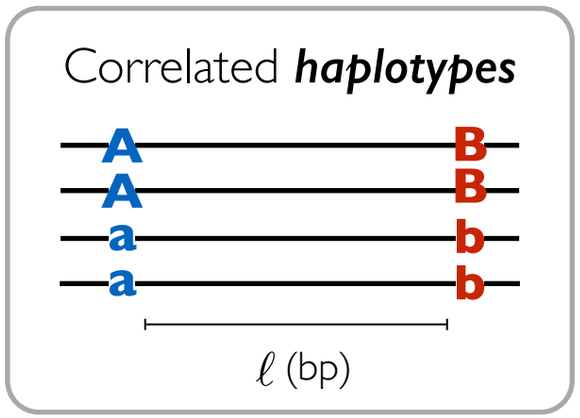
- Genetic diversity is "old" ($T_c \sim 10^3 - 10^4$ SNVs/Mb)
- mostly synonymous ($pN/pS \sim 0.1$) ***negative selection***

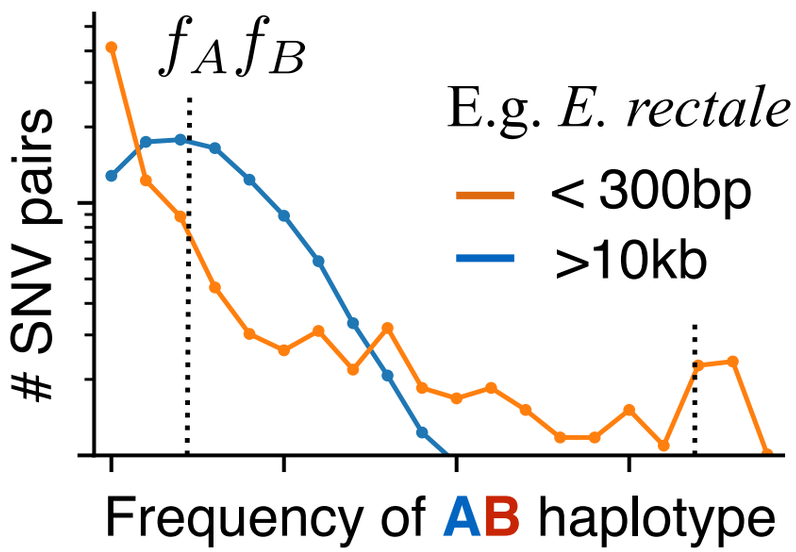
Applications to HMP cohort: general trends across ~40 species



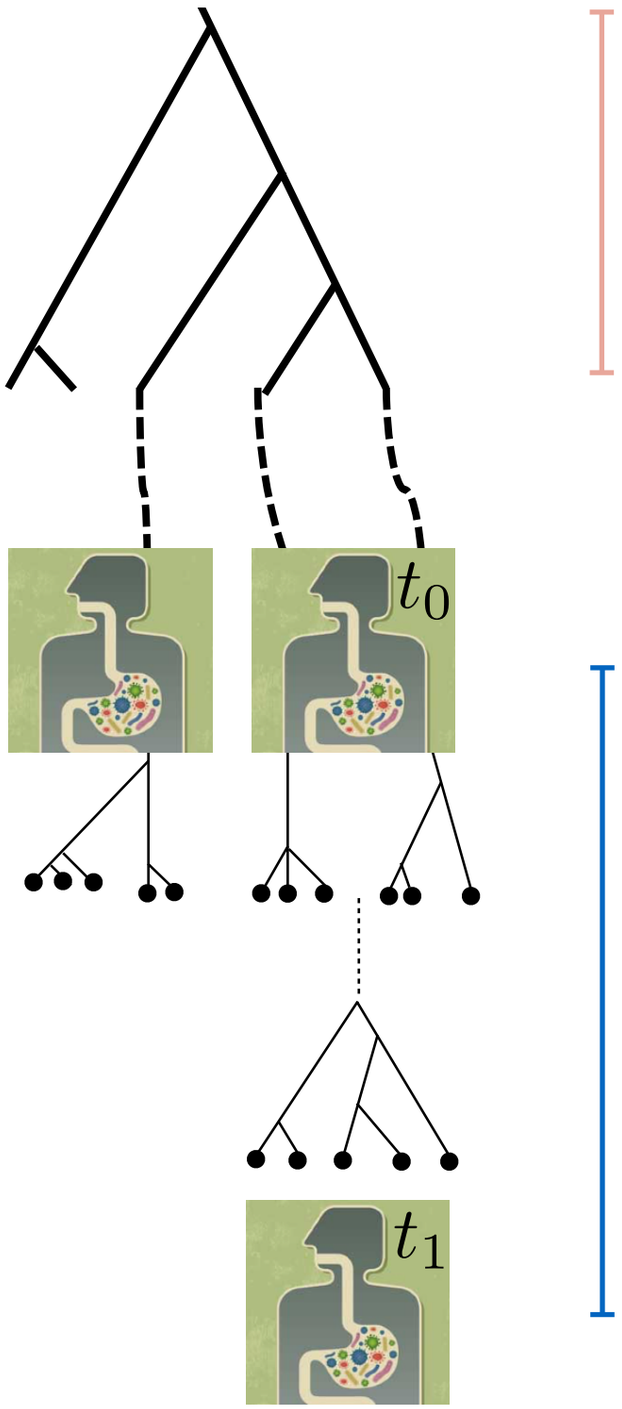
Across-host timescales (~Tc)

- Genetic diversity is "old" ($T_c \sim 10^3 - 10^4$ SNVs/Mb)
- mostly synonymous ($pN/pS \sim 0.1$) ***negative selection***
- Widespread ***bacterial recombination*** ***("quasi-sexual")***





Applications to HMP cohort: general trends across ~40 species

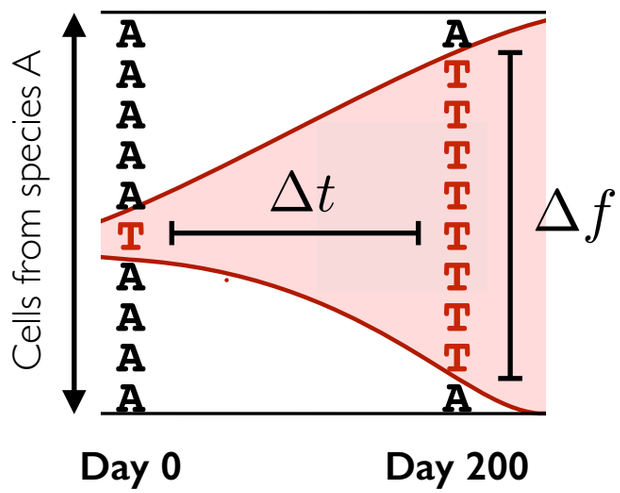


Across-host timescales (~Tc)

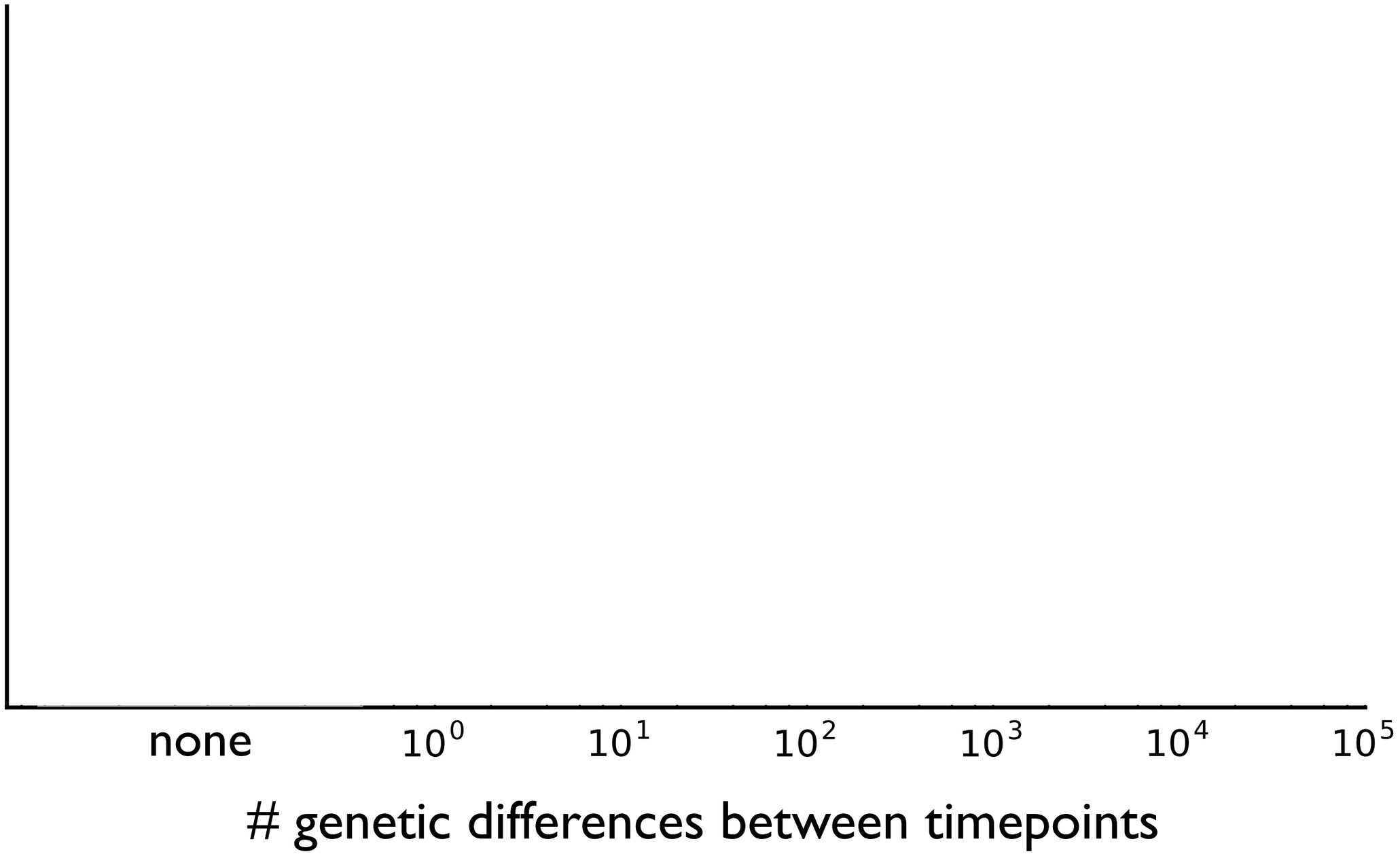
- Genetic diversity is "old" ($T_c \sim 10^3 - 10^4$ SNVs/Mb)
- mostly synonymous ($pN/pS \sim 0.1$) ***negative selection***
- Widespread ***bacterial recombination*** ***("quasi-sexual")***

Within-host timescales (~6mo)

Scan for host-wide sweeps…

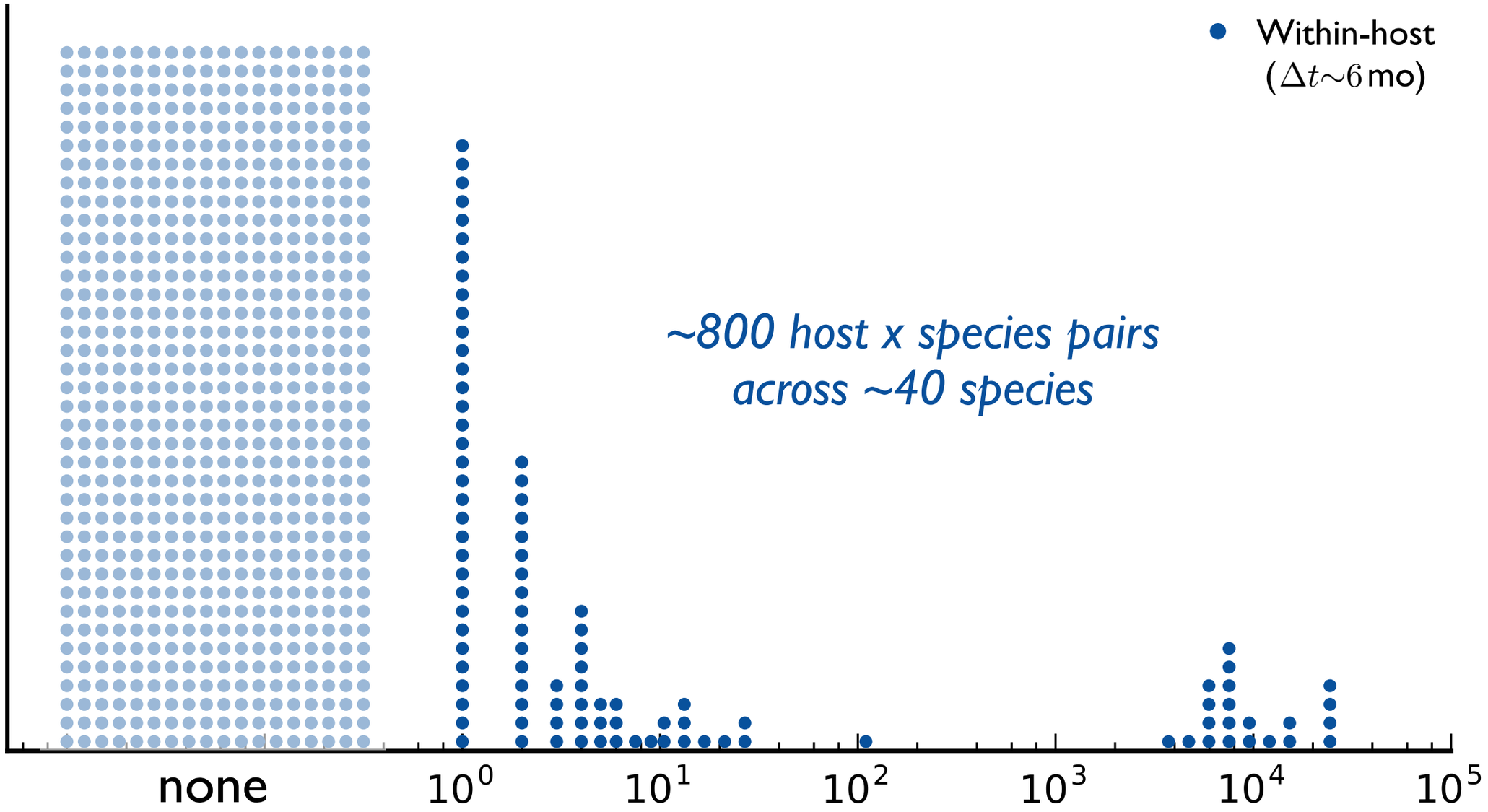


Within-host dynamics over ~6 month timescales



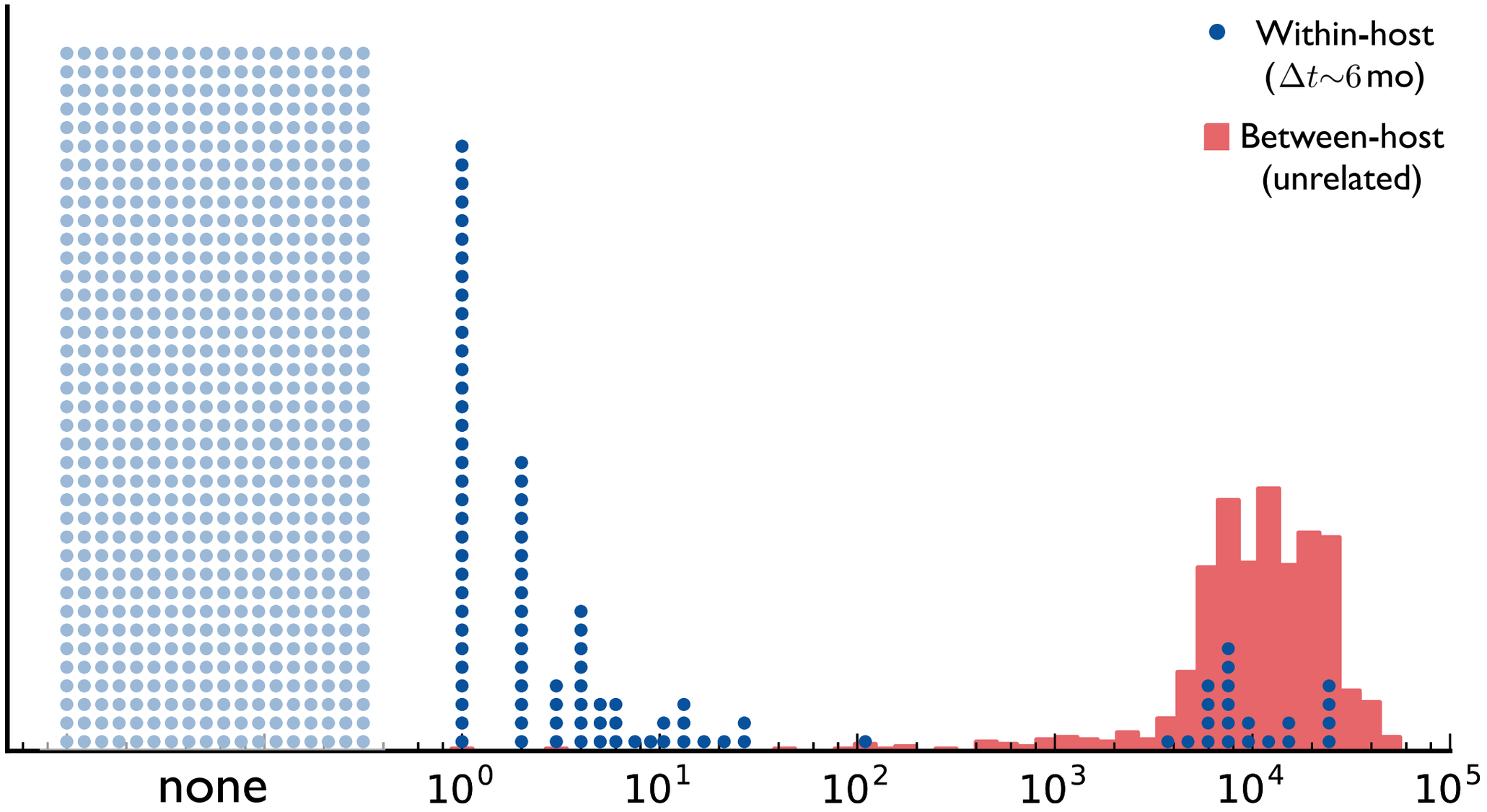
Garud* & Good* et al (*PLoS Bio*, 2019)

Within-host dynamics over ~6 month timescales



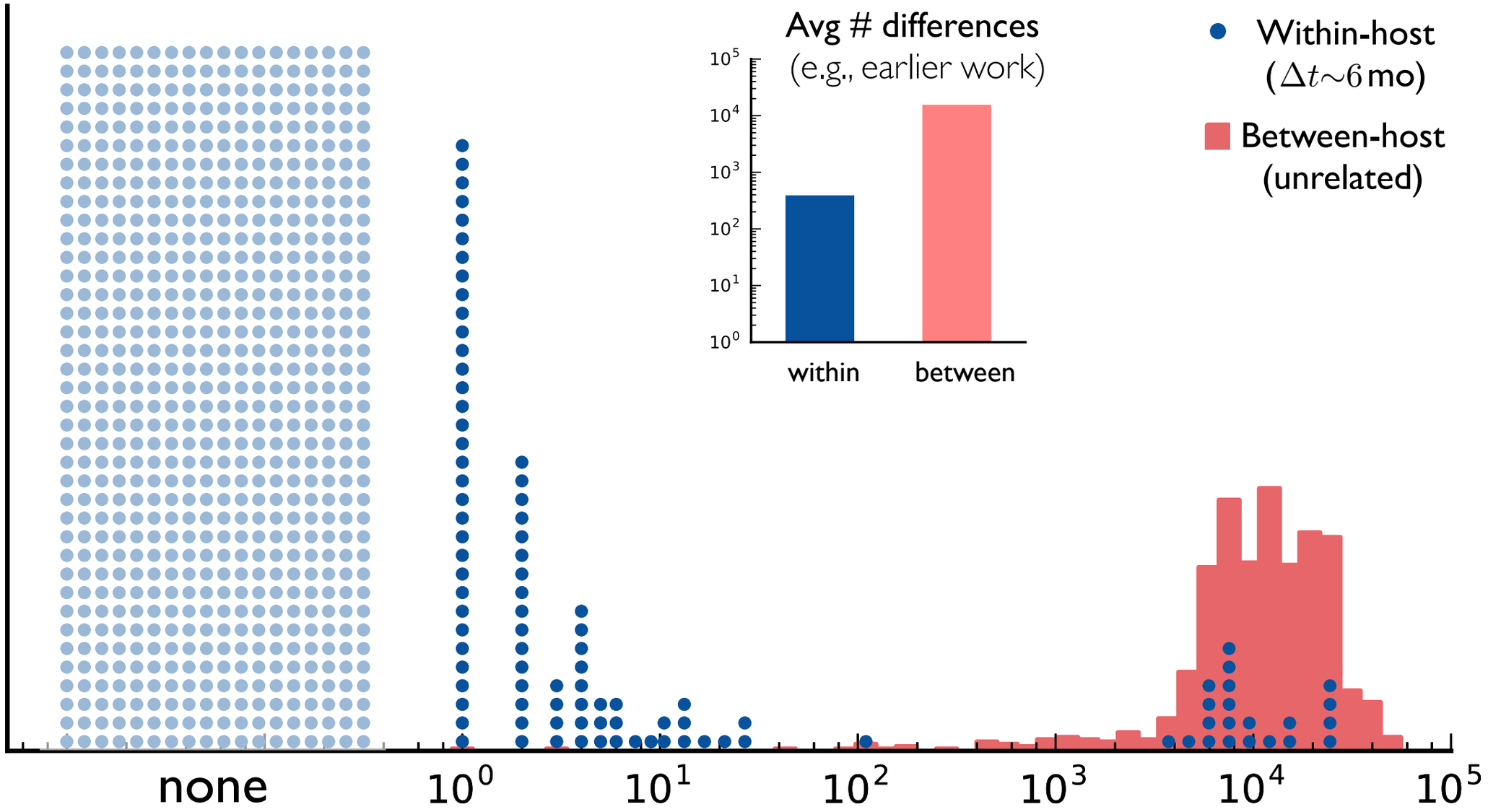
Garud* & Good* et al (*PLoS Bio*, 2019)

Within-host dynamics over ~6 month timescales



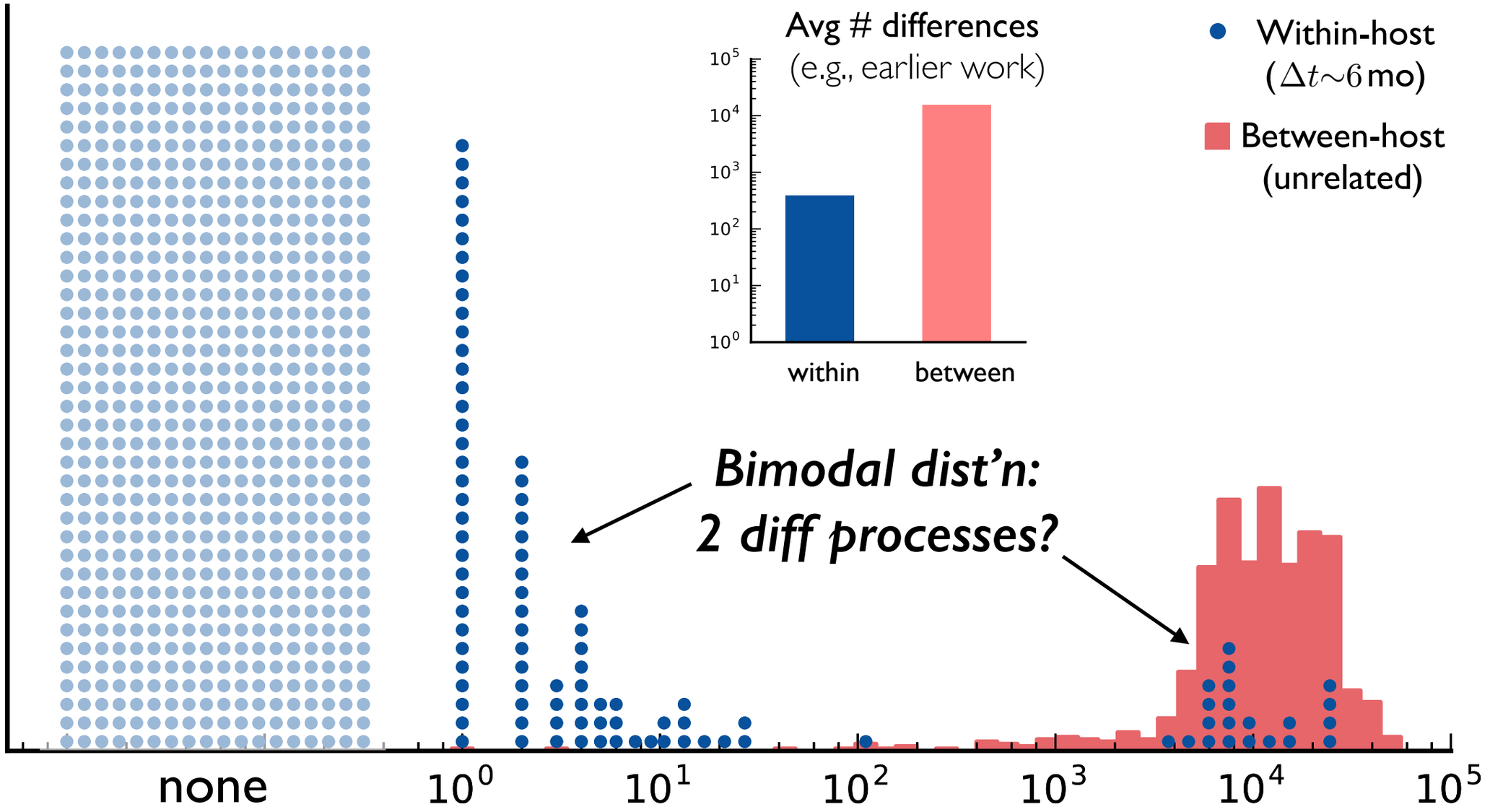
Garud* & Good* et al (*PLoS Bio*, 2019)

Within-host dynamics over ~6 month timescales



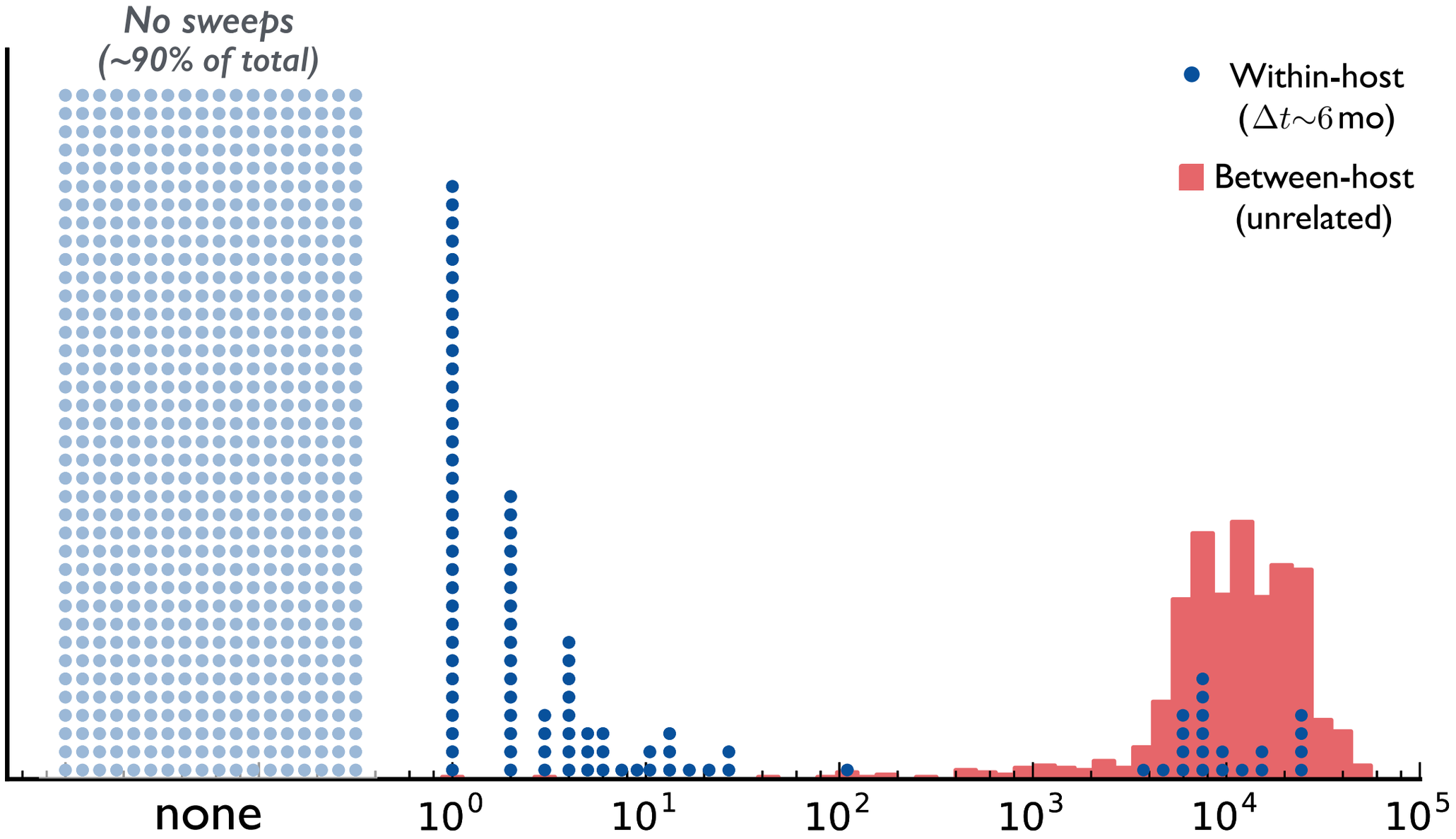
Garud* & Good* et al (*PLoS Bio*, 2019)

Within-host dynamics over ~6 month timescales



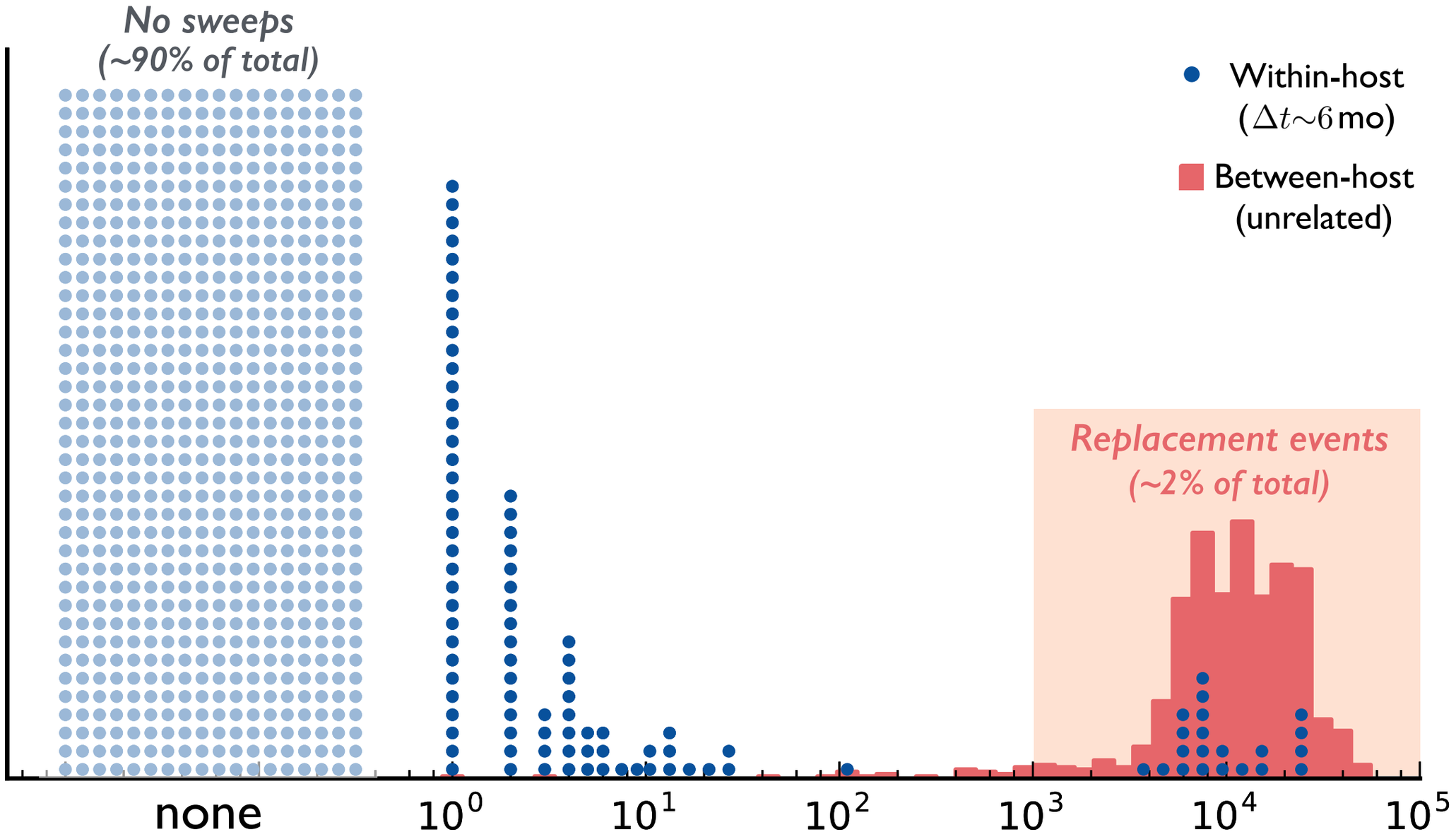
Garud* & Good* et al (*PLoS Bio*, 2019)

Within-host dynamics over ~6 month timescales



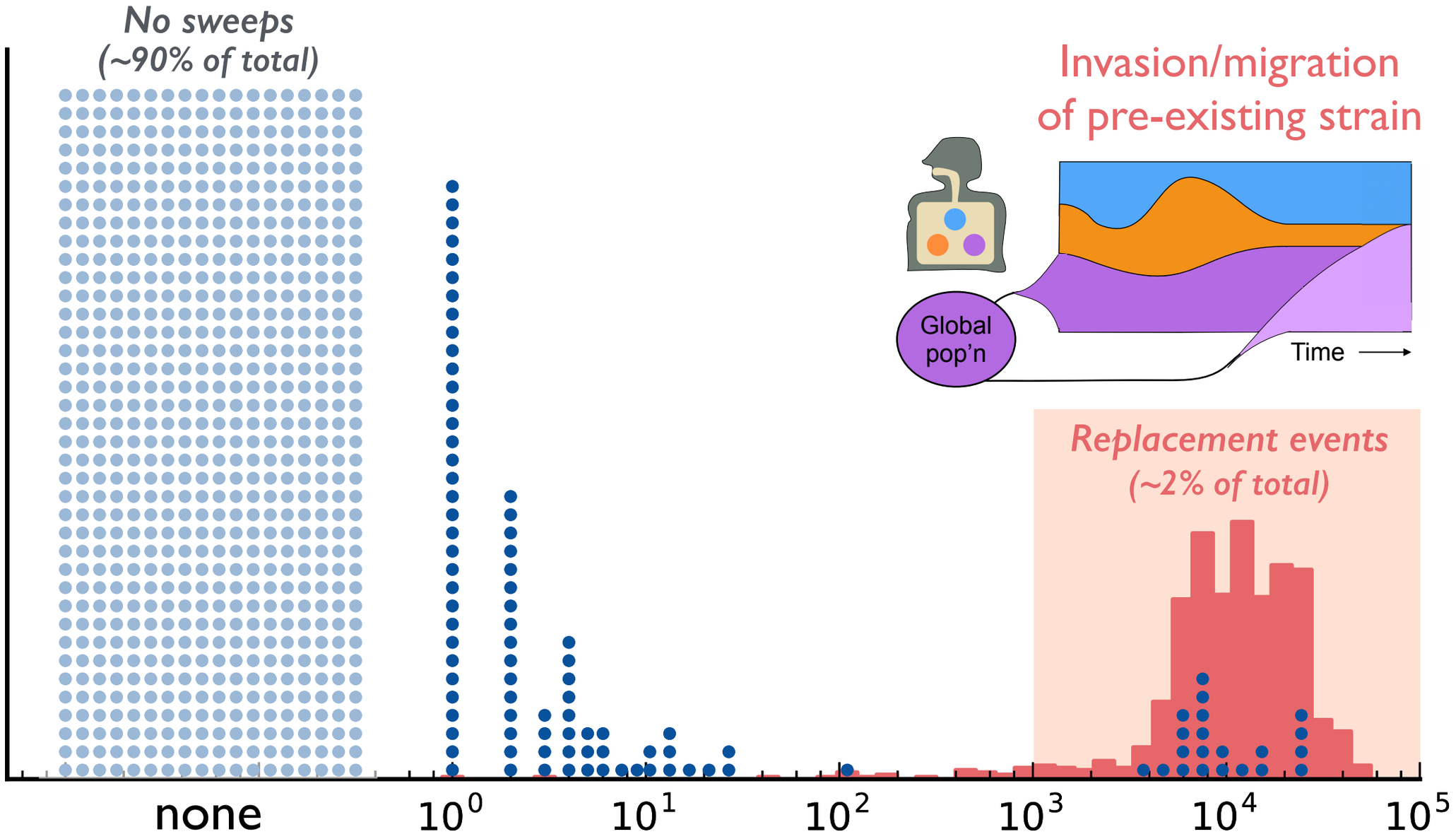
Garud* & Good* et al (*PLoS Bio*, 2019)

Within-host dynamics over ~6 month timescales



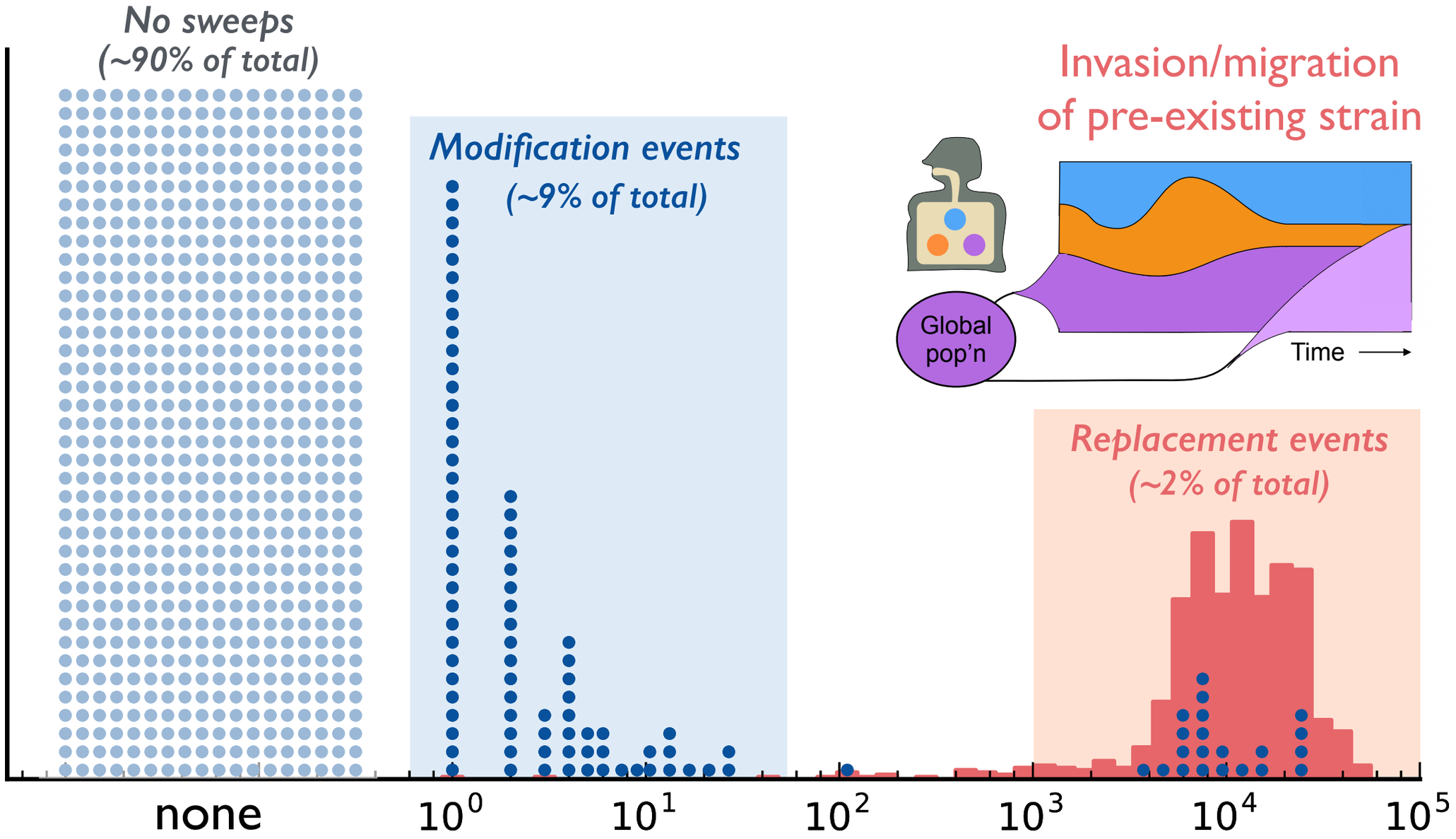
Garud* & Good* et al (*PLoS Bio*, 2019)

Within-host dynamics over ~6 month timescales



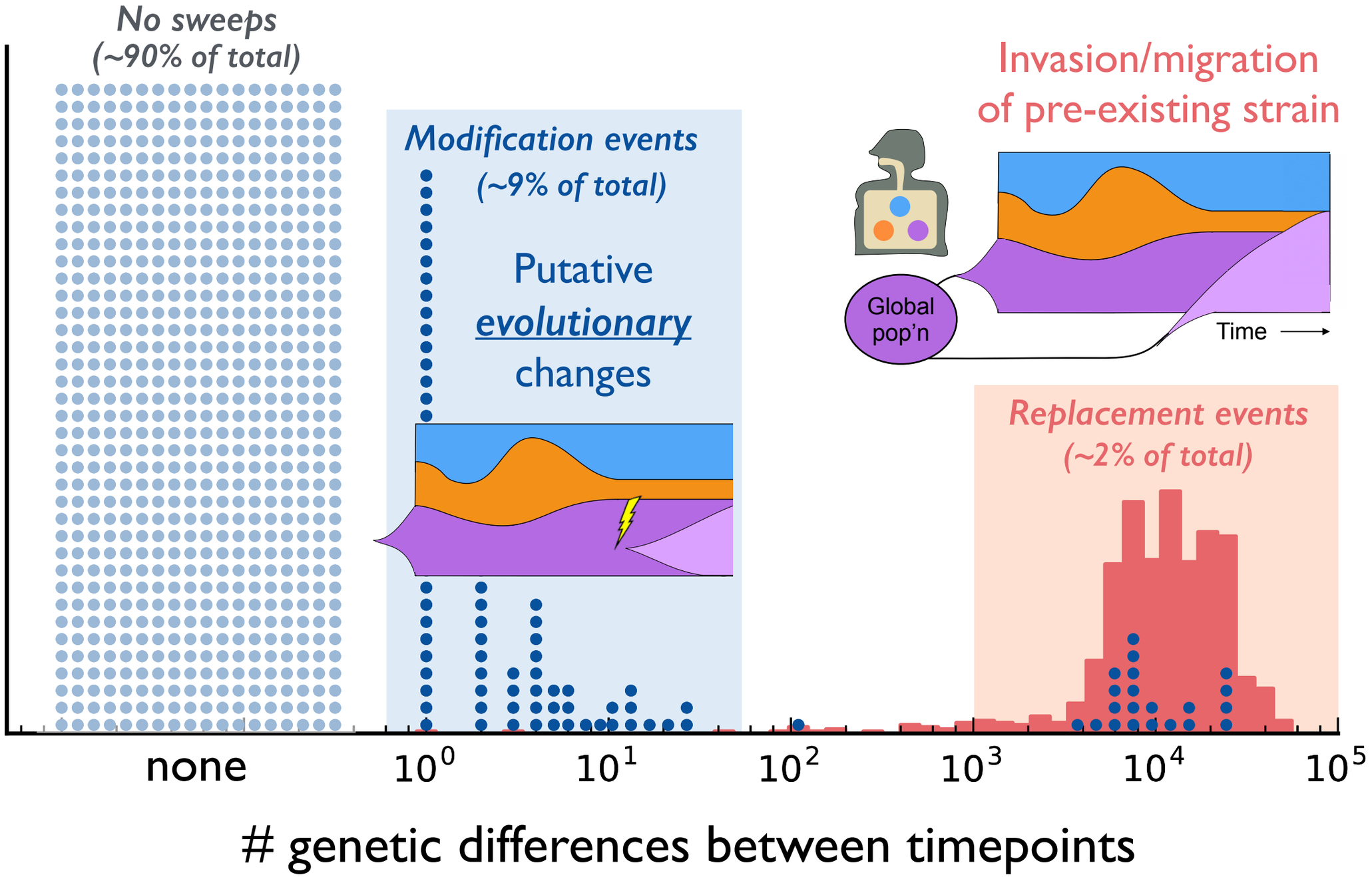
Garud* & Good* et al (*PLoS Bio*, 2019)

Within-host dynamics over ~6 month timescales



Garud* & Good* et al (*PLoS Bio*, 2019)

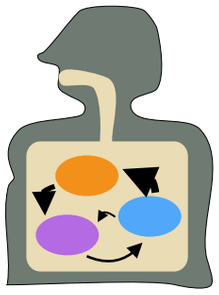
Within-host dynamics over ~6 month timescales



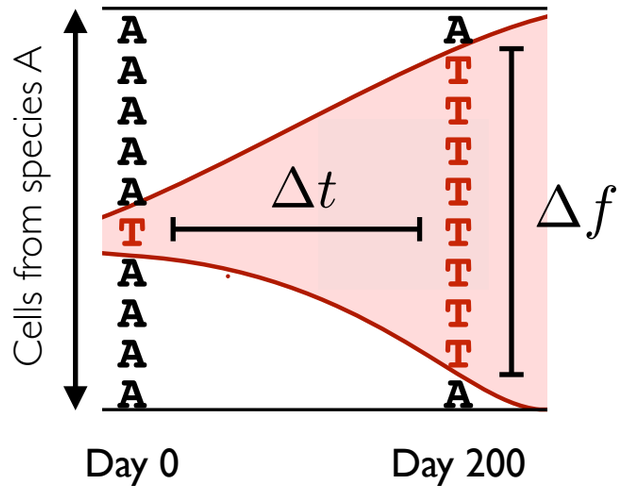
Garud* & Good* et al (*PLoS Bio*, 2019)

Key takeaways

- **Comparing 2 timepoints:** native microbiota ***can*** acquire genetic diffs on human-relevant timescales

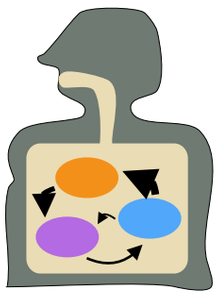


→ ***mixture of "strain replacement" and "evolutionary modification"***

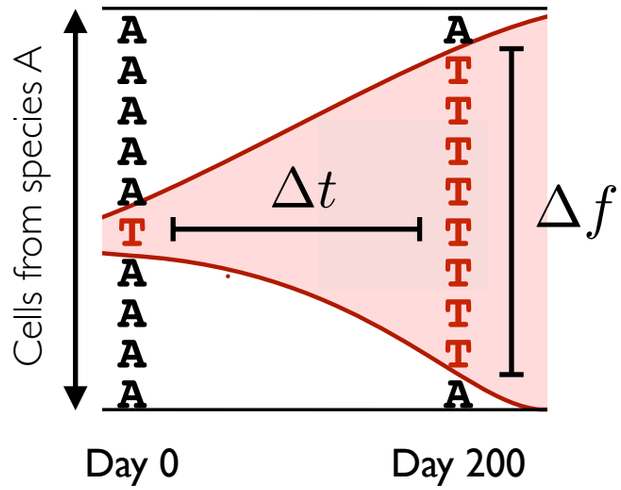


Key takeaways

- **Comparing 2 timepoints:** native microbiota ***can*** acquire genetic diffs on human-relevant timescales



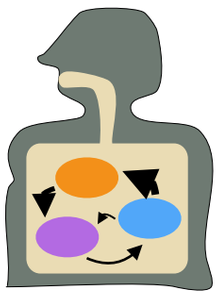
→ ***mixture of "strain replacement" and "evolutionary modification"***



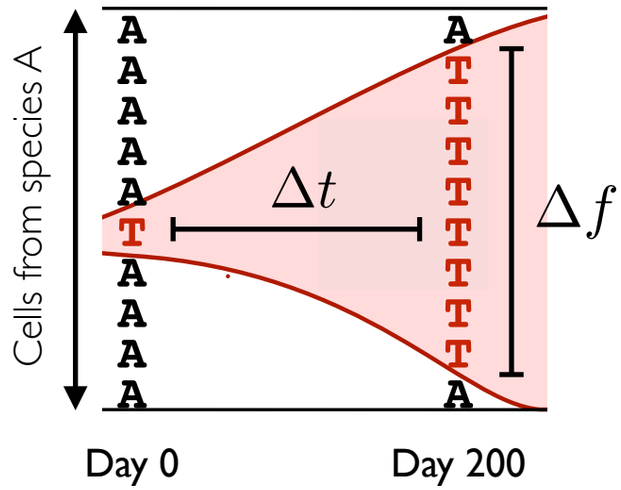
- **Next steps:** what do the ***population genetics*** of this process look like?

Key takeaways

- **Comparing 2 timepoints:** native microbiota ***can*** acquire genetic diffs on human-relevant timescales



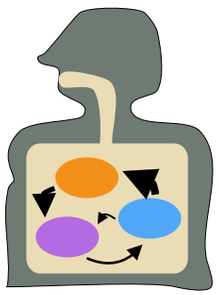
→ ***mixture of "strain replacement" and "evolutionary modification"***



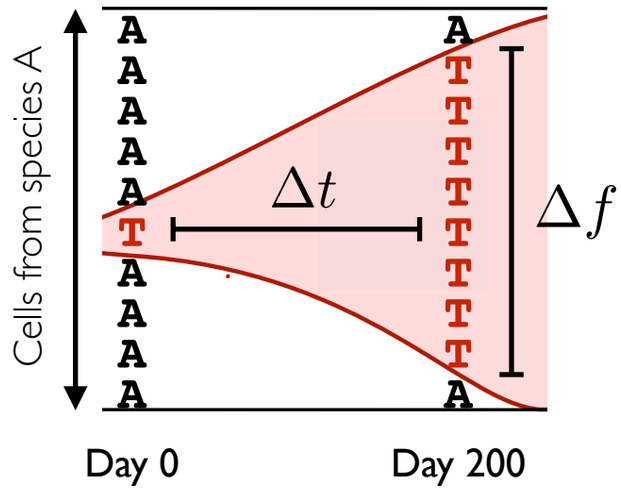
- **Next steps:** what do the ***population genetics*** of this process look like?
  - How important are natural selection, genetic drift, recombination w/in hosts?

Key takeaways

- **Comparing 2 timepoints:** native microbiota ***can*** acquire genetic diffs on human-relevant timescales



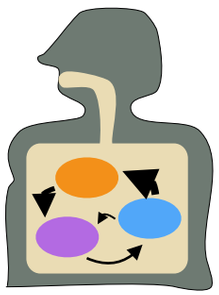
→ ***mixture of "strain replacement" and "evolutionary modification"***



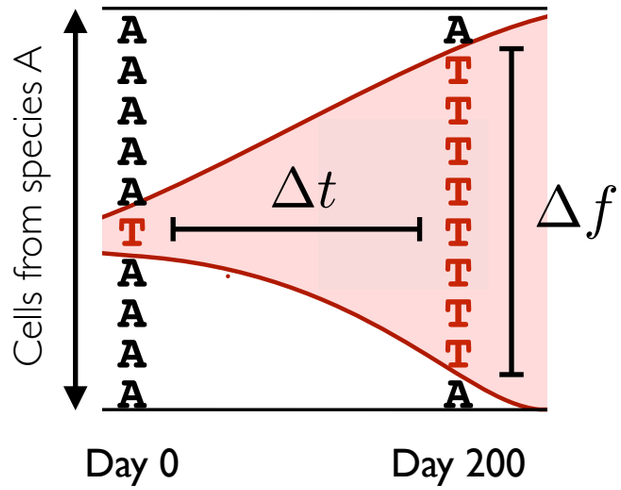
- **Next steps:** what do the ***population genetics*** of this process look like?
  - How important are natural selection, genetic drift, recombination w/in hosts?
  - Driven by sudden environmental changes (e.g. ABX)? or continual evolution?

Key takeaways

- **Comparing 2 timepoints:** native microbiota ***can*** acquire genetic diffs on human-relevant timescales



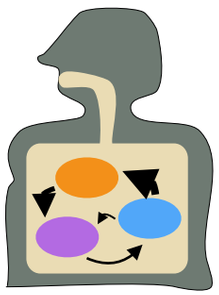
→ ***mixture of "strain replacement" and "evolutionary modification"***



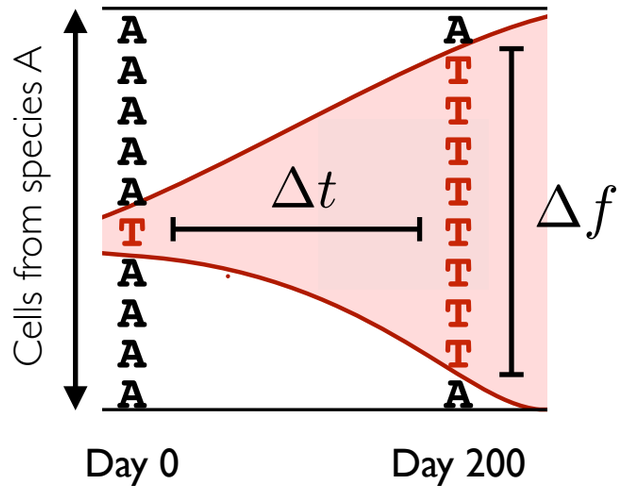
- **Next steps:** what do the ***population genetics*** of this process look like?
  - How important are natural selection, genetic drift, recombination w/in hosts?
  - Driven by sudden environmental changes (e.g. ABX)? or continual evolution?
  - What do "sweeps" look like? Selection strengths? de novo or pre-existing?

Key takeaways

- **Comparing 2 timepoints:** native microbiota ***can*** acquire genetic diffs on human-relevant timescales



→ ***mixture of "strain replacement" and "evolutionary modification"***

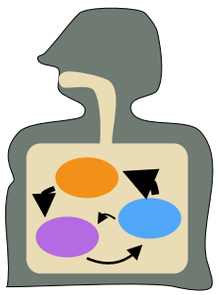


- **Next steps:** what do the ***population genetics*** of this process look like?
  - How important are natural selection, genetic drift, recombination w/in hosts?
  - Driven by sudden environmental changes (e.g. ABX)? or continual evolution?
  - What do "sweeps" look like? Selection strengths? de novo or pre-existing?

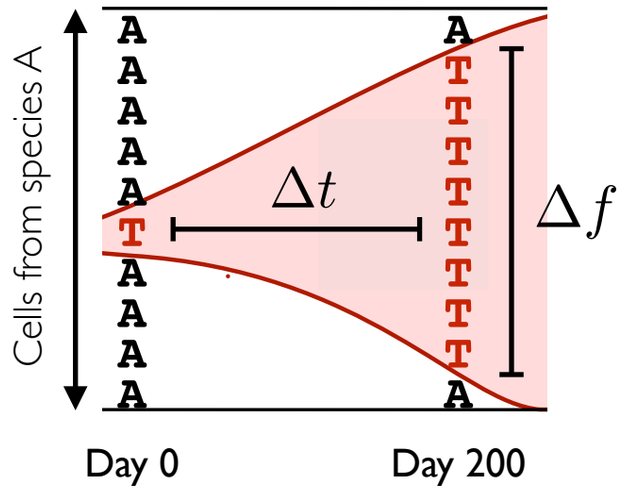
Does it matter if ***"strain replacement"*** vs ***"evolutionary modification"*** ?

Key takeaways

- **Comparing 2 timepoints:** native microbiota ***can*** acquire genetic diffs on human-relevant timescales



→ ***mixture of "strain replacement" and "evolutionary modification"***

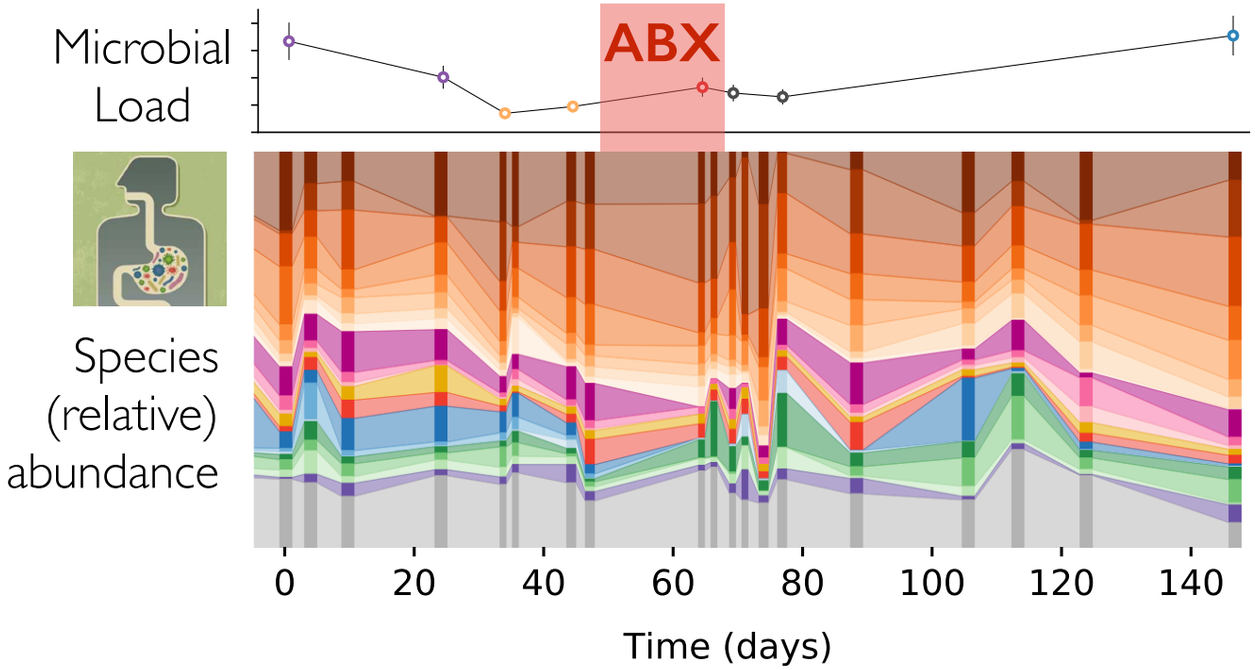


- **Next steps:** what do the ***population genetics*** of this process look like?
  - How important are natural selection, genetic drift, recombination w/in hosts?
  - Driven by sudden environmental changes (e.g. ABX)? or continual evolution?
  - What do "sweeps" look like? Selection strengths? de novo or pre-existing?

Does it matter if ***"strain replacement"*** vs ***"evolutionary modification"*** ?

→ ***requires denser longitudinal sampling***

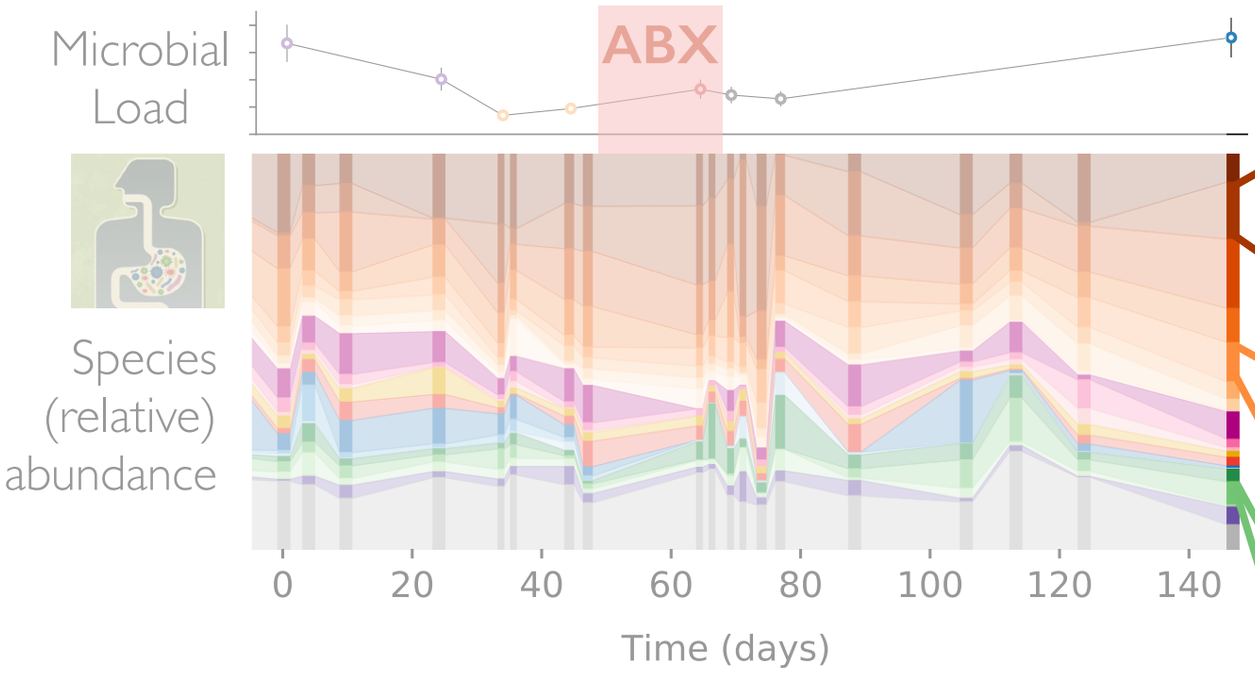
Next steps: dense time series data to infer *dynamics of this process*

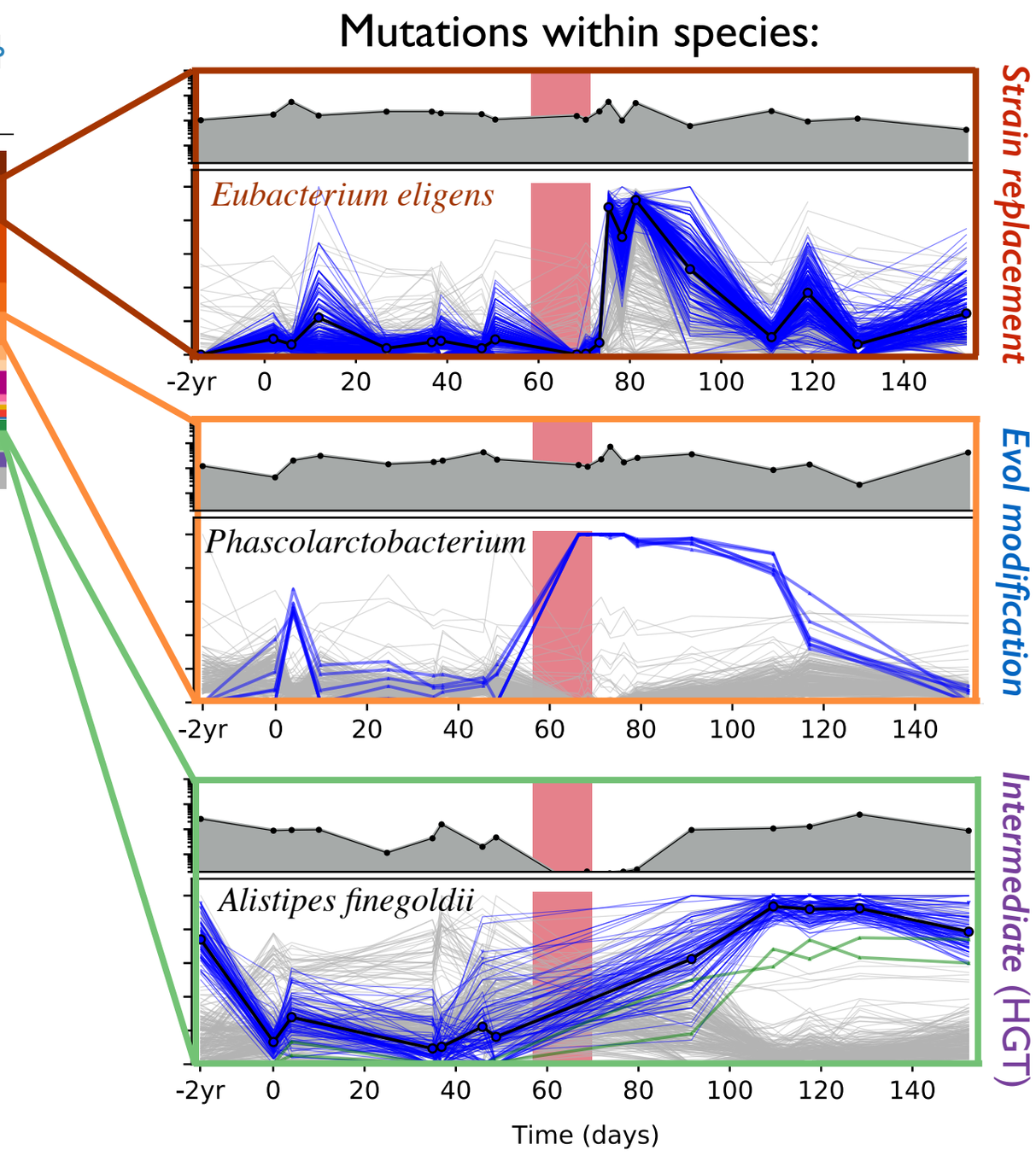


Morteza Roodgar

Mike Snyder (Stanford)

Next steps: dense time series data to infer *<u>dynamics</u> of this process*



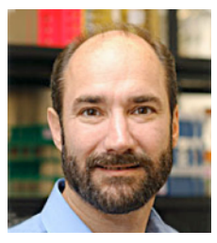


+

33 other species

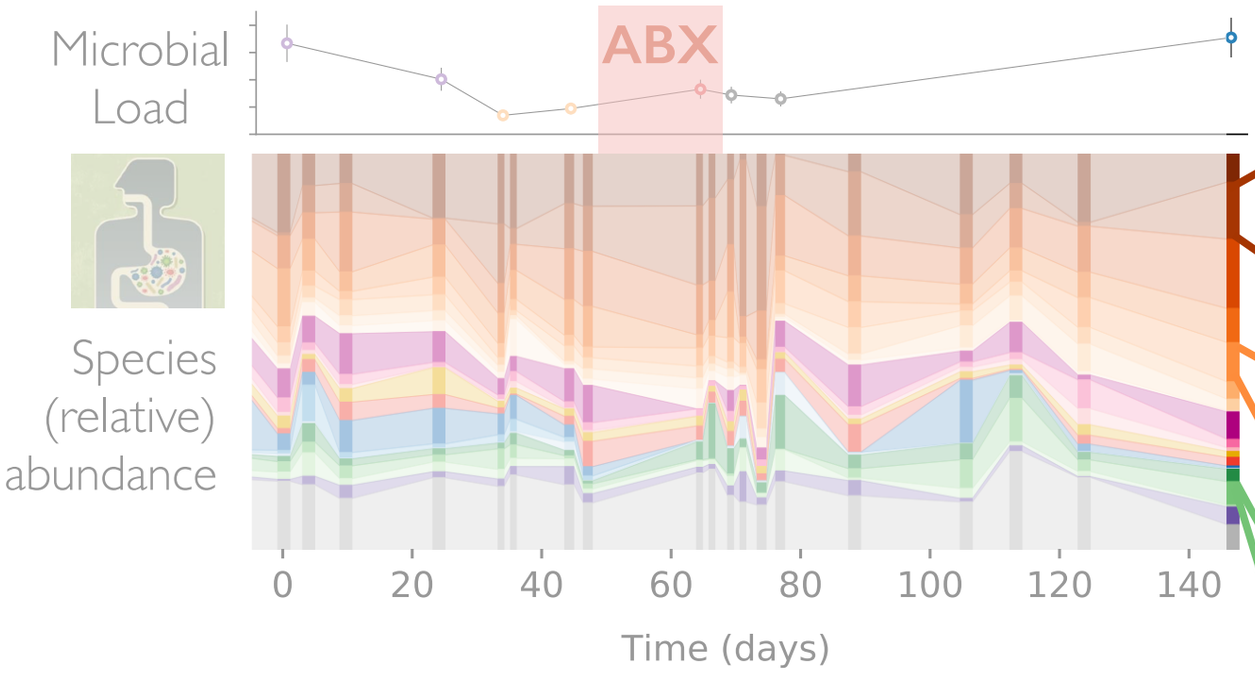
(18 w/ genetic changes)

Morteza Roodgar



Mike Snyder (Stanford)

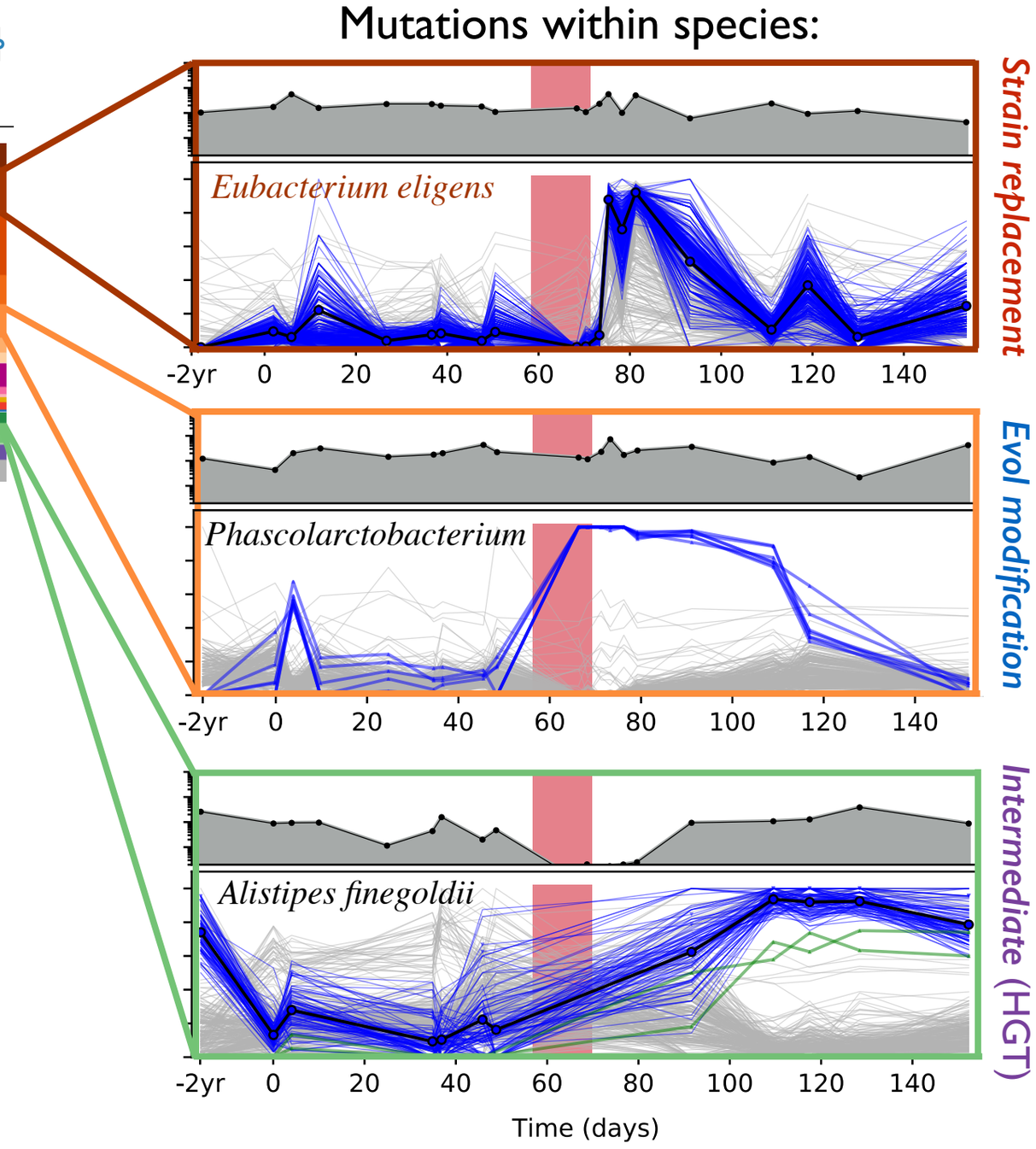
Next steps: dense time series data to infer *dynamics of this process*



Question: how do native gut microbiota respond to ABX perturbations at the ***genetic level***?

Morteza Roodgar

Mike Snyder (Stanford)

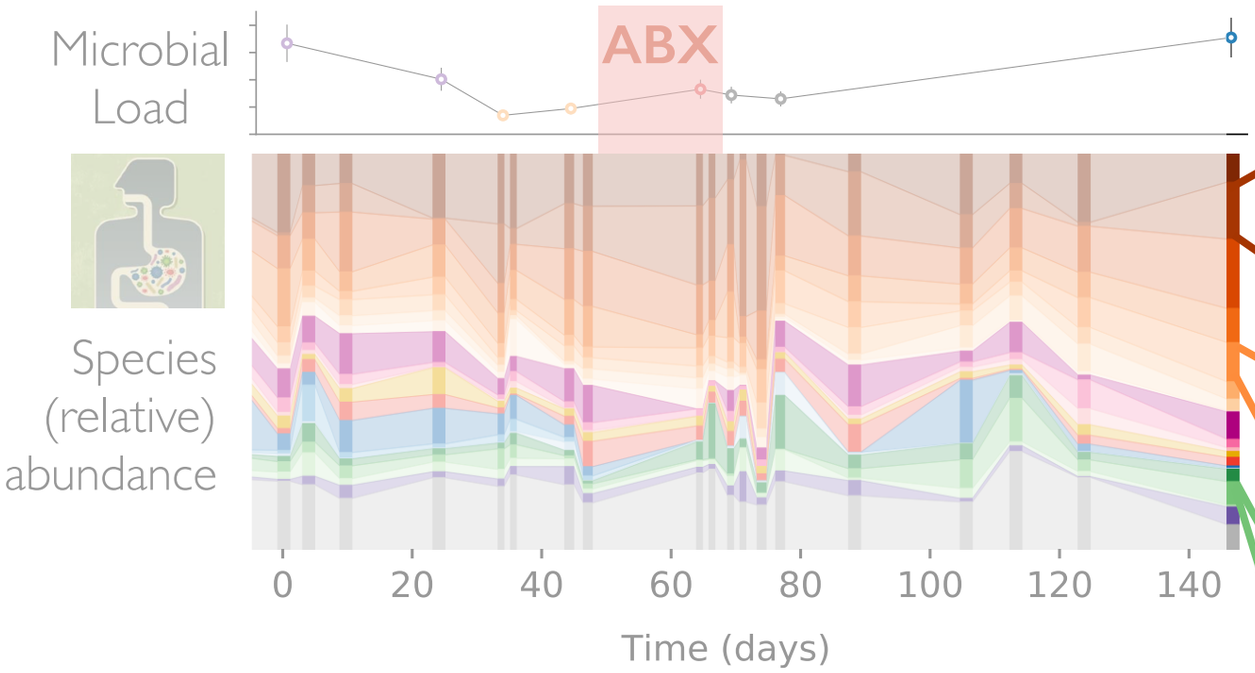


+

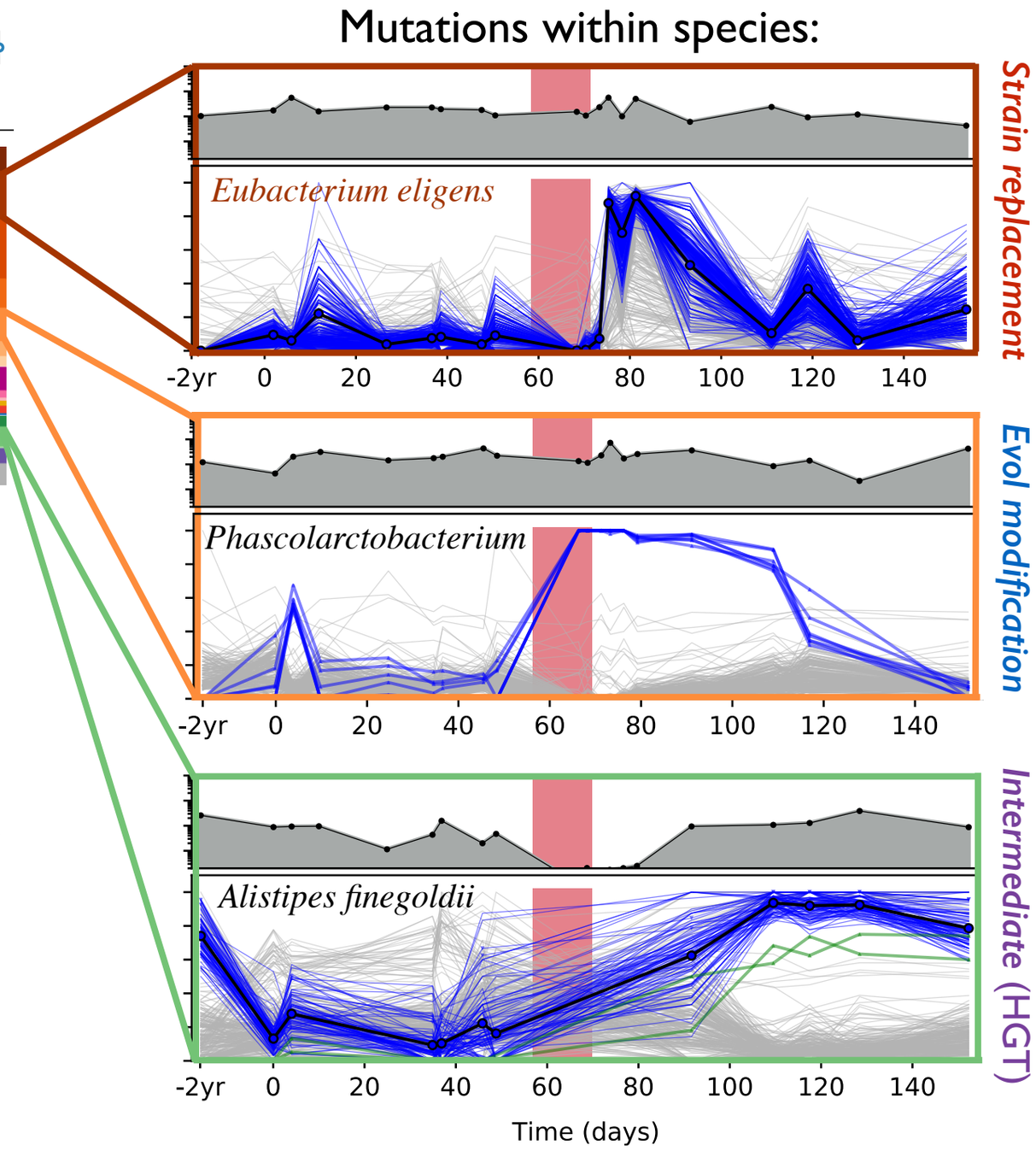
33 other species

(18 w/ genetic changes)

Next steps: dense time series data to infer *<u>dynamics</u> of this process*



ABX can drive ***rapid genetic changes*** w/in species this complex community



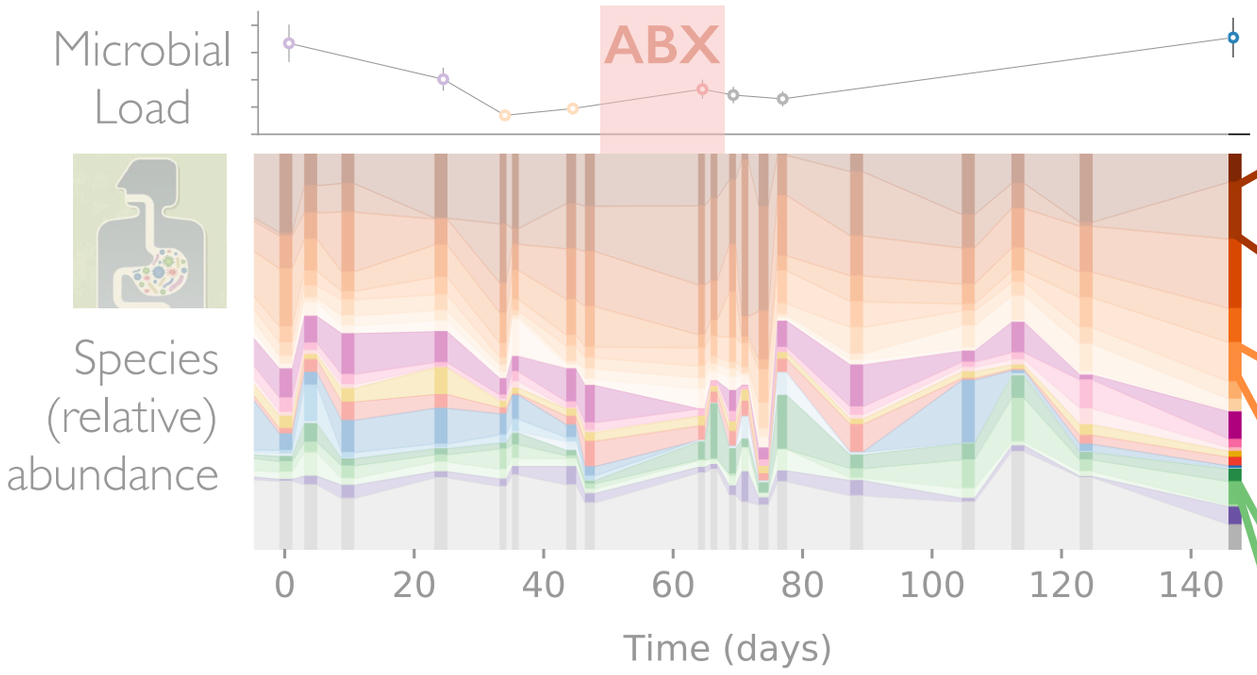
+

33 other species

(18 w/ genetic changes)

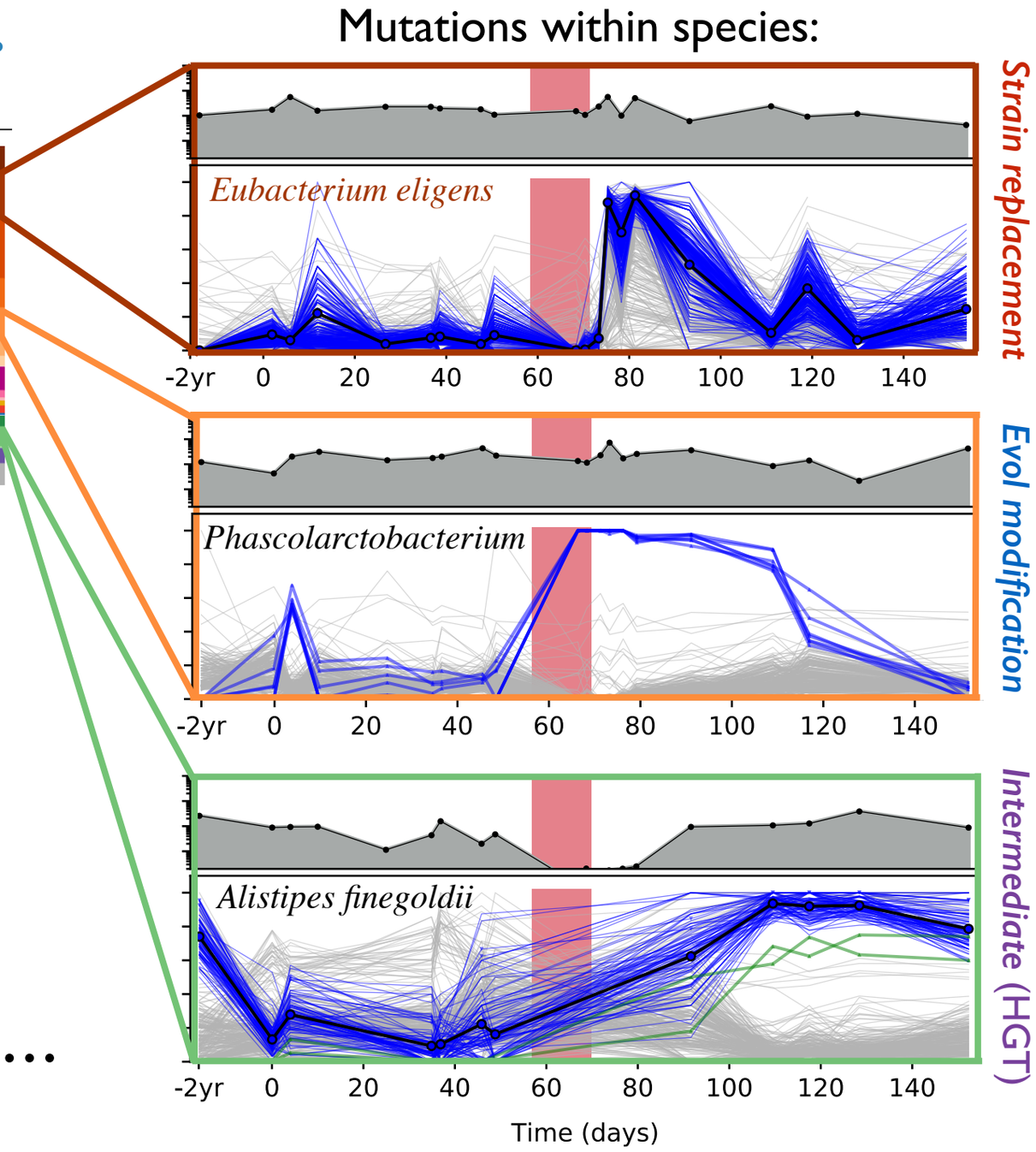
Roodgar* & Good* et al (*Genome Research*, 2021)

Next steps: dense time series data to infer *<u>dynamics</u> of this process*



ABX can drive ***rapid genetic changes*** w/in species this complex community

↳ ***but not consistent with simple <u>extinction & recolonization</u> picture…***



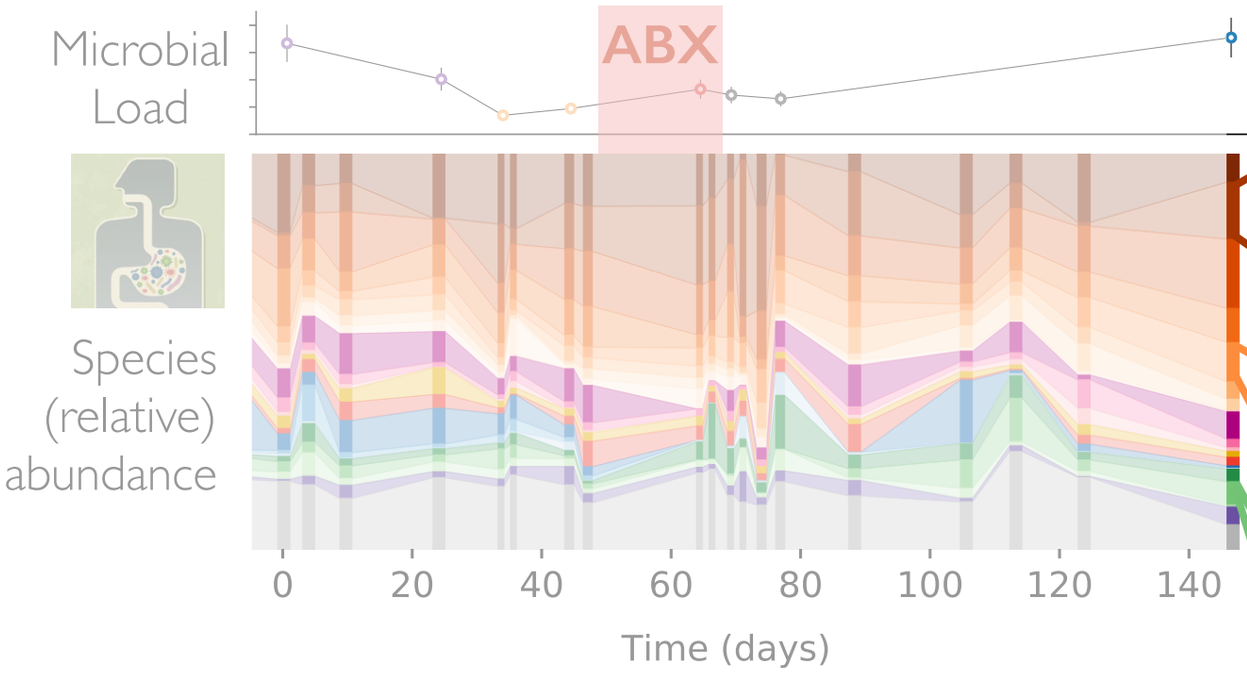
+

33 other species

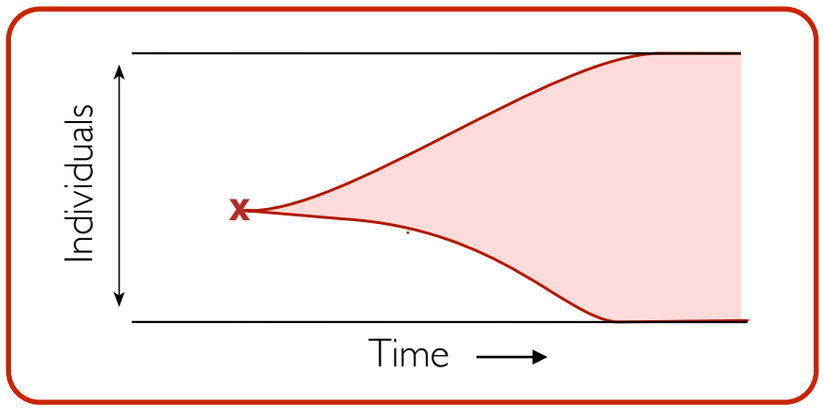
(18 w/ genetic changes)

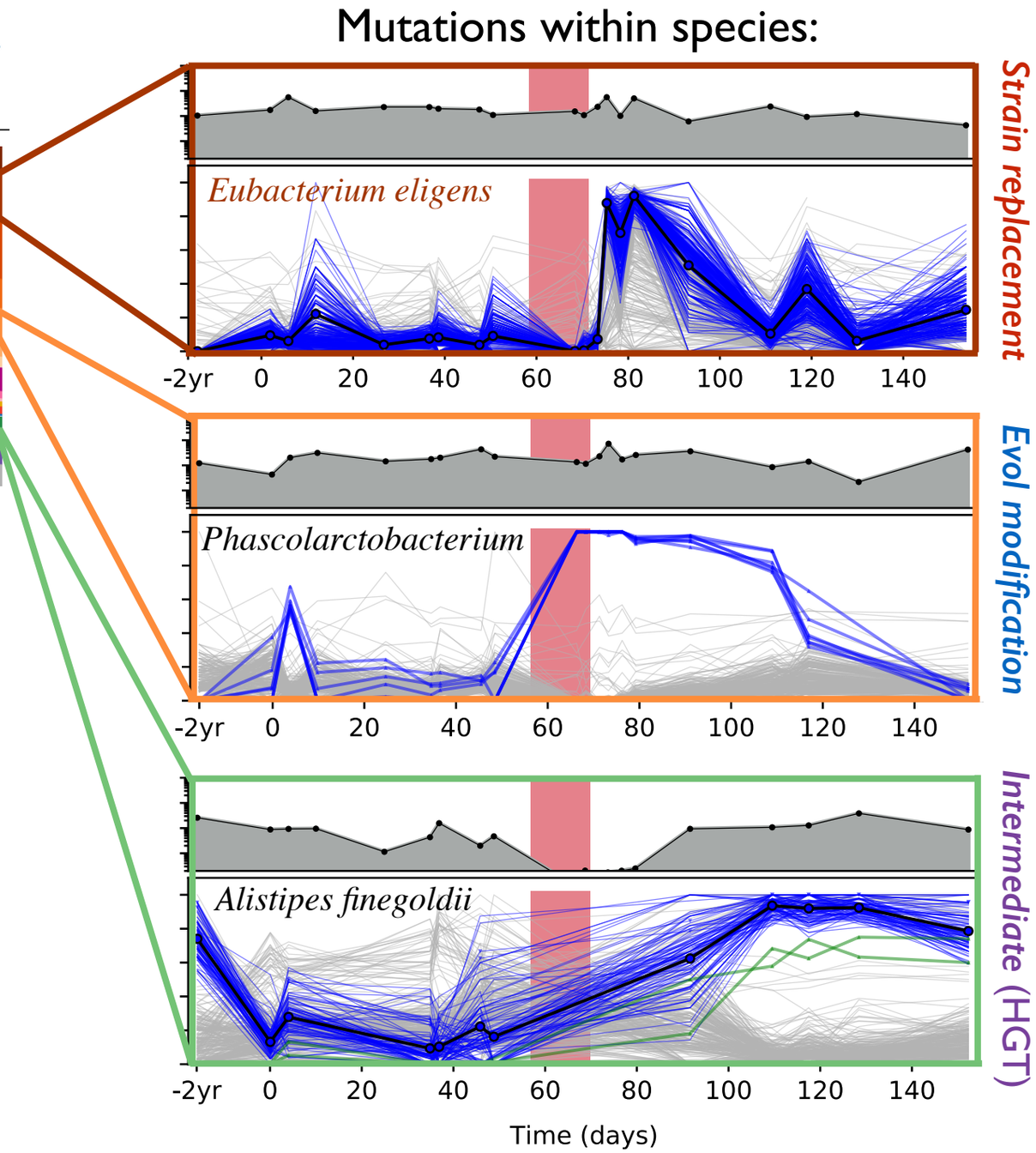
Roodgar* & Good* et al (*Genome Research*, 2021)

Next steps: dense time series data to infer *dynamics* of this process



➔ ***but also inconsistent w/ simplest models of ABX resistance evolution***





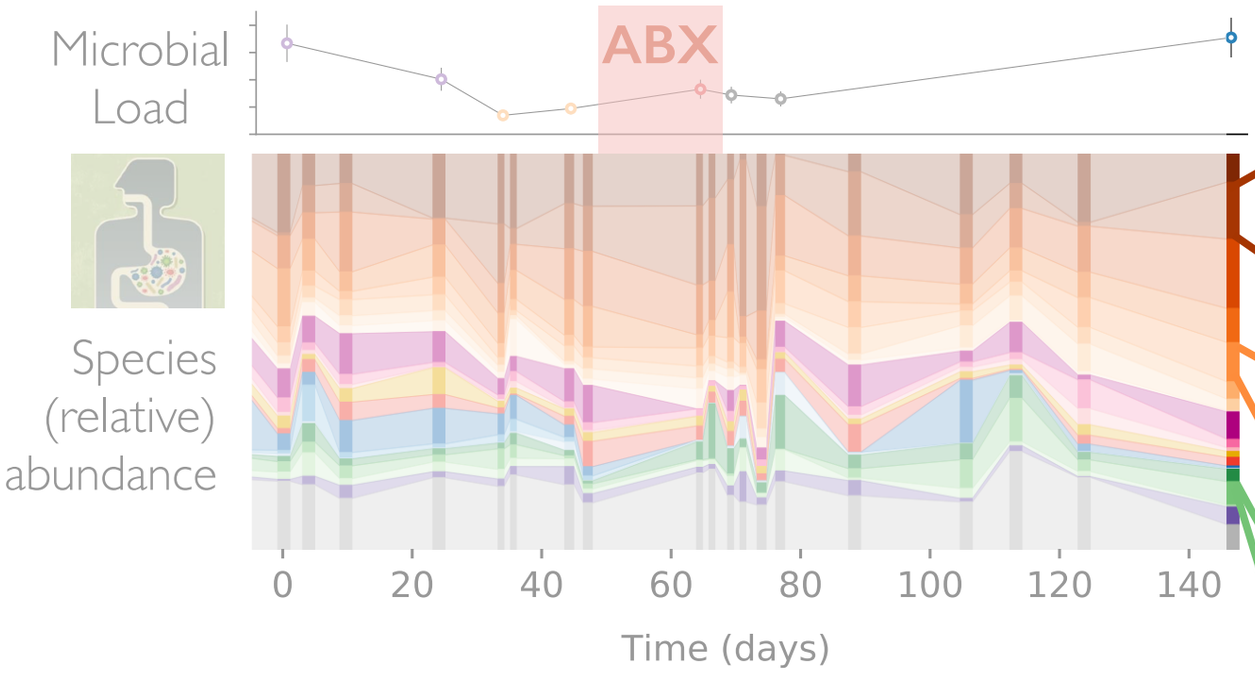
+

33 other species

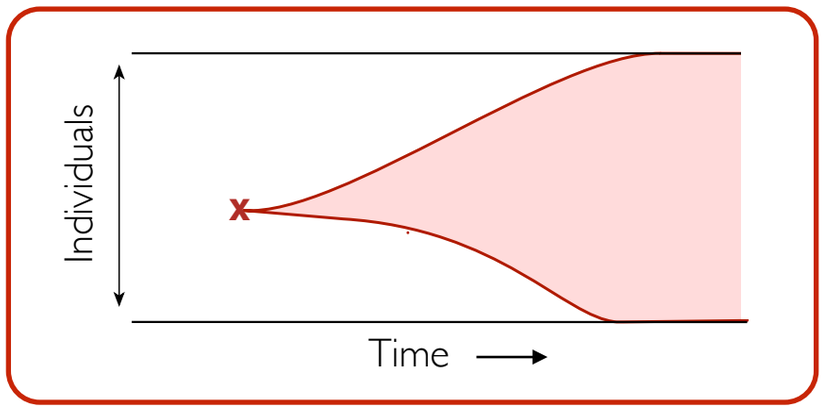
(18 w/ genetic changes)

Roodgar* & Good* et al (*Genome Research*, 2021)

Next steps: dense time series data to infer *dynamics* of this process

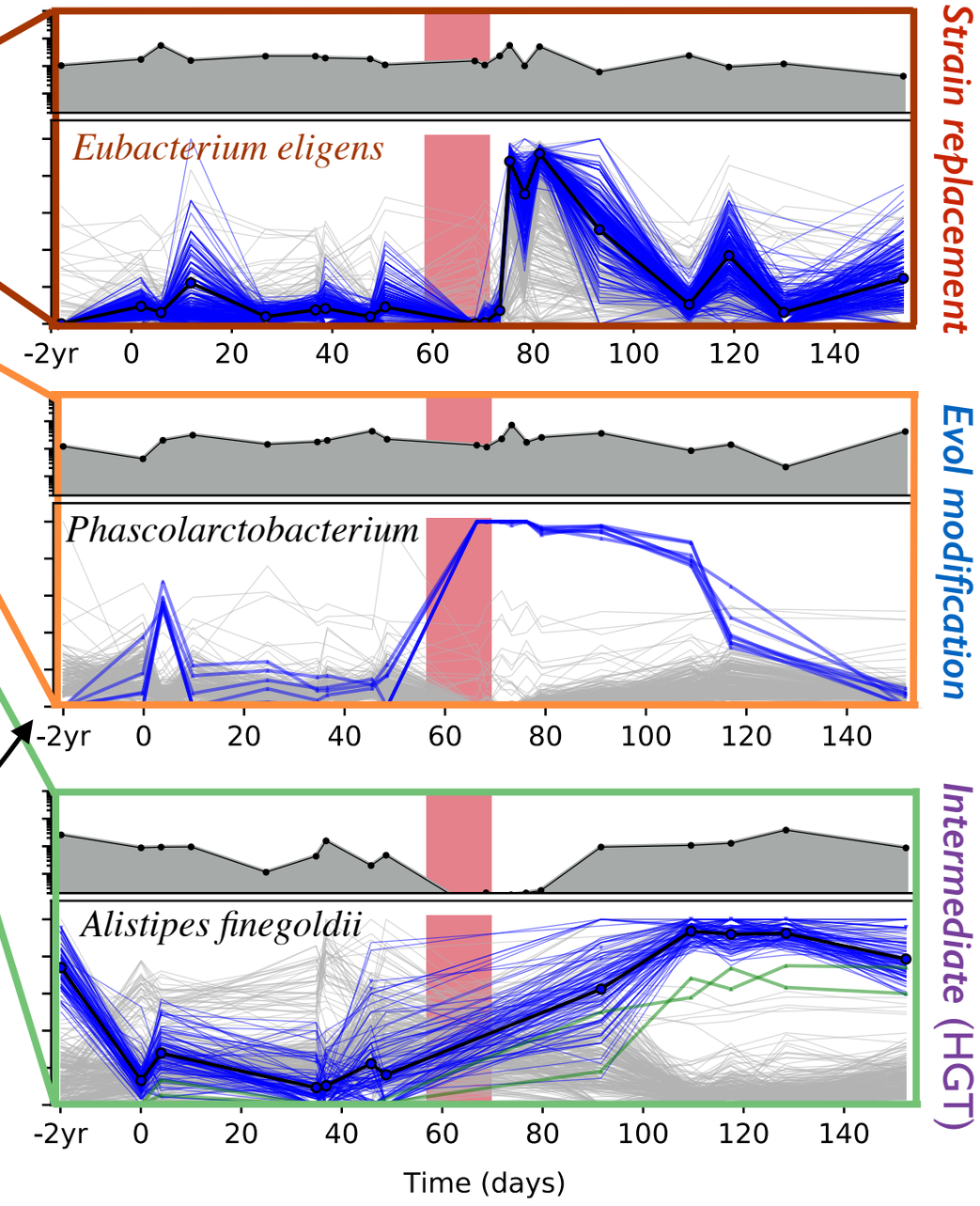


→ ***but also inconsistent w/ simplest models of ABX resistance evolution***



Very different from cartoon!

Mutations within species:



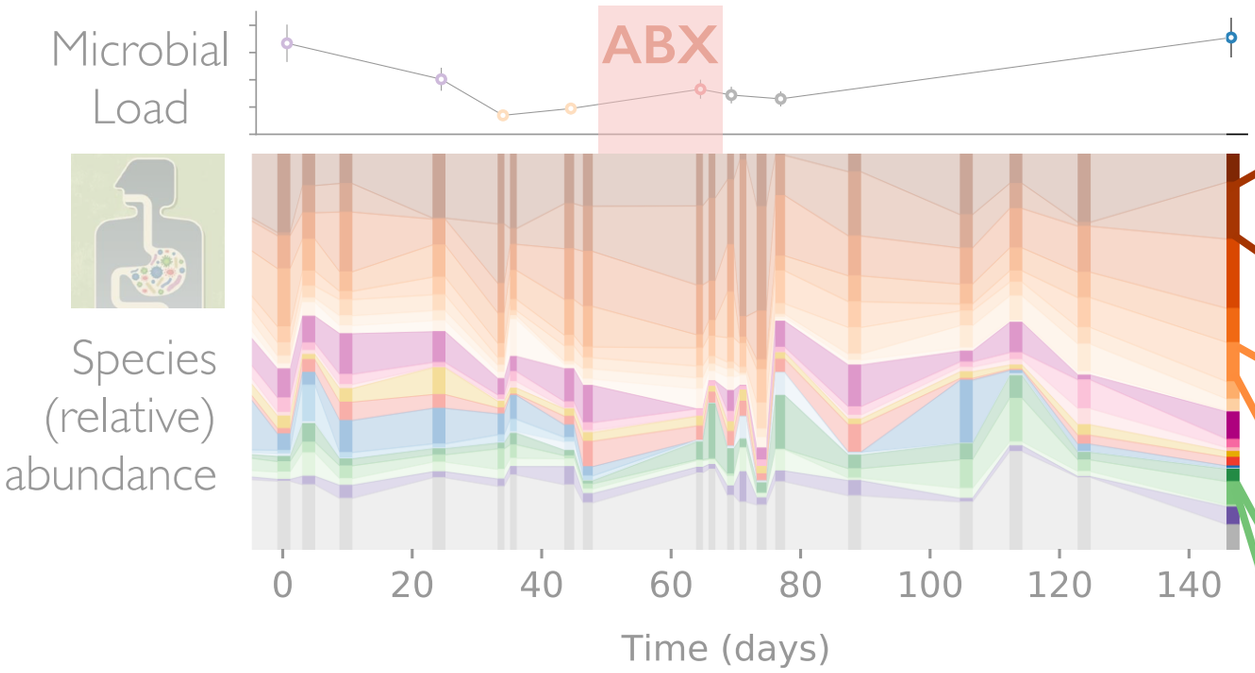
\+

33 other species

(18 w/ genetic changes)

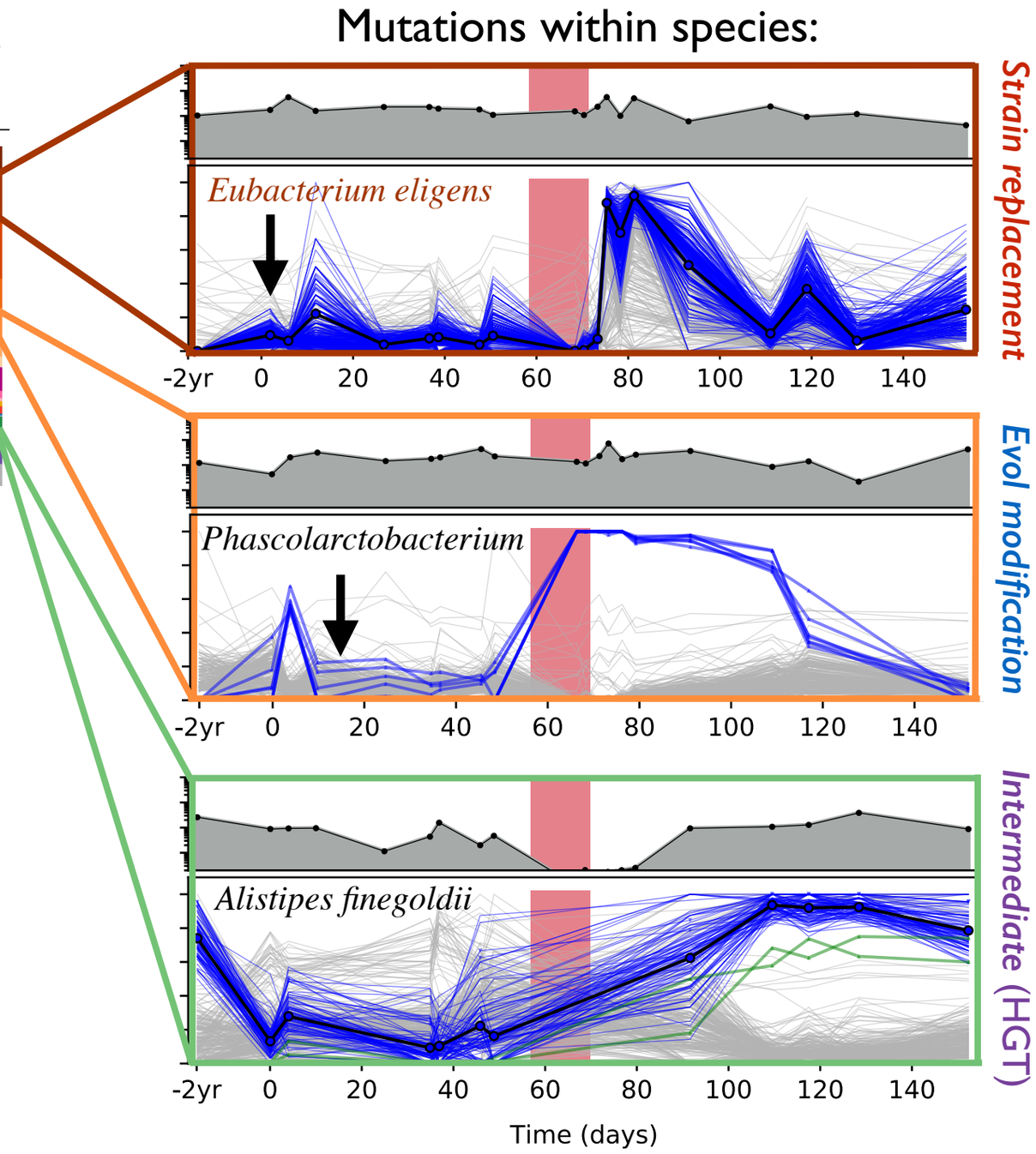
Roodgar* & Good* et al (*Genome Research*, 2021)

Next steps: dense time series data to infer *dynamics* of this process



Instead, common trends:

- Sweeping variants often present at low freqs before ABX



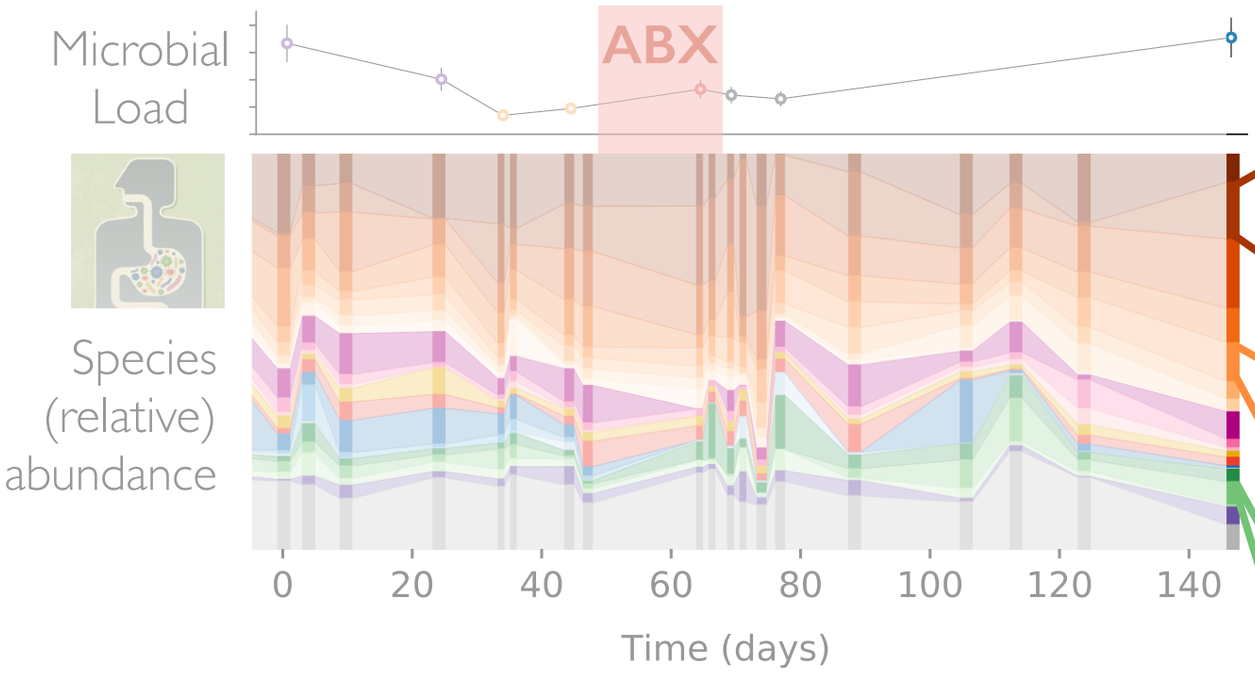
+

33 other species

(18 w/ genetic changes)

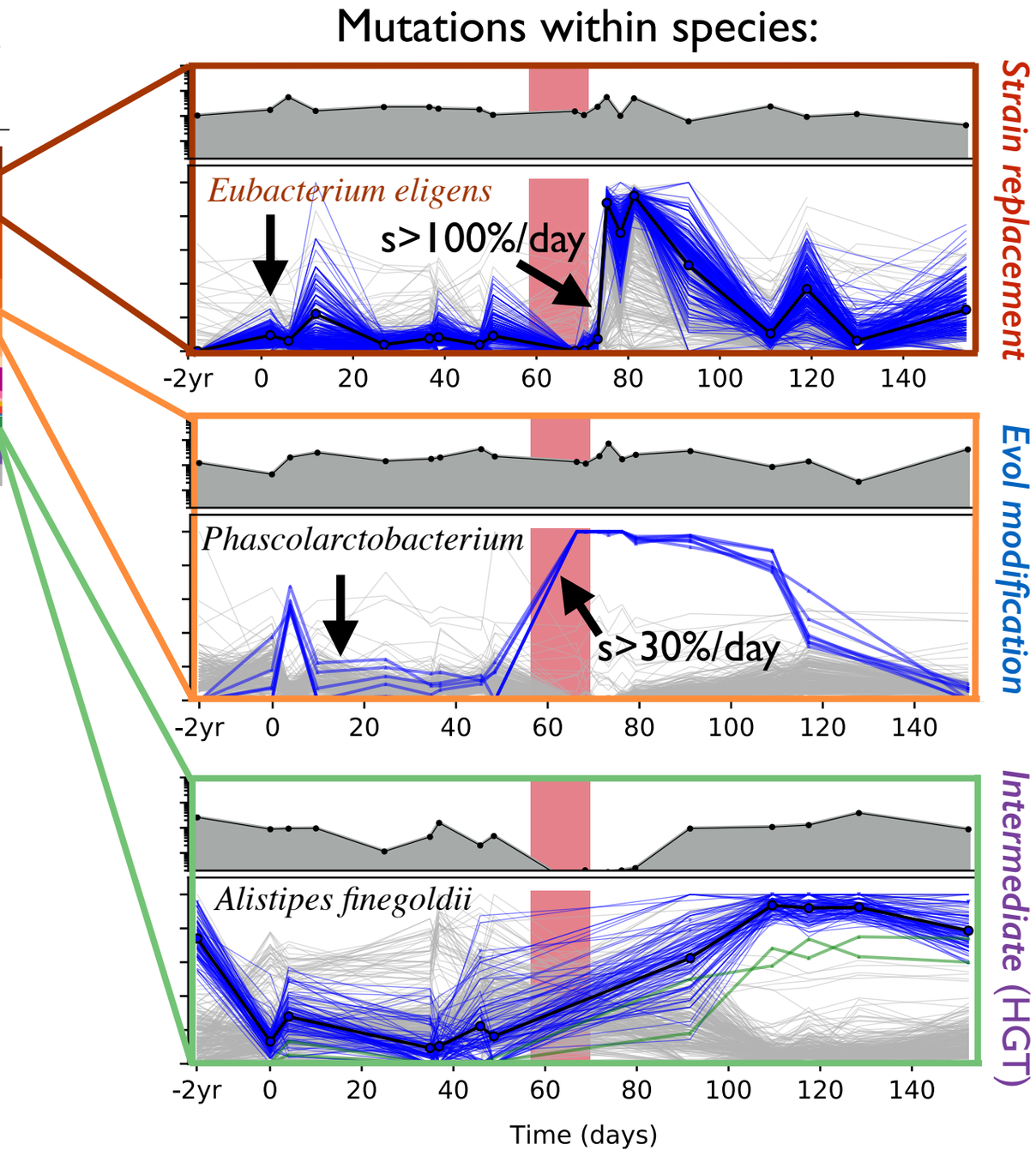
Roodgar* & Good* et al (*Genome Research*, 2021)

Next steps: dense time series data to infer *dynamics* of this process



Instead, common trends:

- Sweeping variants often present at low freqs before ABX



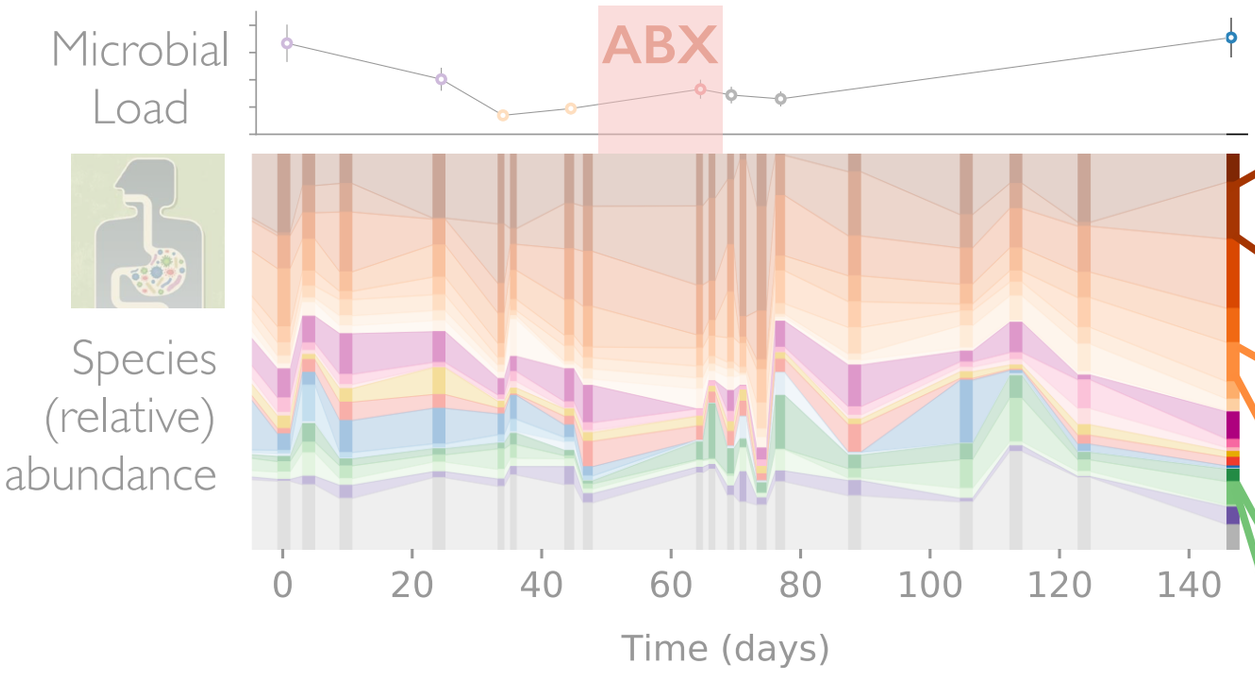
+

33 other species

(18 w/ genetic changes)

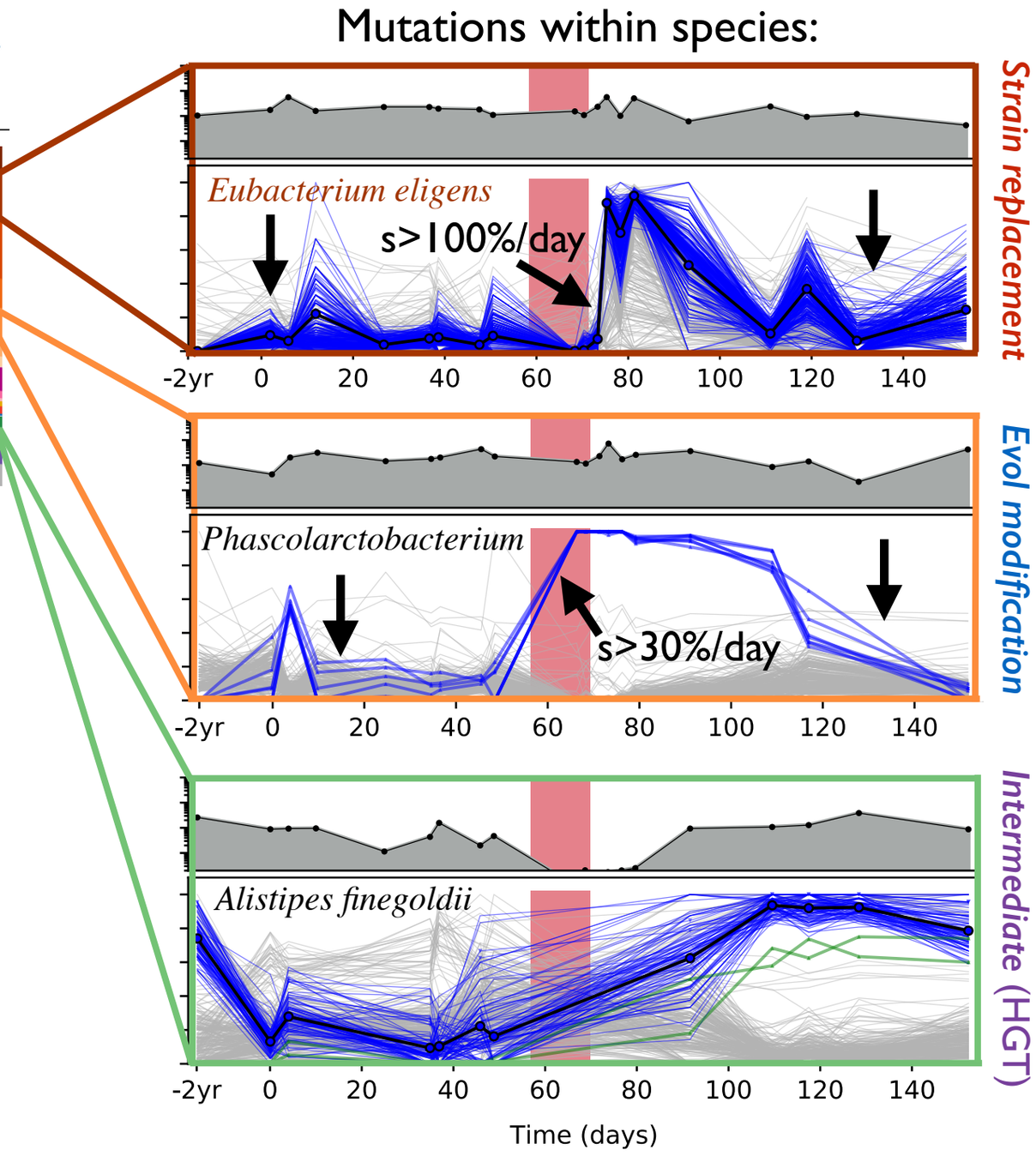
Roodgar* & Good* et al (*Genome Research*, 2021)

Next steps: dense time series data to infer *dynamics* of this process



Instead, common trends:

- Sweeping variants often present at low freqs before ABX
- But few fix — many return back to initial levels w/in a few months



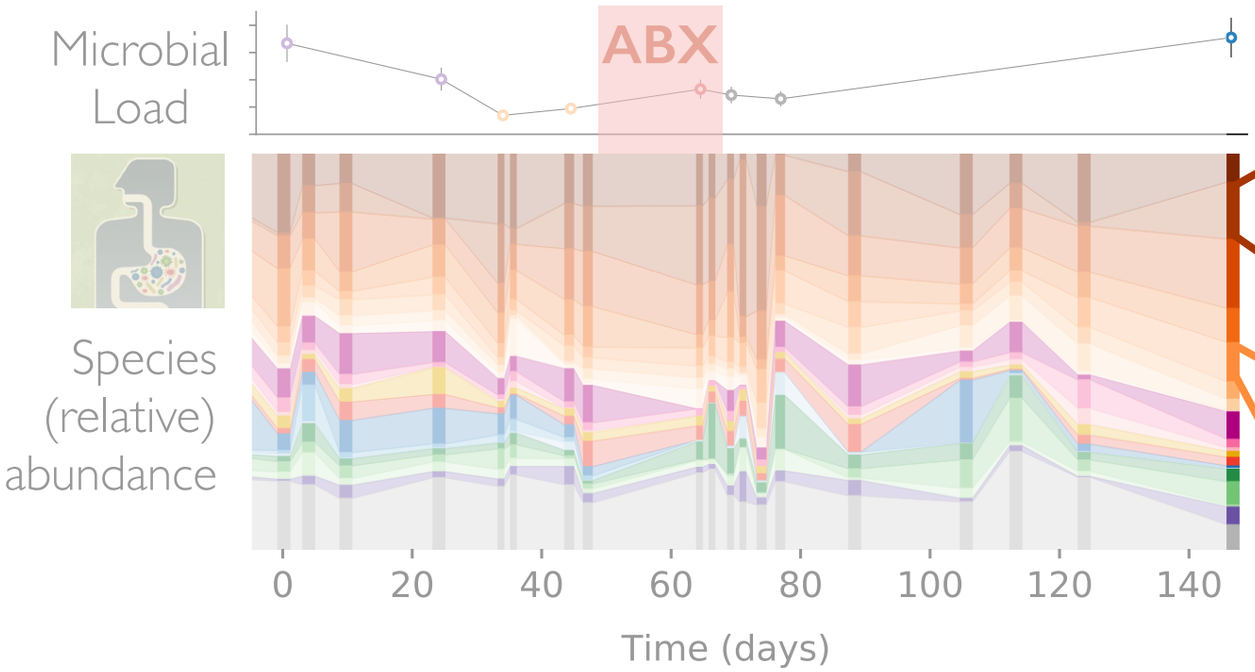
+

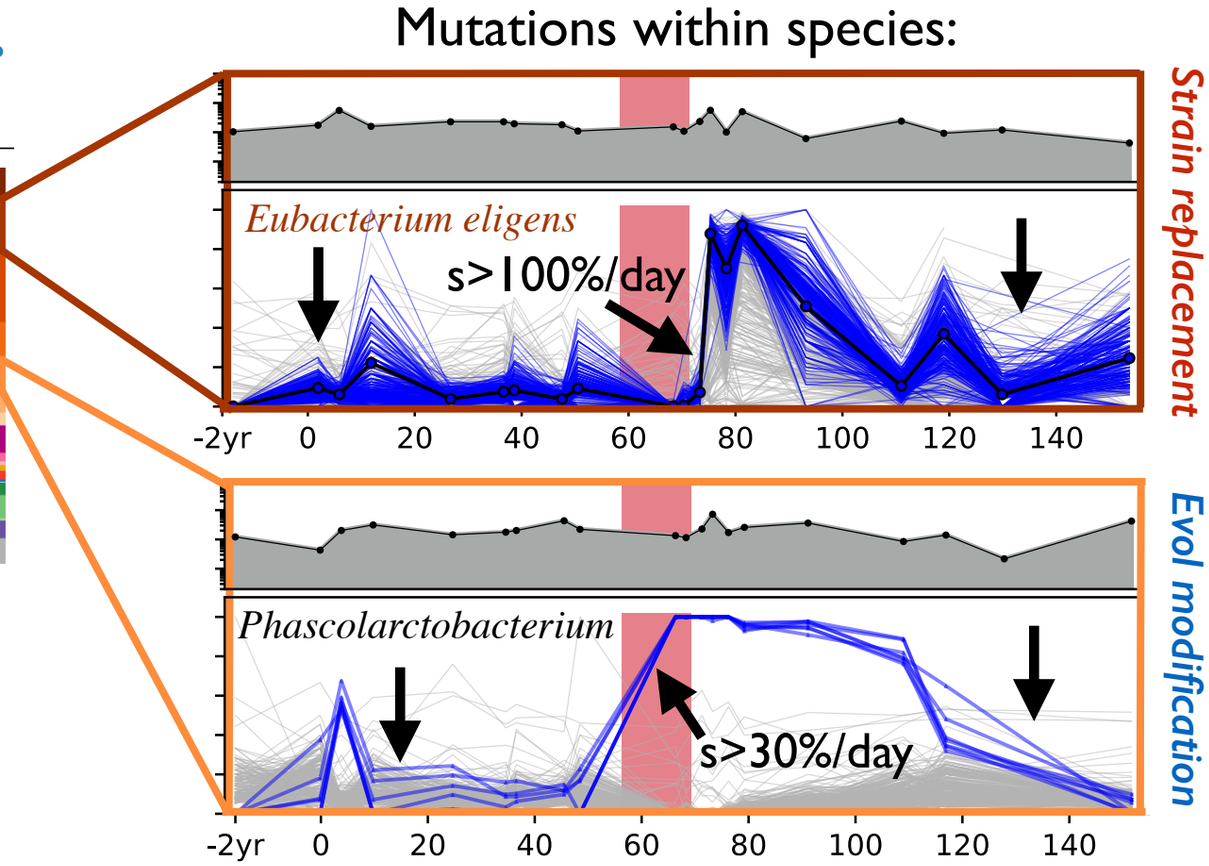
33 other species

(18 w/ genetic changes)

Roodgar* & Good* et al (*Genome Research*, 2021)

Next steps: dense time series data to infer *dynamics* of this process





Instead, common trends:

- Sweeping variants often present at low freqs before ABX
- But few fix — many return back to initial levels w/in a few months

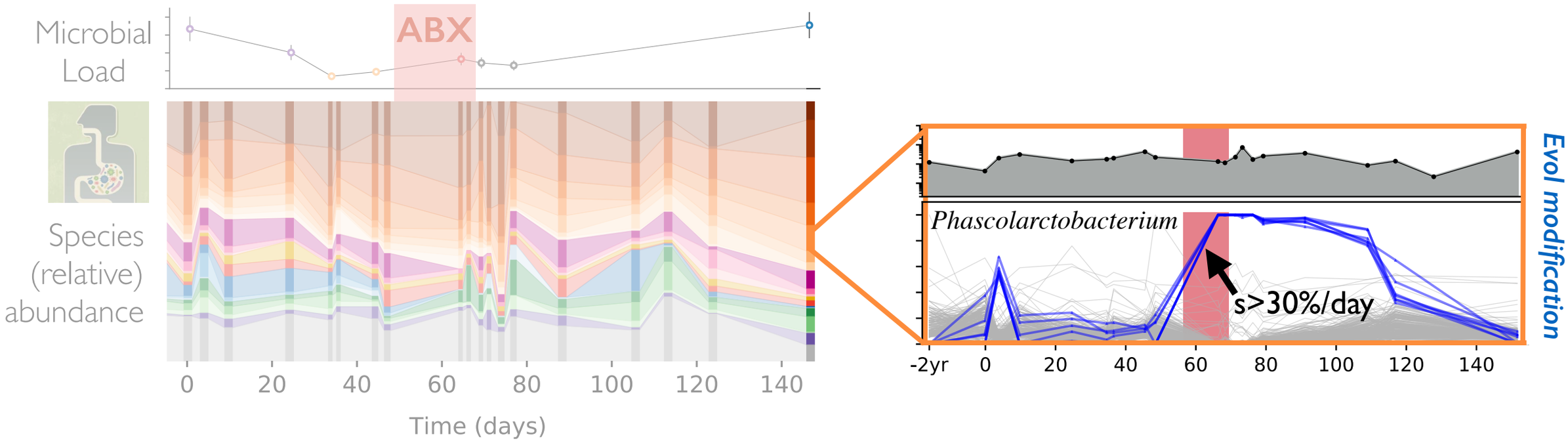
+ 34 other species (19 w/ genetic changes)

Evidence for add'l ecological structure <u>within species</u> in this complex community?

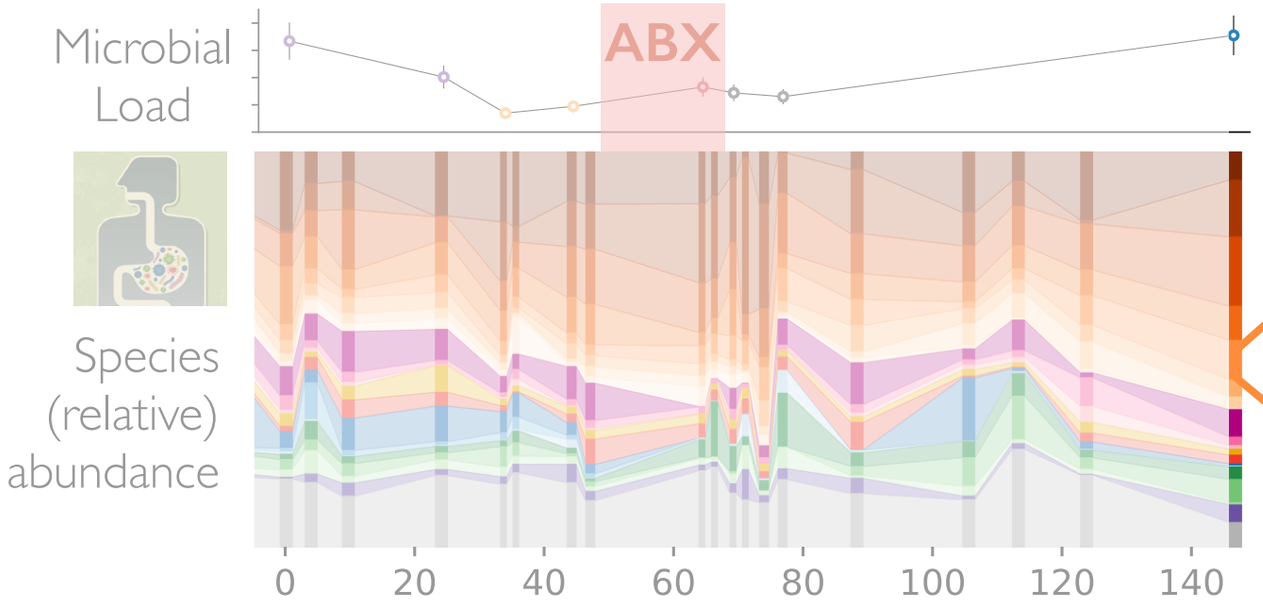
See also: Zhao* & Liberman* et al (*Cell Host & Microbe*, 2019)

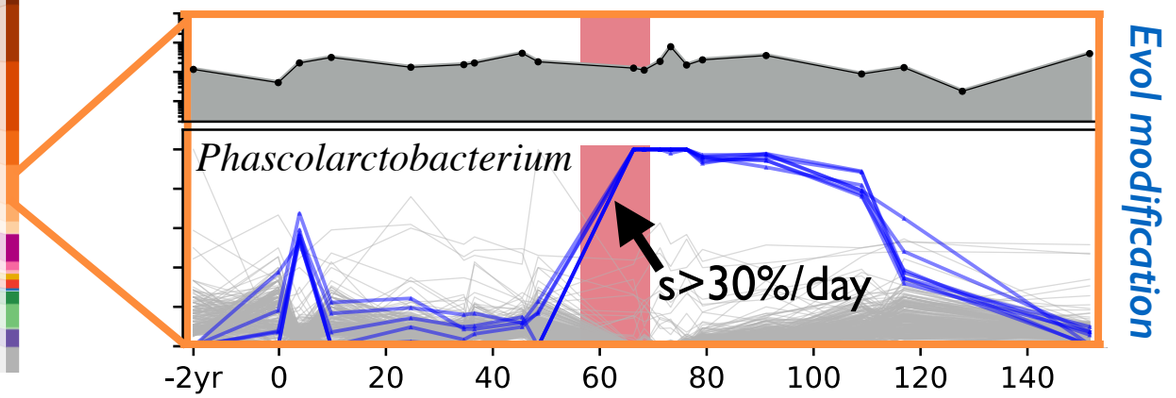
Roodgar* & Good* et al (*Genome Research*, 2021)

Problem: observational sequencing is limited by throughput



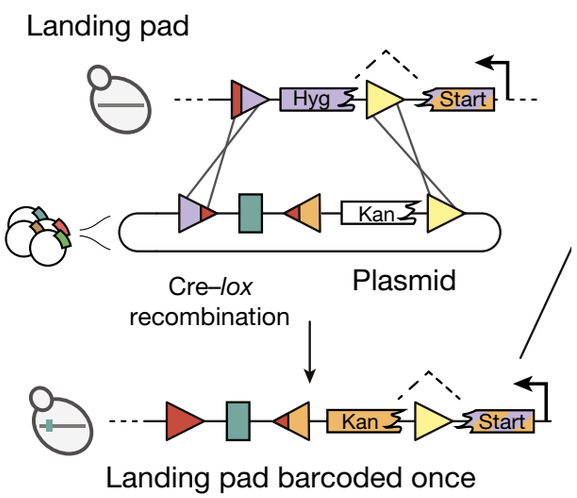
Problem: observational sequencing is limited by throughput

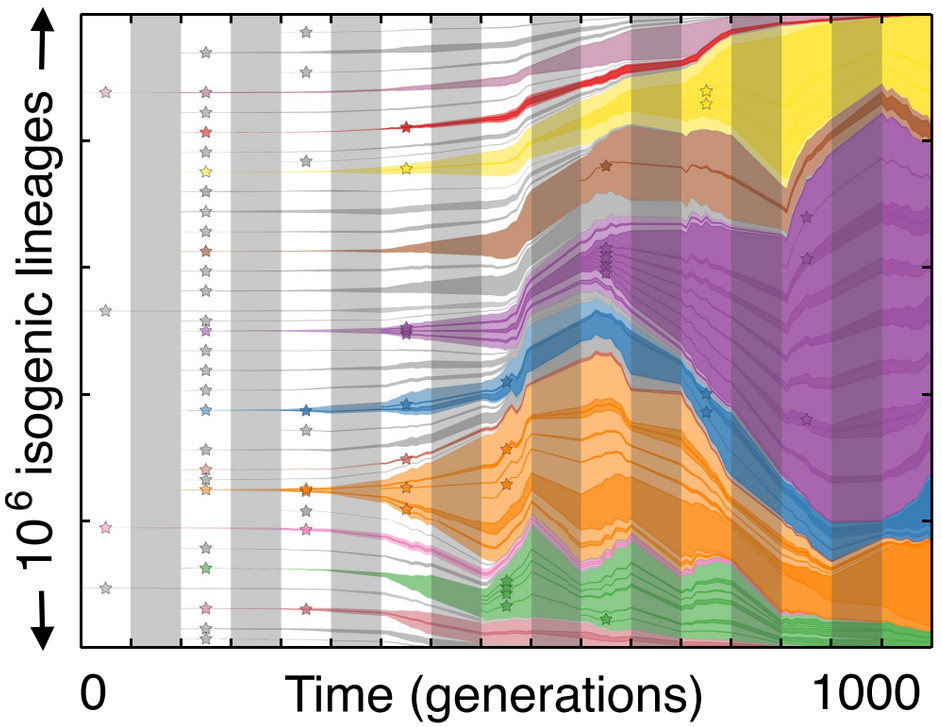




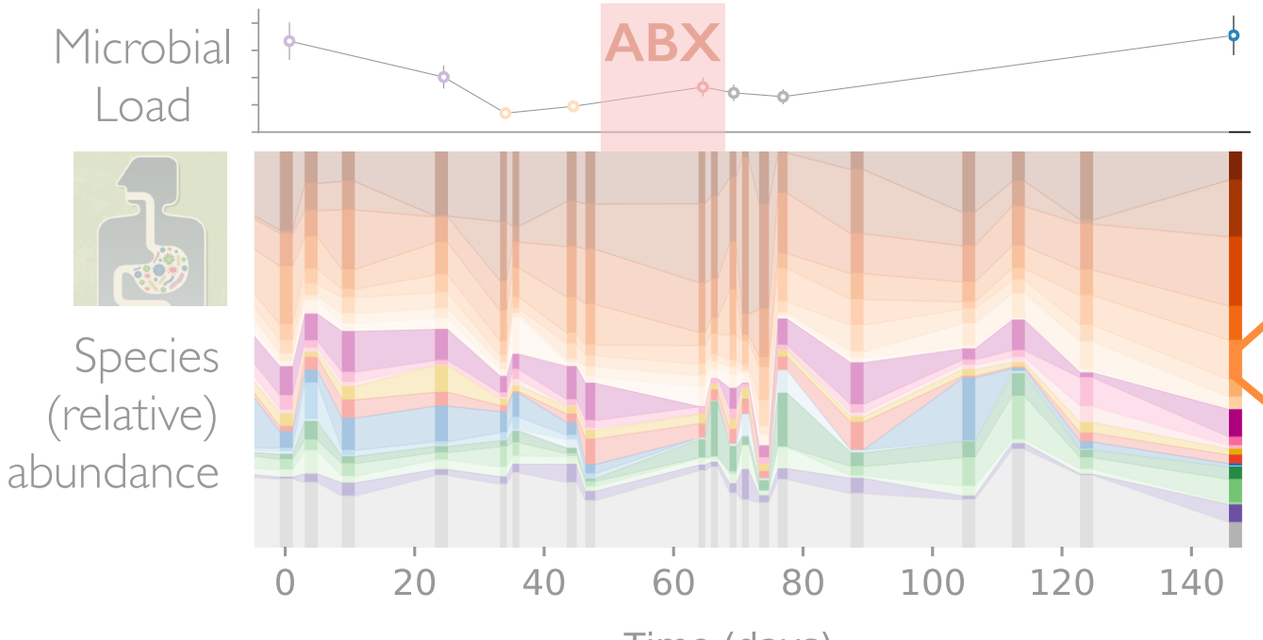
vs

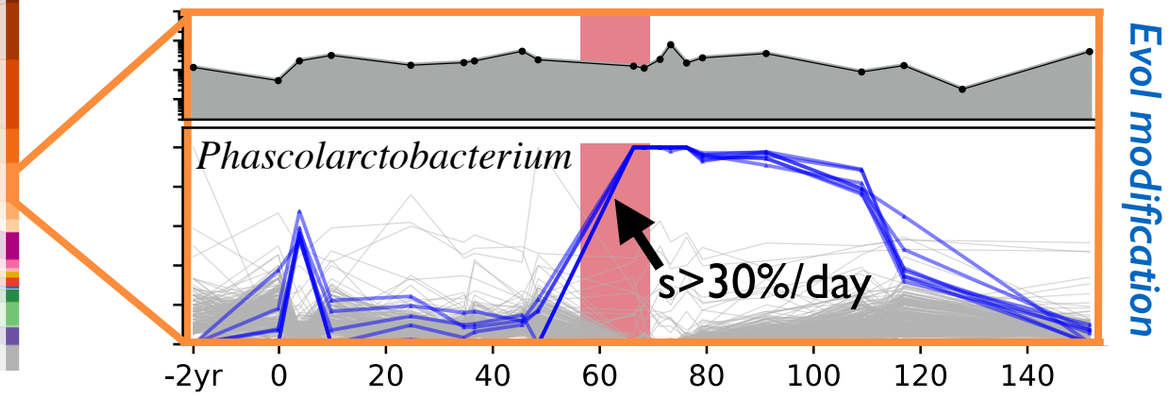
Genetic barcoding in lab yeast
(e.g. Nguyen Ba et al 2019)





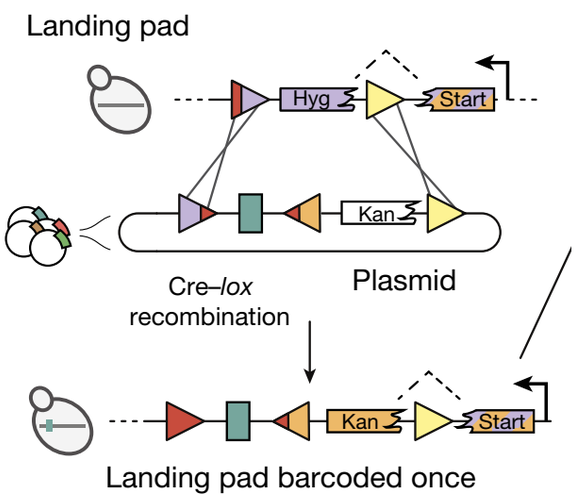
Problem: observational sequencing is limited by throughput

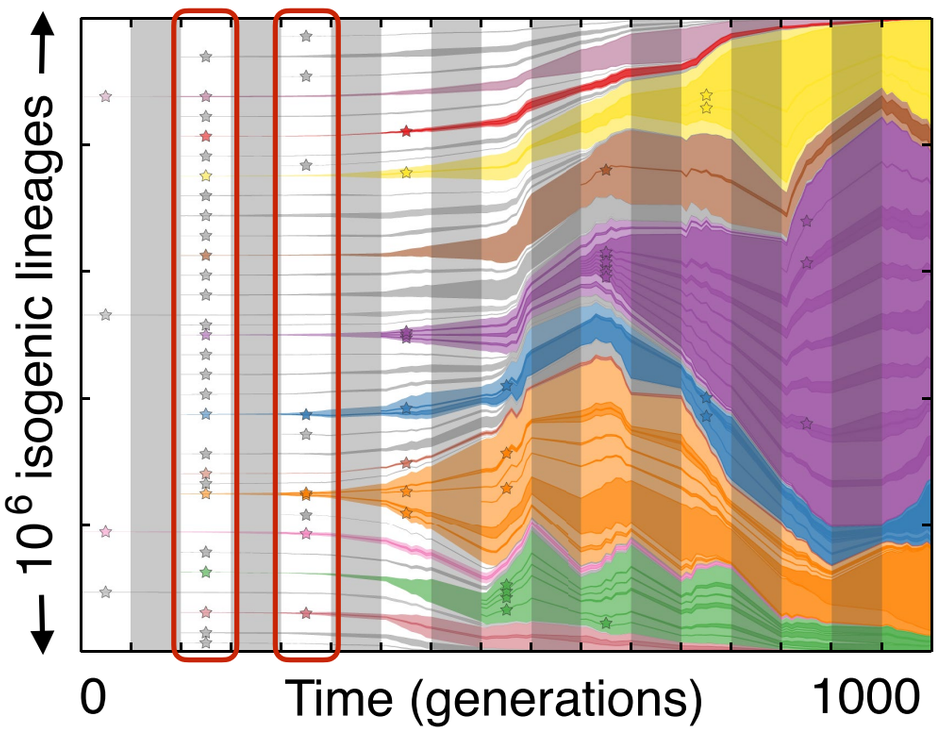




vs

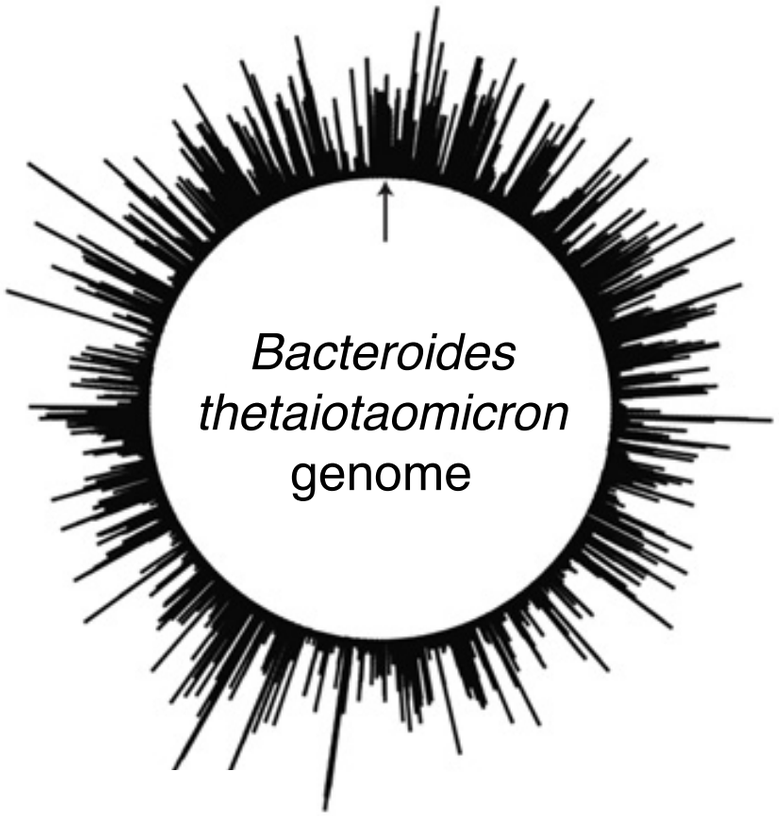
Genetic barcoding in lab yeast
(e.g. Nguyen Ba et al 2019)



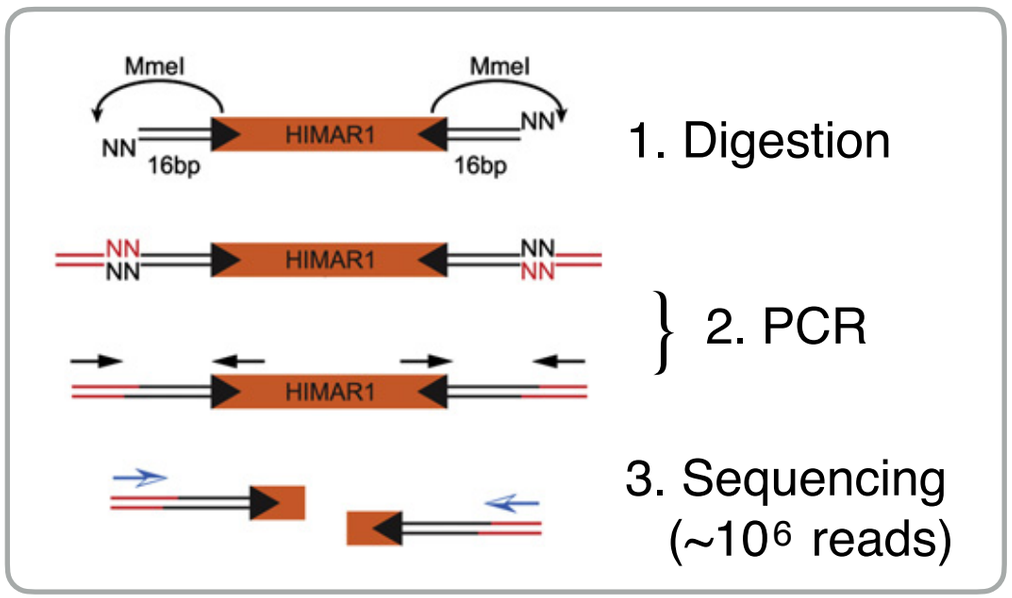


Fitness measurements of ~1000 ben. mut'ns in a single population

High-resolution lineage tracking w/ genome-wide TnSeq libraries



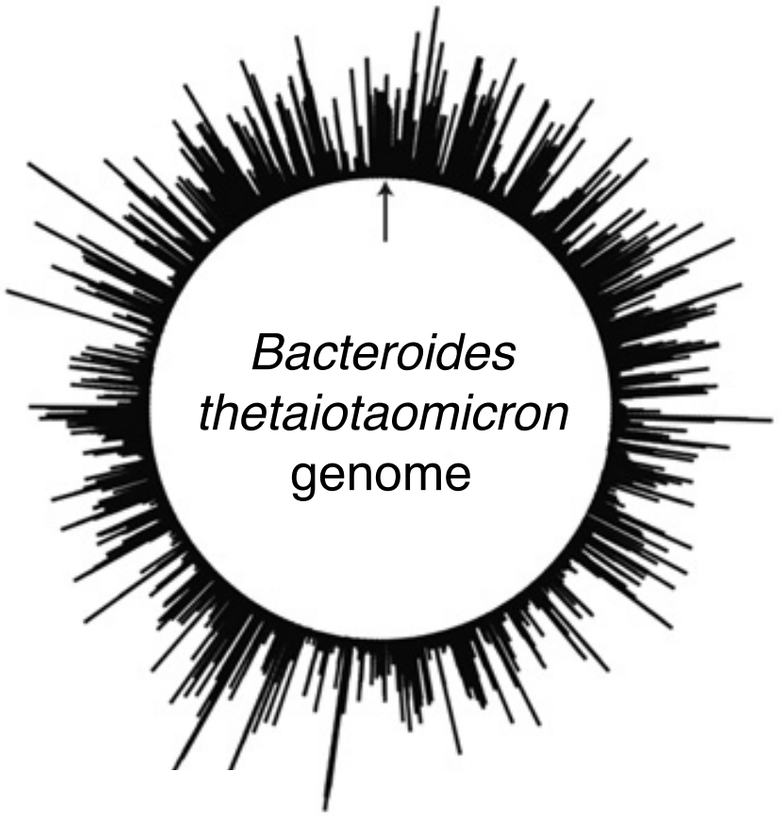
Insertion location = "barcode"



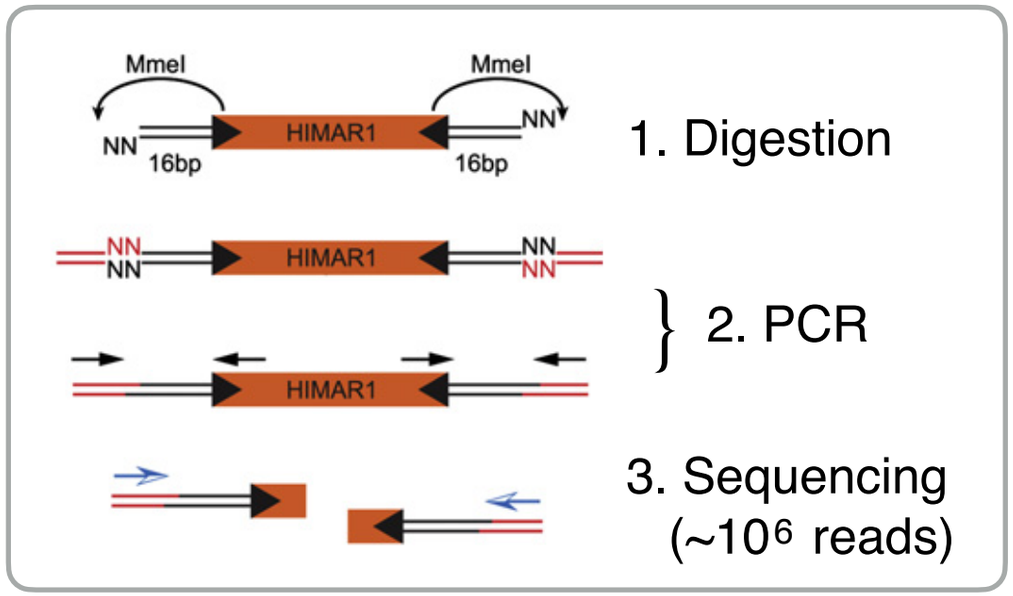
— 10 insertions / kb (~1 insertion / cell)

Goodman et al (*Cell Host Microbe* 2009)

High-resolution lineage tracking w/ genome-wide TnSeq libraries

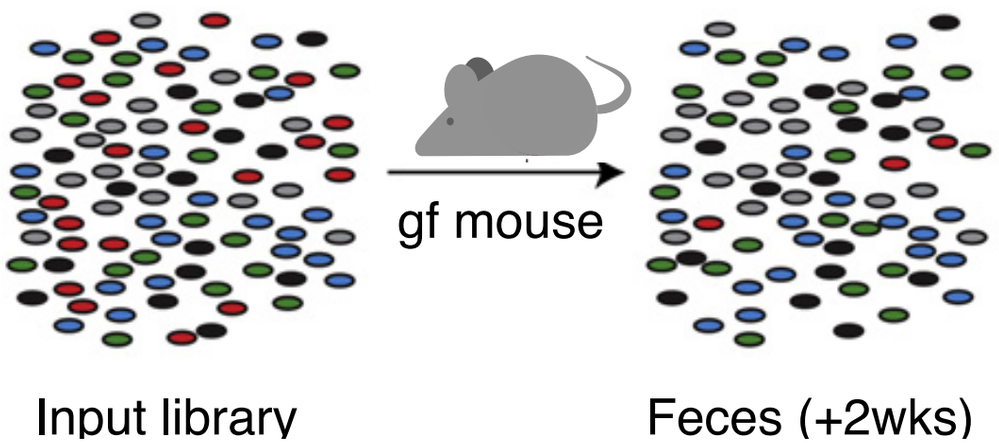


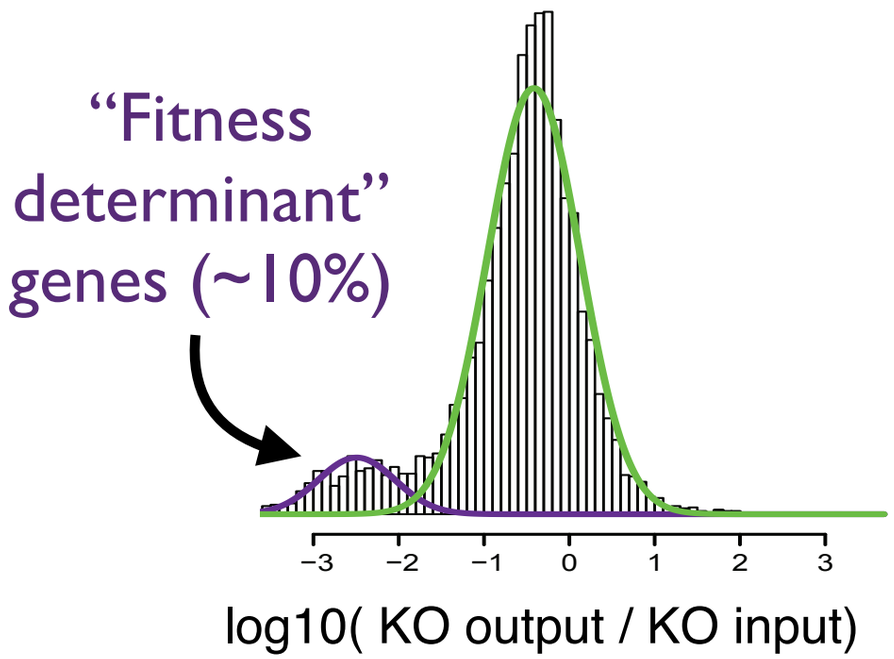
Insertion location = "barcode"



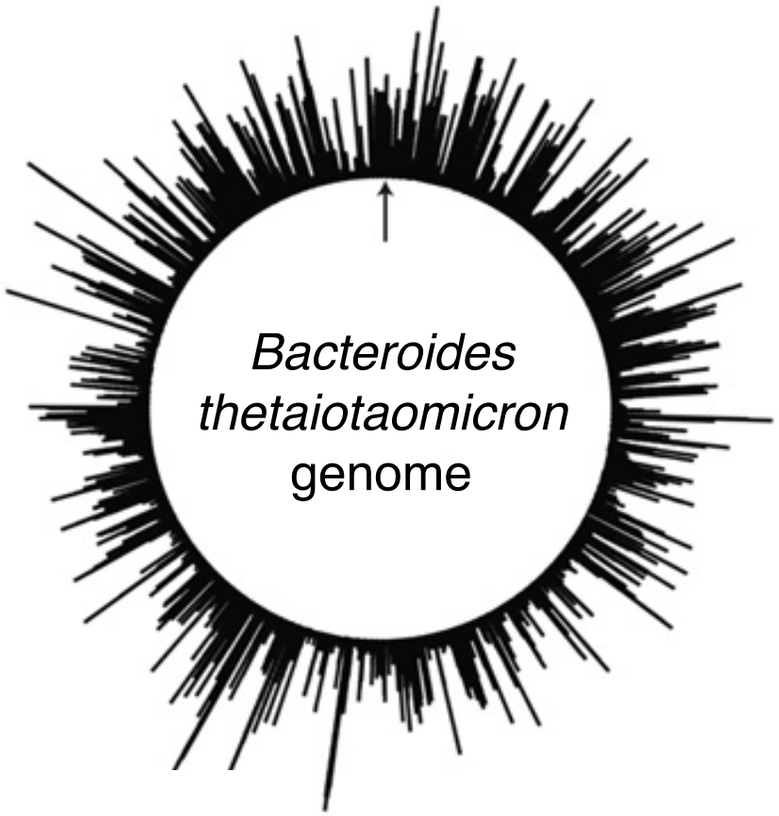
— 10 insertions / kb (~1 insertion / cell)

Goodman et al (*Cell Host Microbe* 2009)



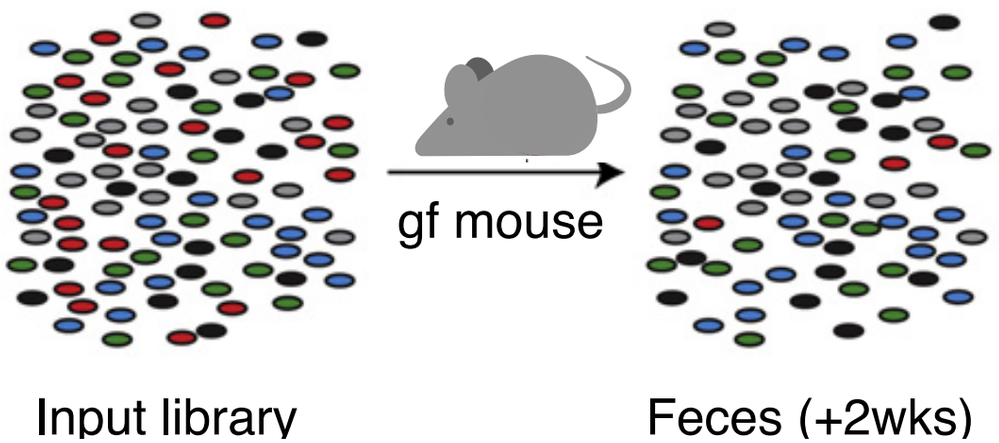


High-resolution lineage tracking w/ genome-wide TnSeq libraries

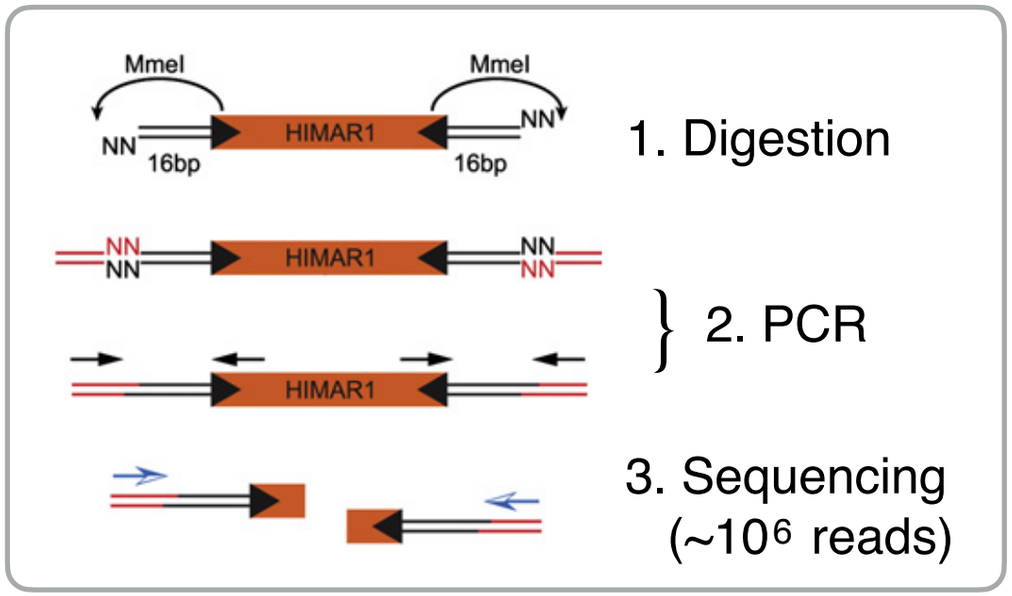


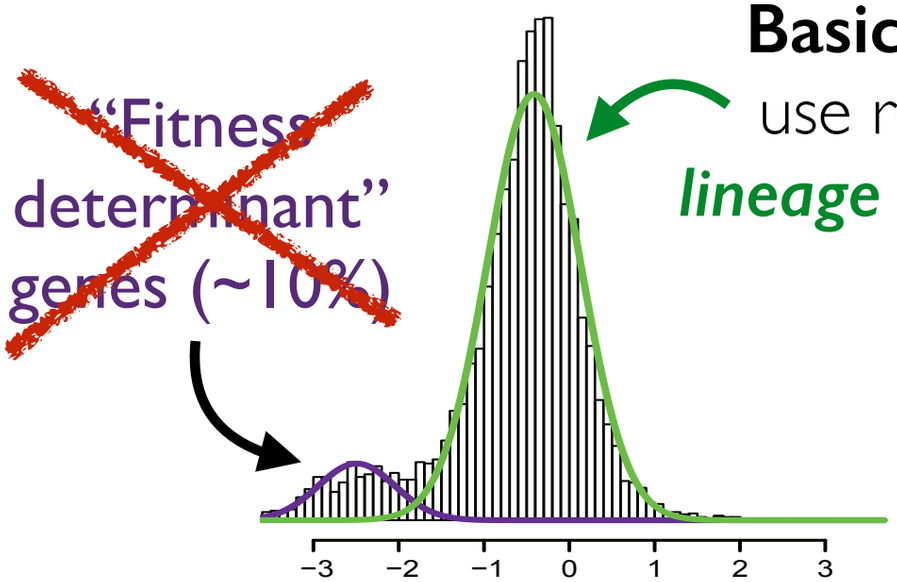
— 10 insertions / kb (~1 insertion / cell)

Goodman et al (*Cell Host Microbe* 2009)



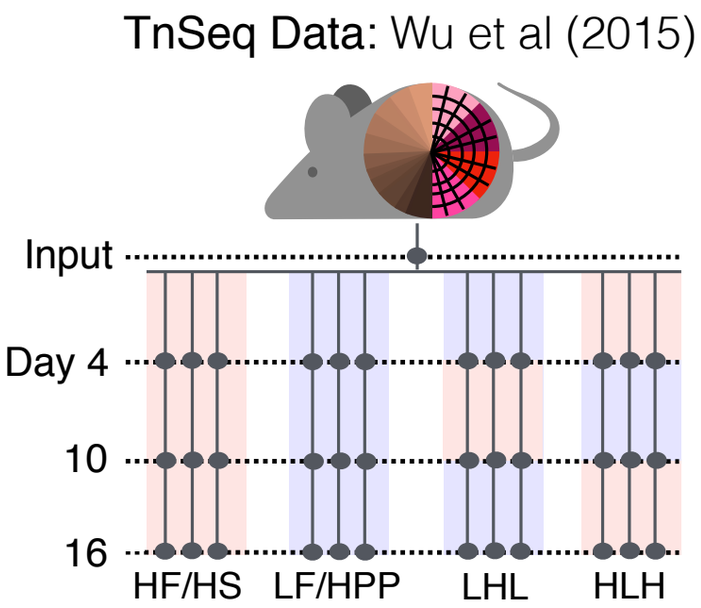
Insertion location = "barcode"



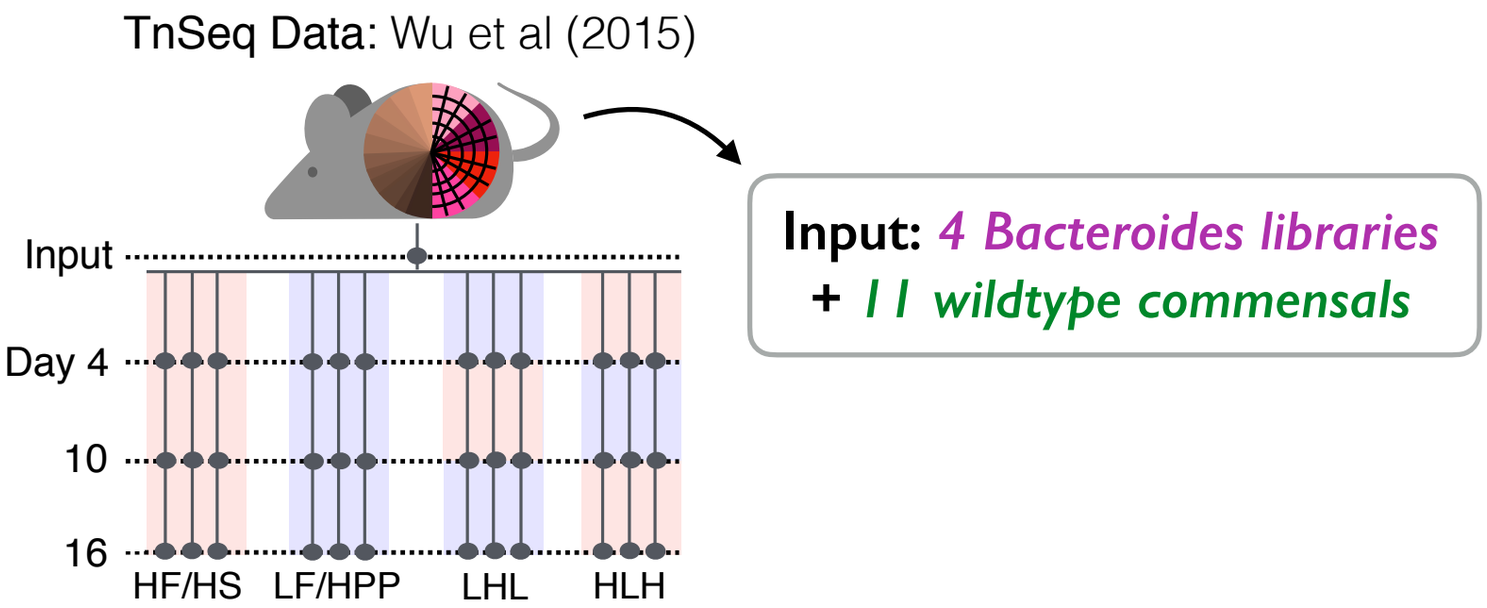


Daniel Wong

Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

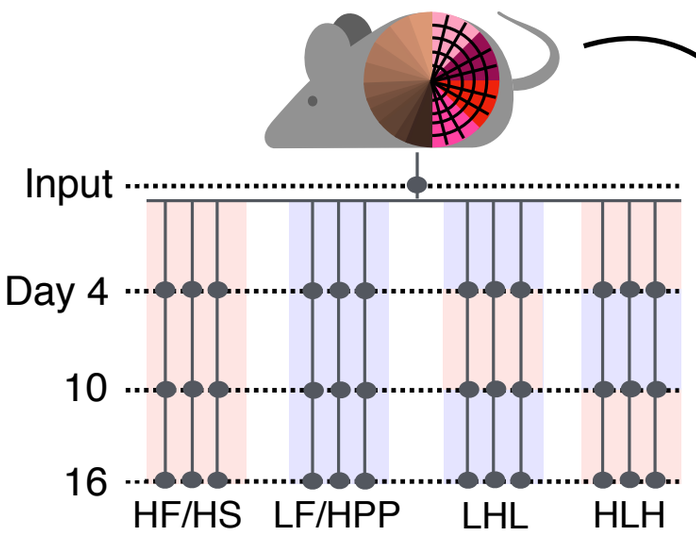


Fine-scale lineage dynamics reveal rapid adaptation *in vivo*



Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)

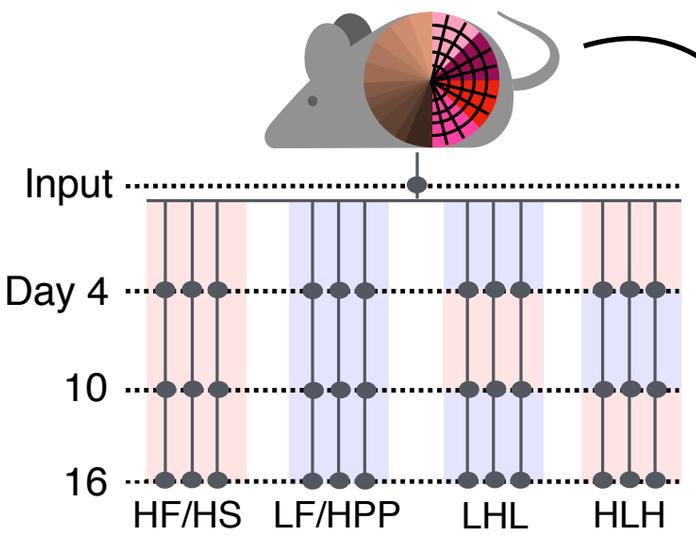


Input: *4 Bacteroides libraries*
+ *11 wildtype commensals*

←16 replicate mice →
(different diets)

Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)



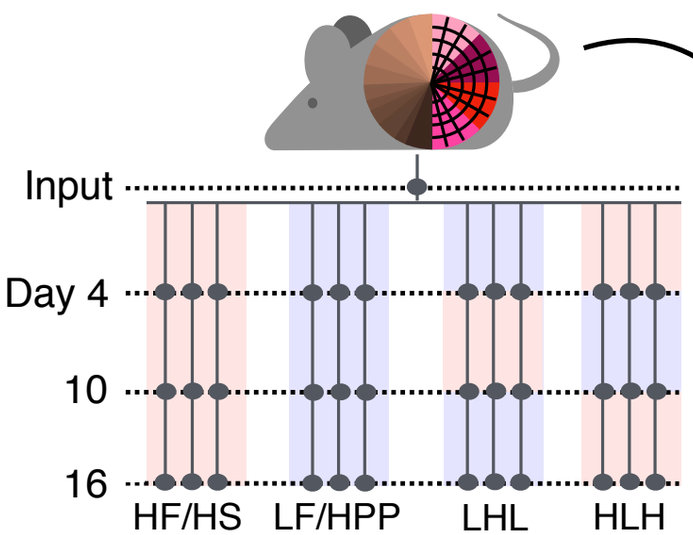
Input: *4 Bacteroides libraries*
+ *11 wildtype commensals*

Wu et al: ~10-20% of genes important in at least one diet

←16 replicate mice →
(different diets)

Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)



←16 replicate mice →
(different diets)

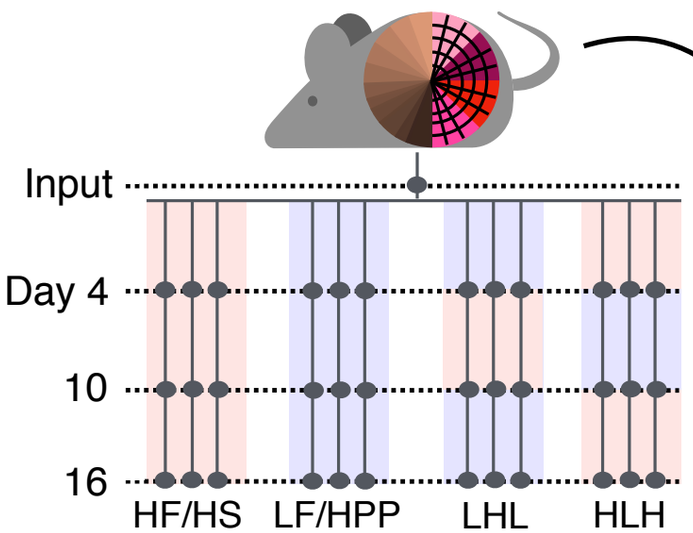
Input: *4 Bacteroides libraries*
+ *11 wildtype commensals*

Wu et al: ~10-20% of genes important in at least one diet

After pruning these genes…
>400k trackable lineages

Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)

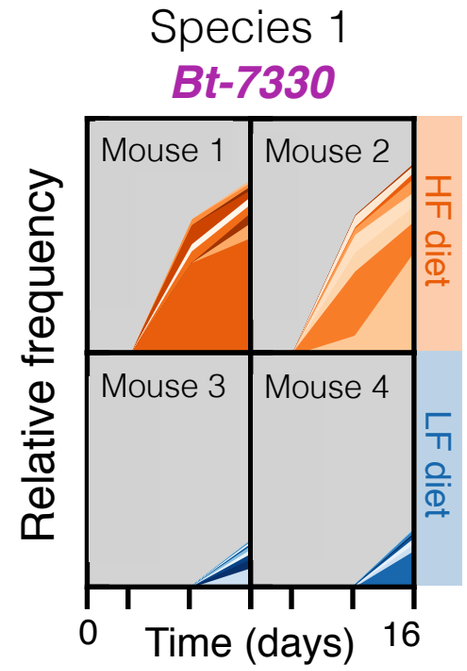


←16 replicate mice →
(different diets)

Input: *4 Bacteroides libraries*
+ *11 wildtype commensals*

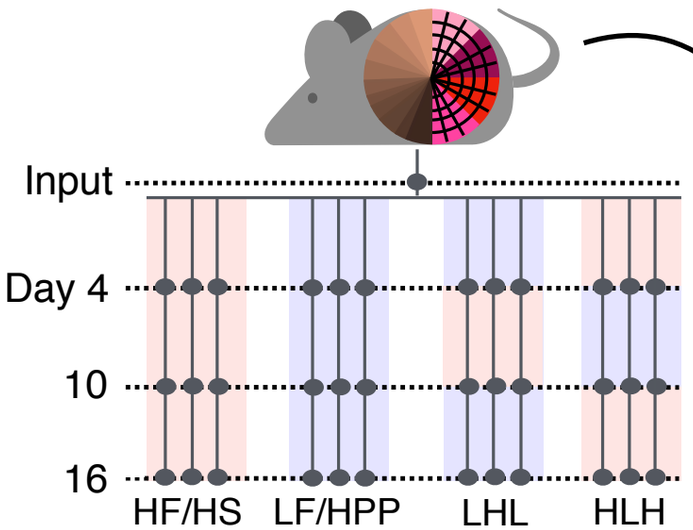
Wu et al: ~10-20% of genes important in at least one diet

After pruning these genes…
>400k trackable lineages



Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)



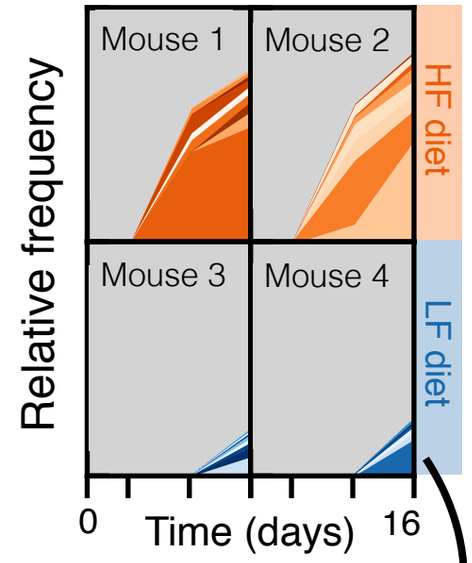
←**16 replicate mice**→
(different diets)

Input: *4 Bacteroides libraries*
+ *11 wildtype commensals*

Wu et al: ~10-20% of genes important in at least one diet

After pruning these genes…
>400k trackable lineages

Species 1
Bt-7330



Selection on ***additional mut'ns*** that accumulate during exp't

(other Tns in same gene decline)

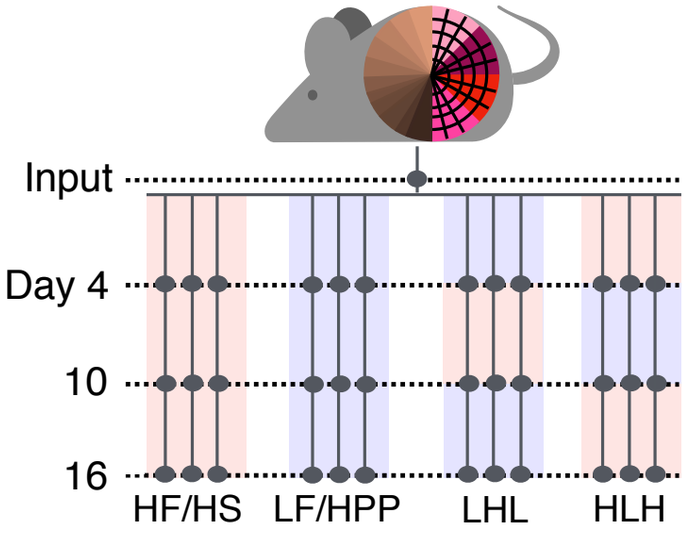
Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

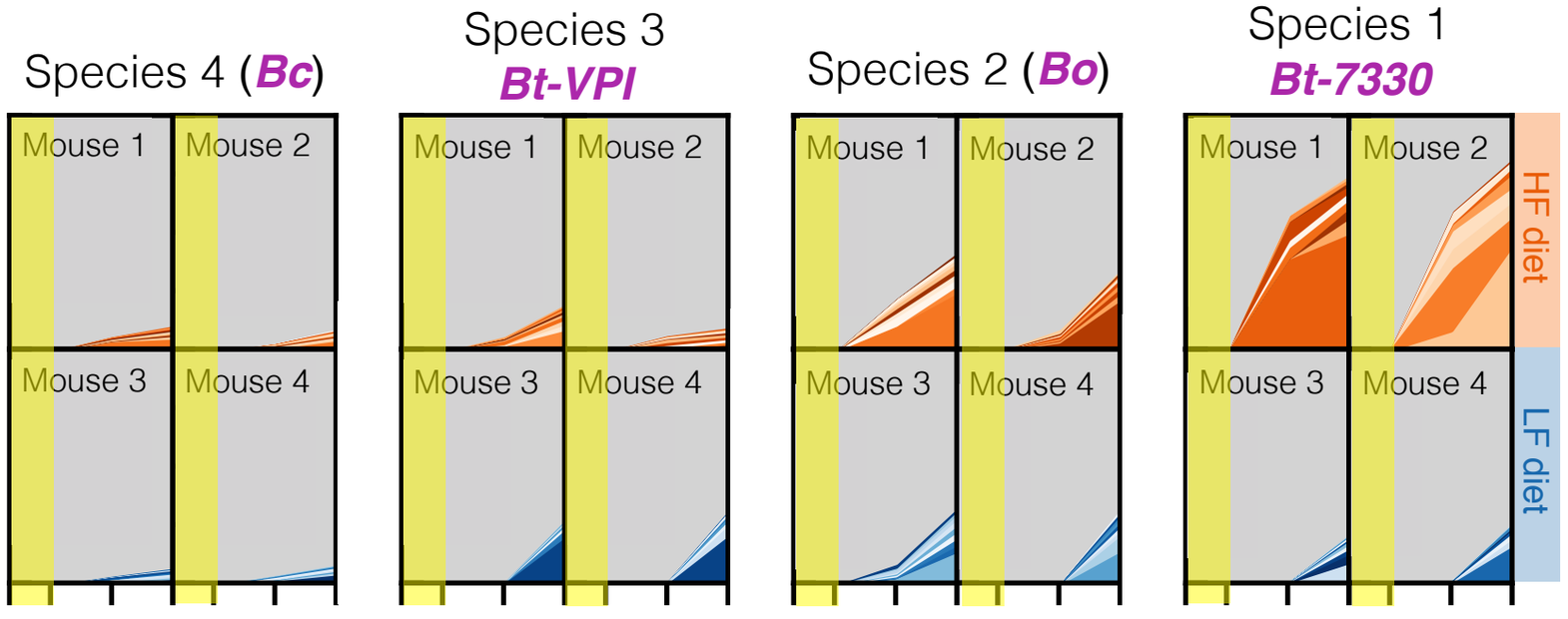
Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

What's going on at day 4?

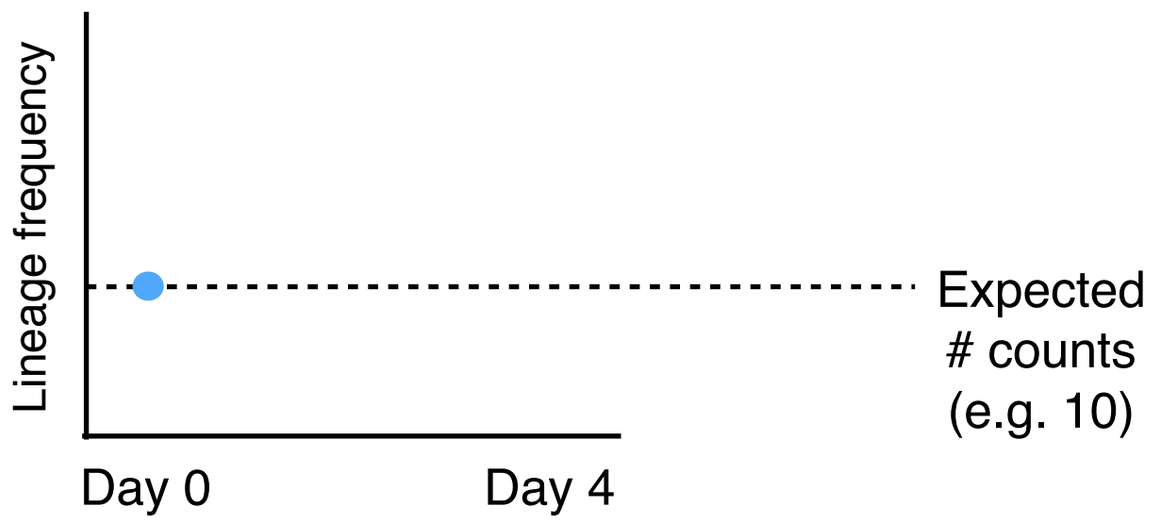
Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)



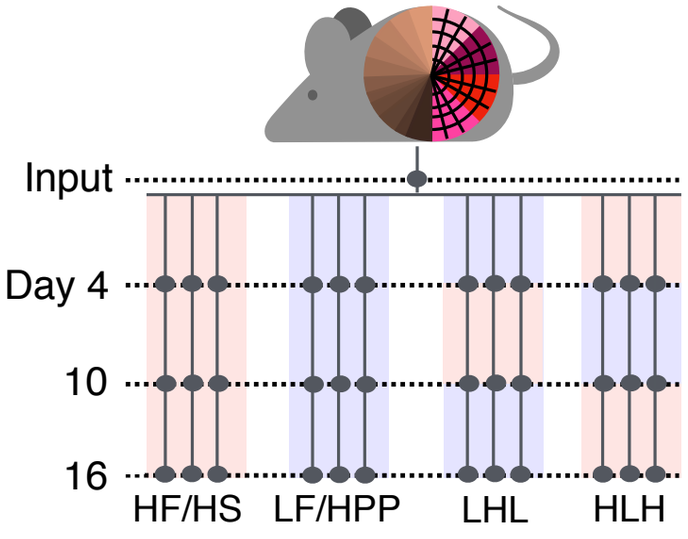


What's going on at day 4?

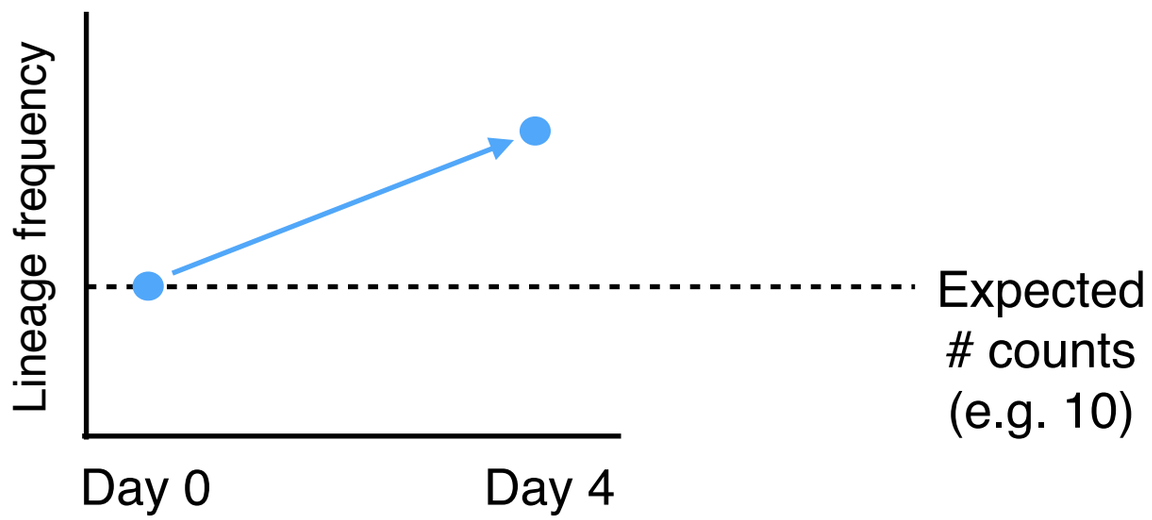


Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)

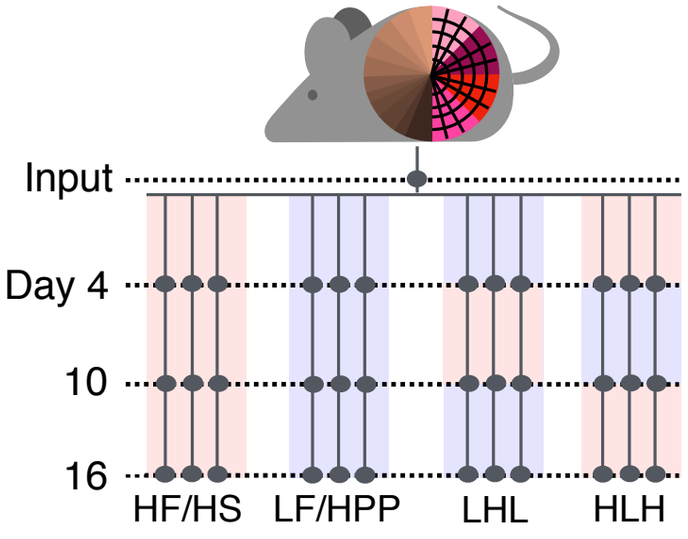


What's going on at day 4?

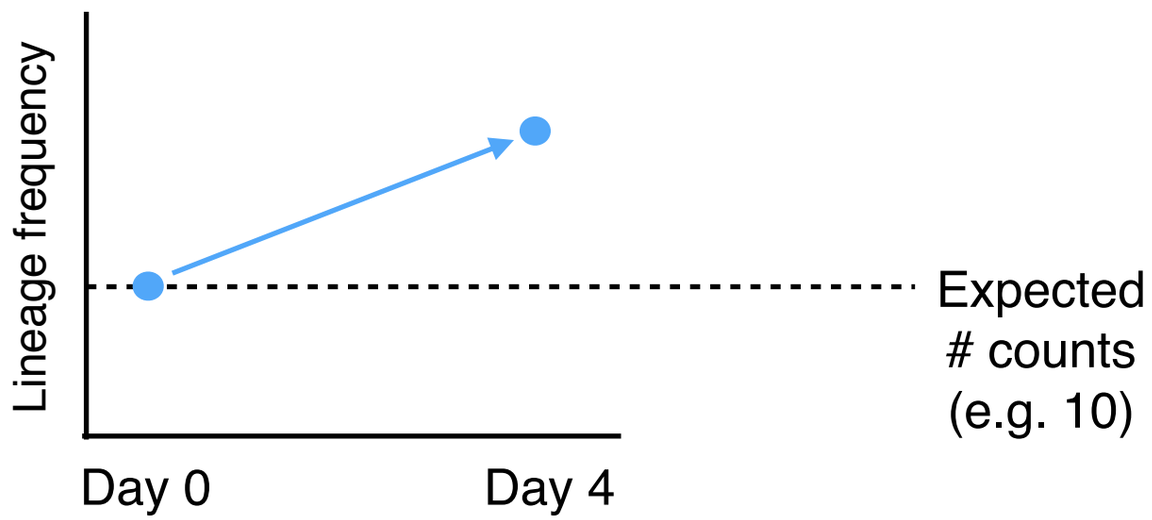


Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)



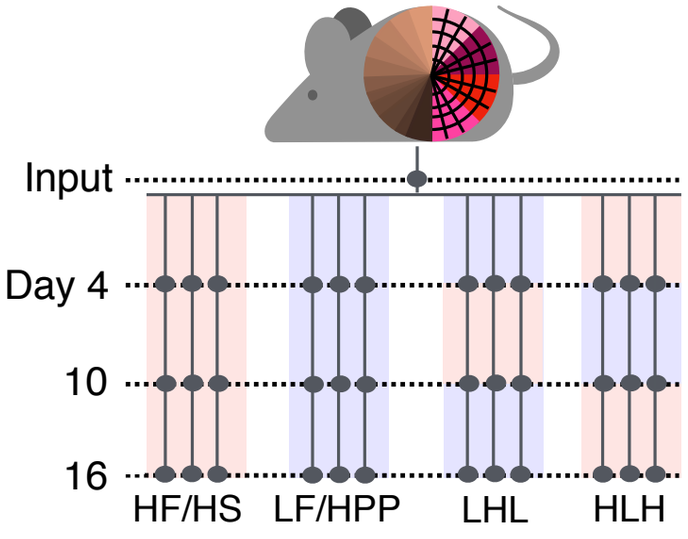
What's going on at day 4?



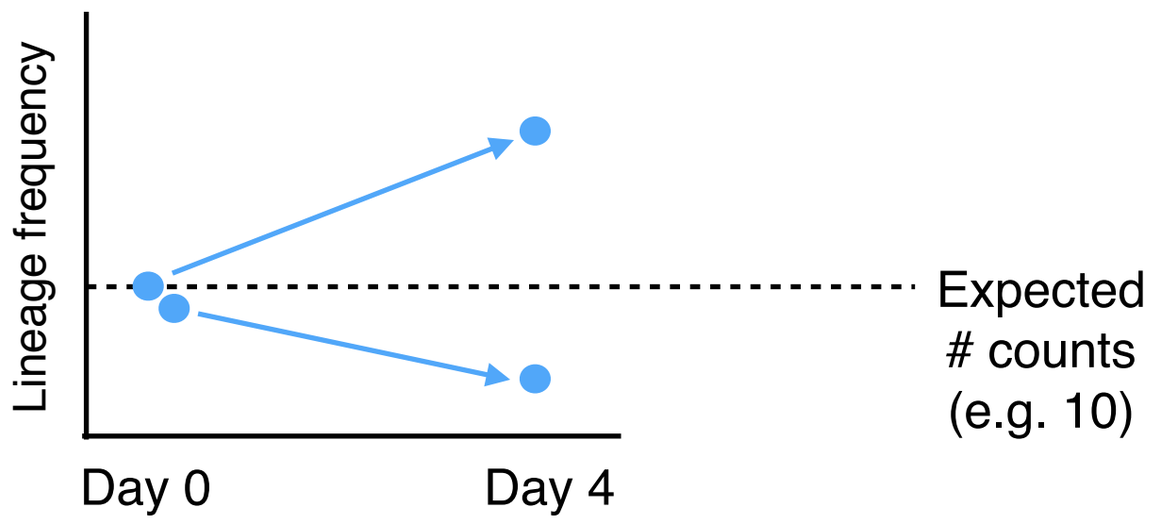
Idea: focus on ***collective behavior***

Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)



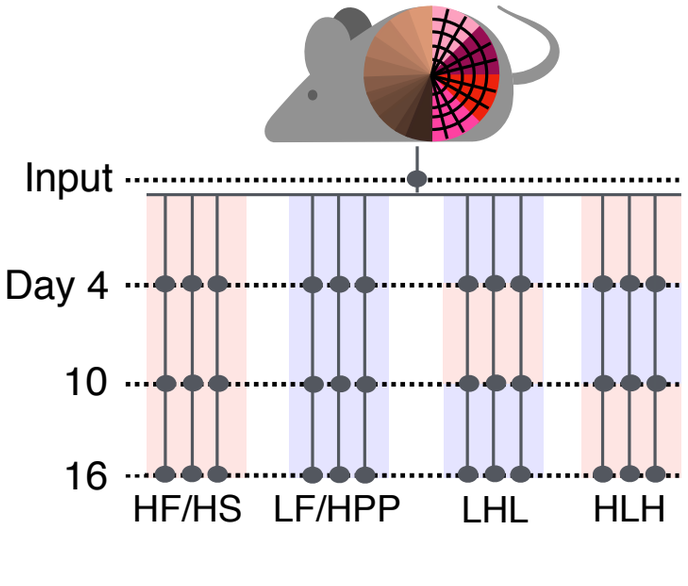
What's going on at day 4?

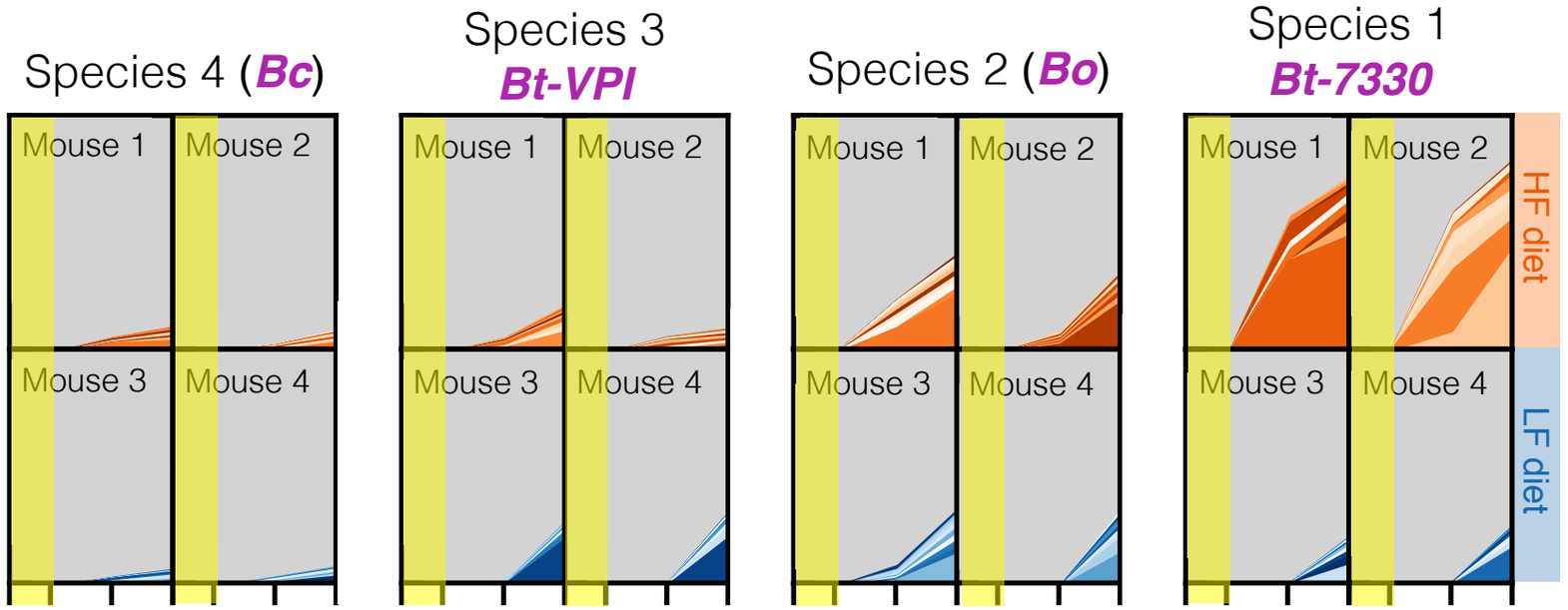


Idea: focus on ***collective behavior***

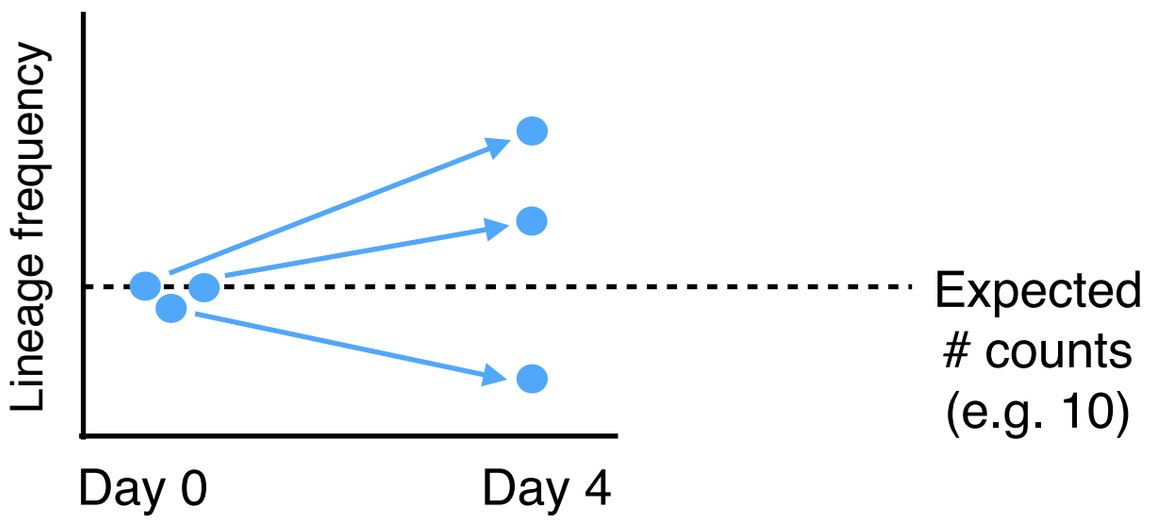
Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)





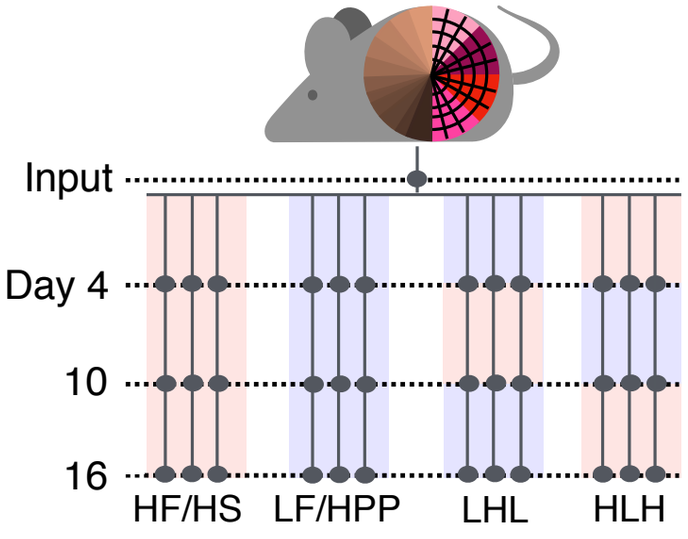
What's going on at day 4?



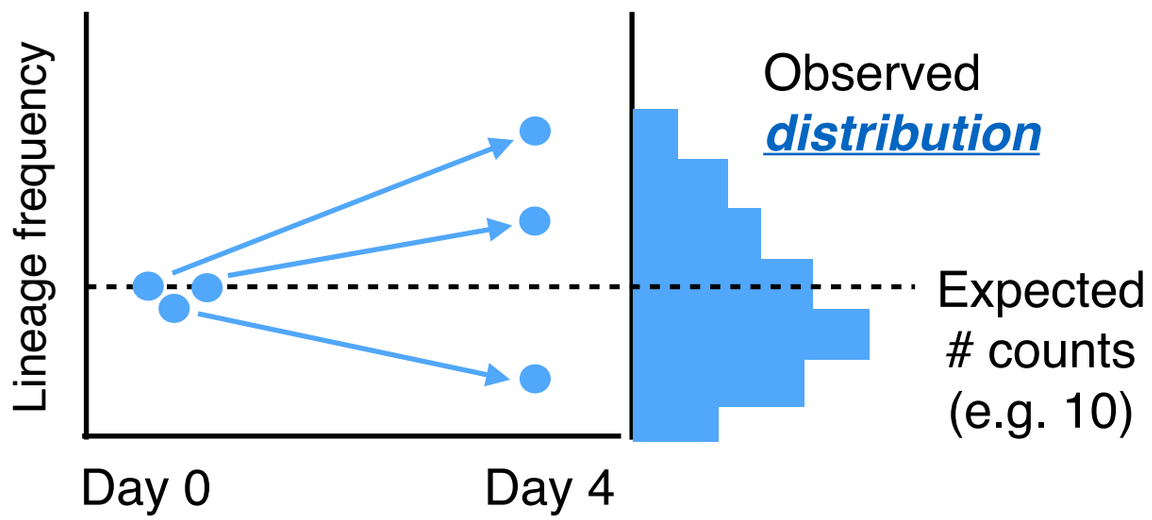
Idea: focus on ***collective behavior***

Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)



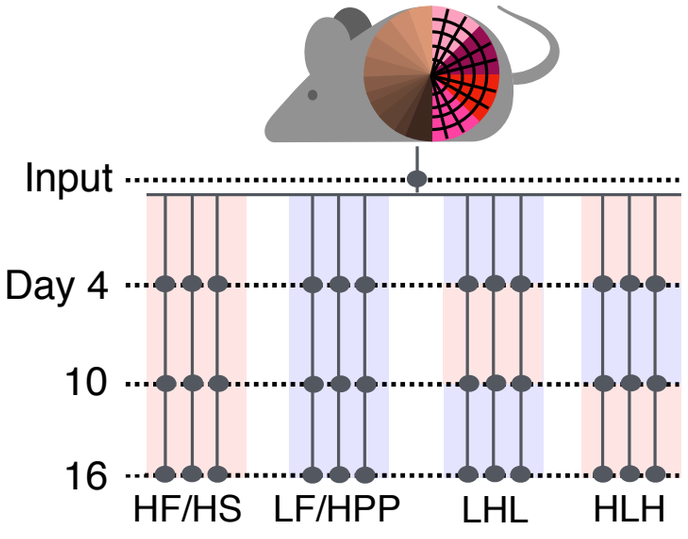
What's going on at day 4?

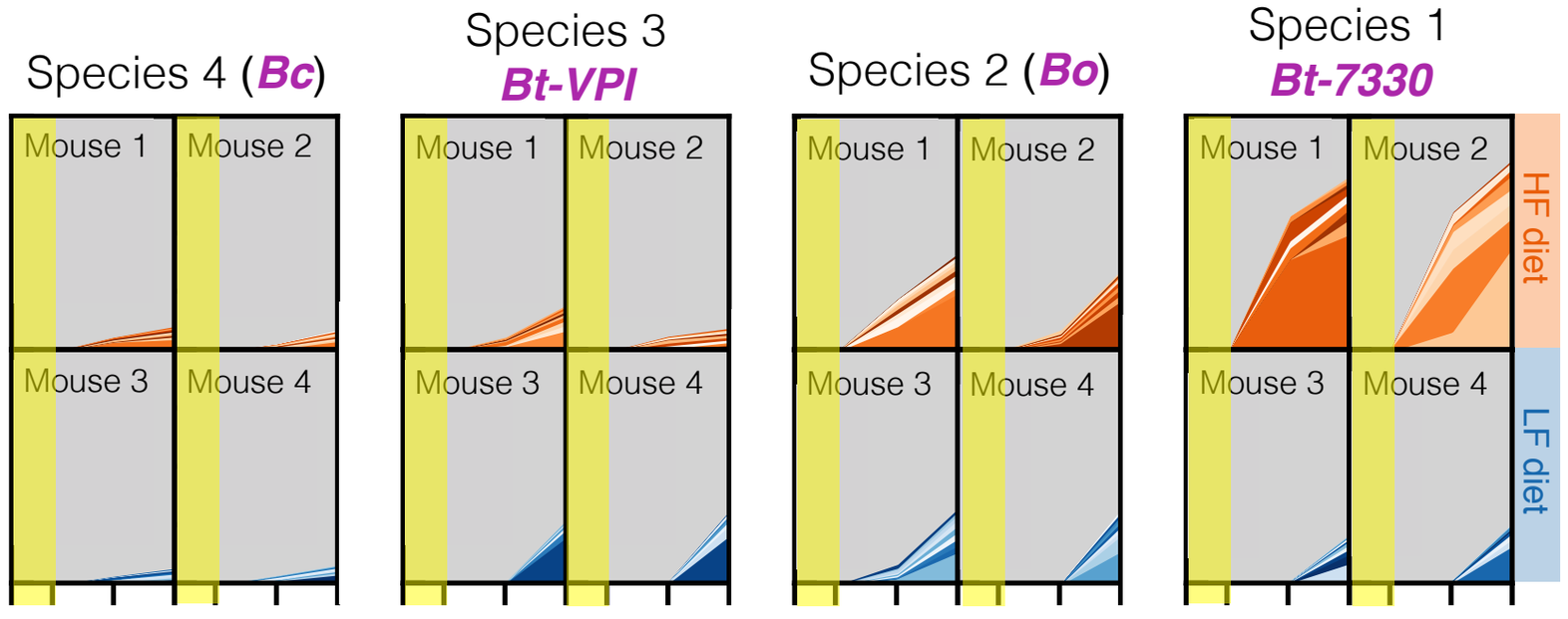


Idea: focus on ***collective behavior***

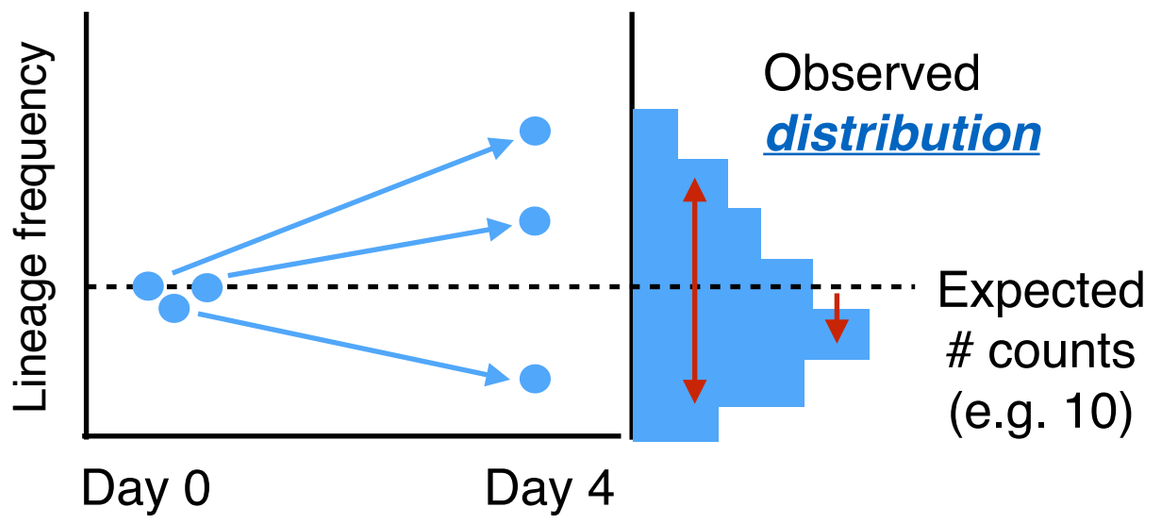
Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

TnSeq Data: Wu et al (2015)



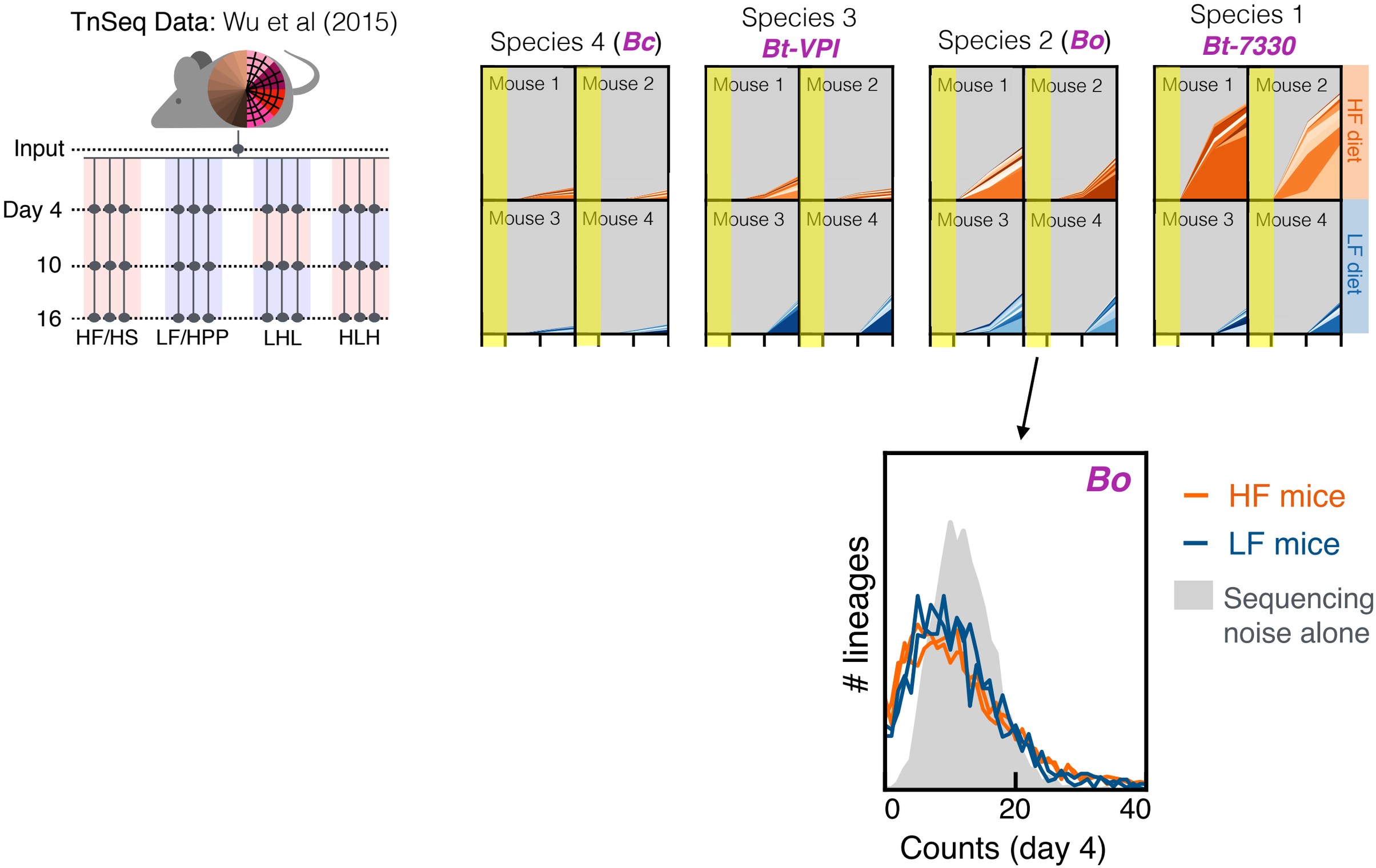


What's going on at day 4?

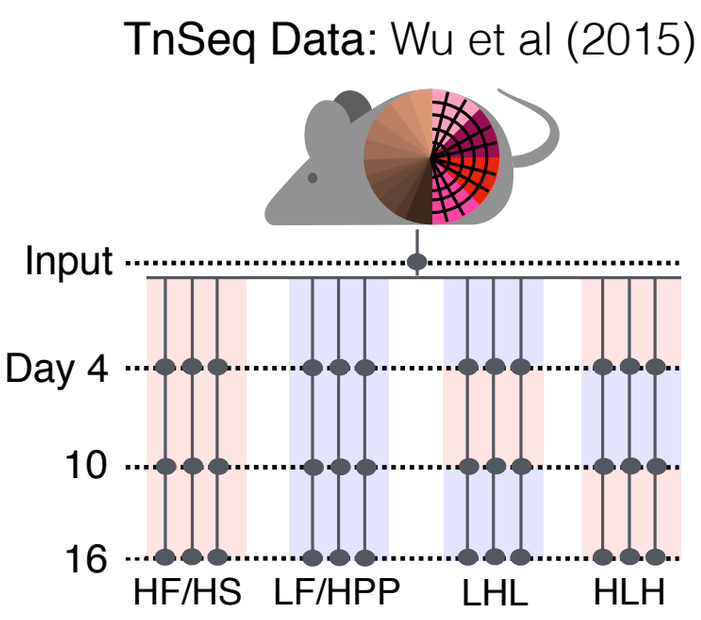


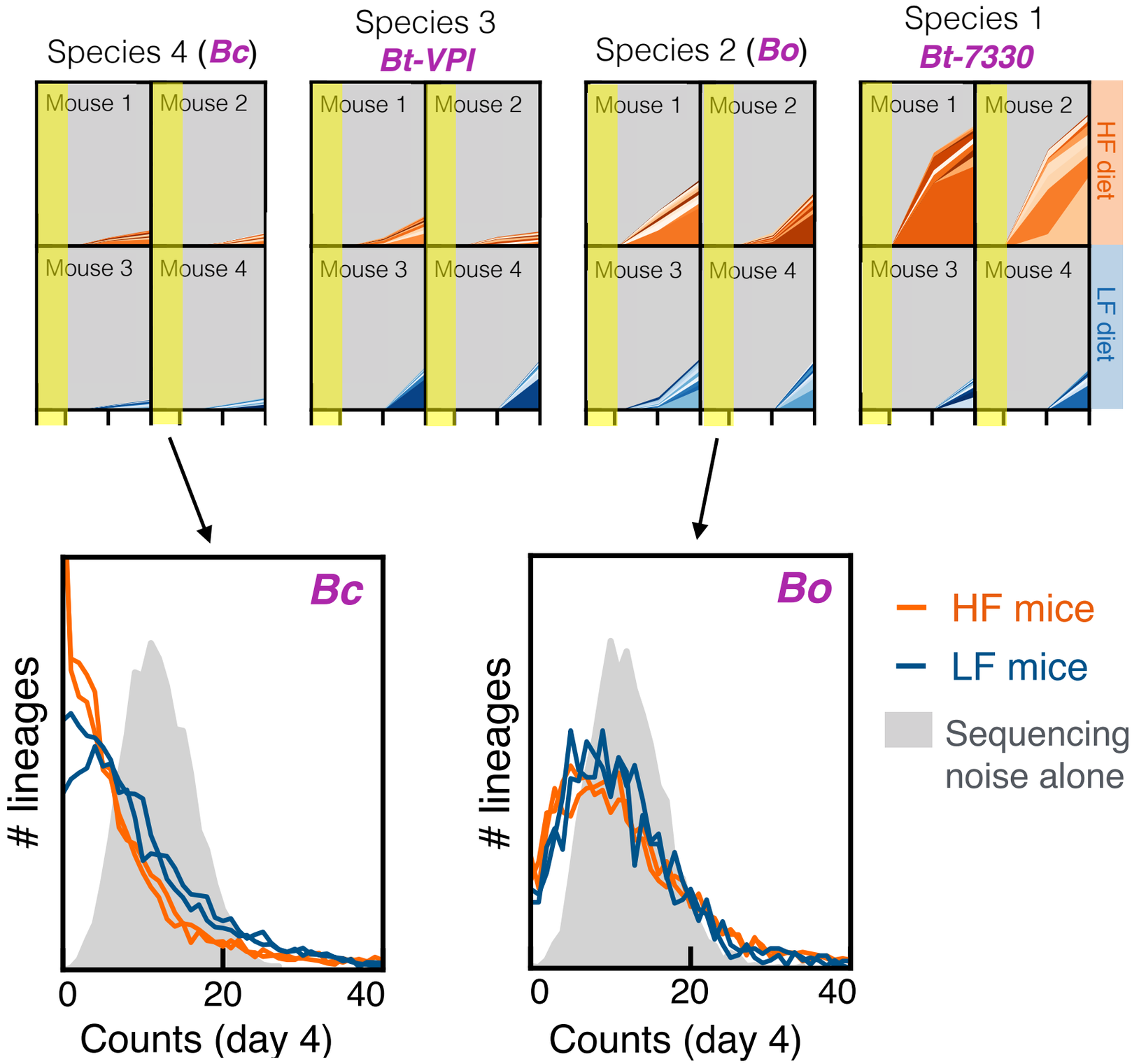
Idea: focus on ***collective behavior***

Fine-scale lineage dynamics reveal rapid adaptation *in vivo*



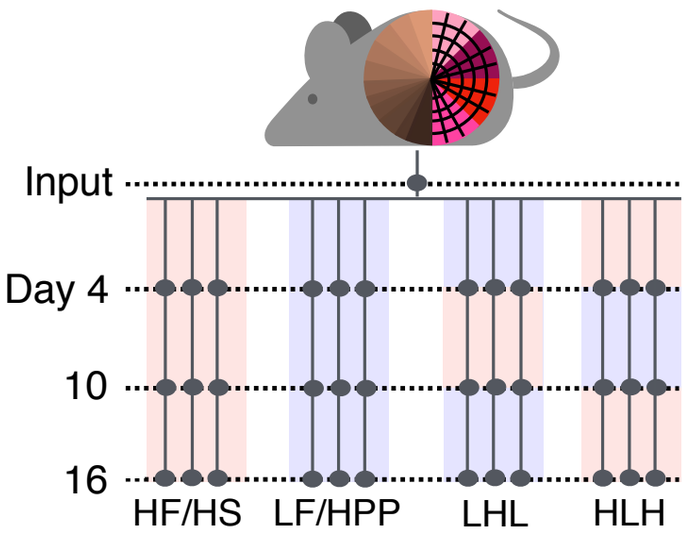
Fine-scale lineage dynamics reveal rapid adaptation *in vivo*



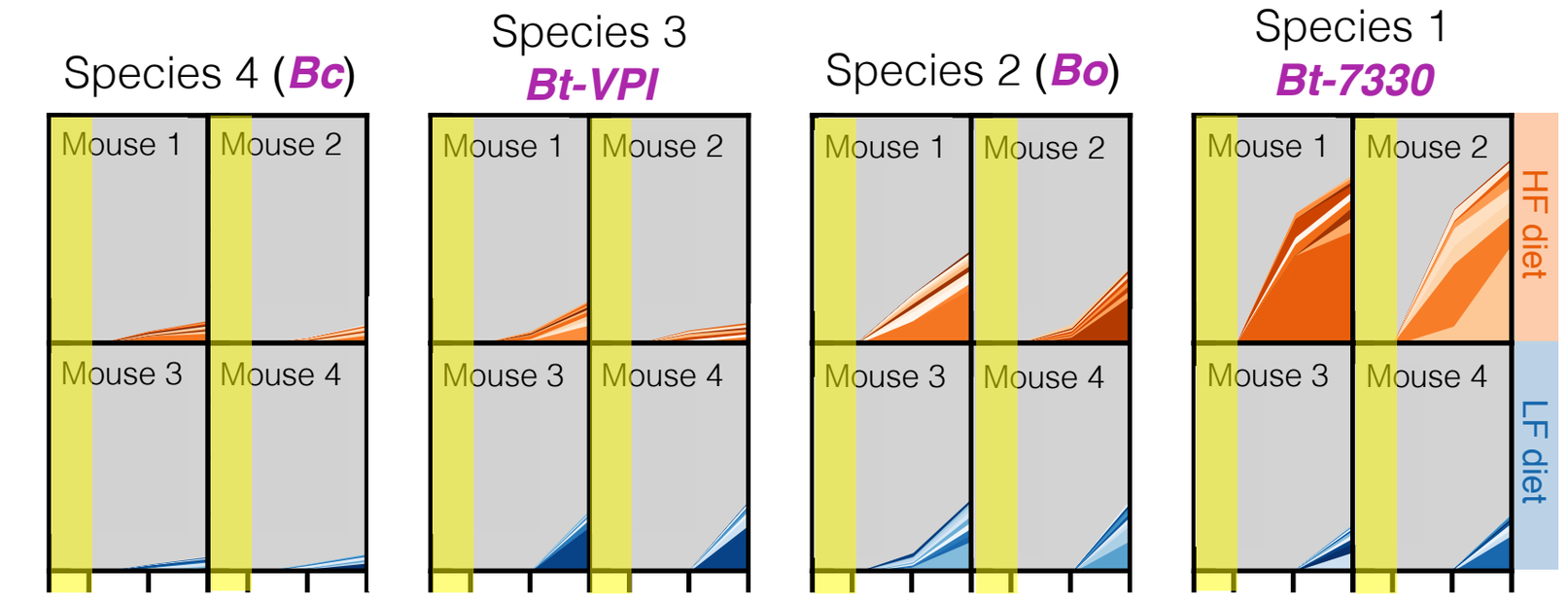


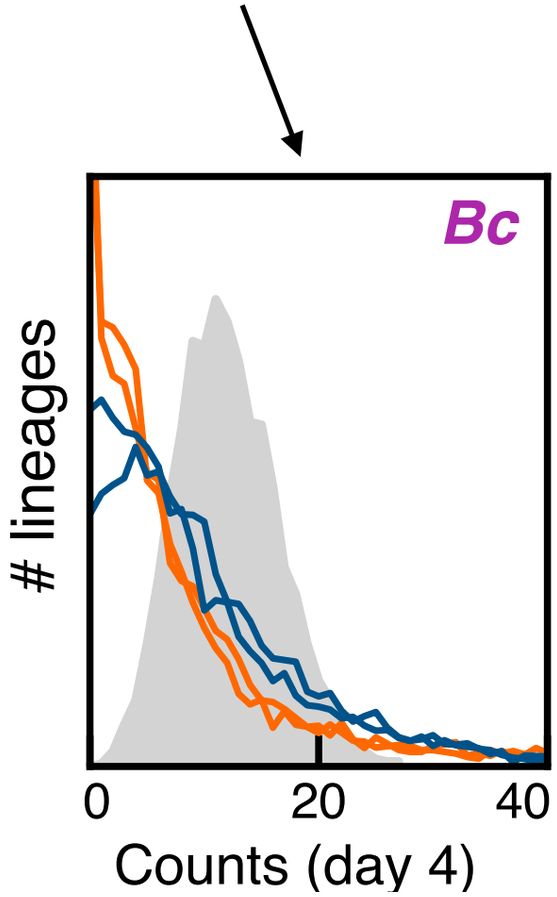
Fine-scale lineage dynamics reveal rapid adaptation *in vivo*

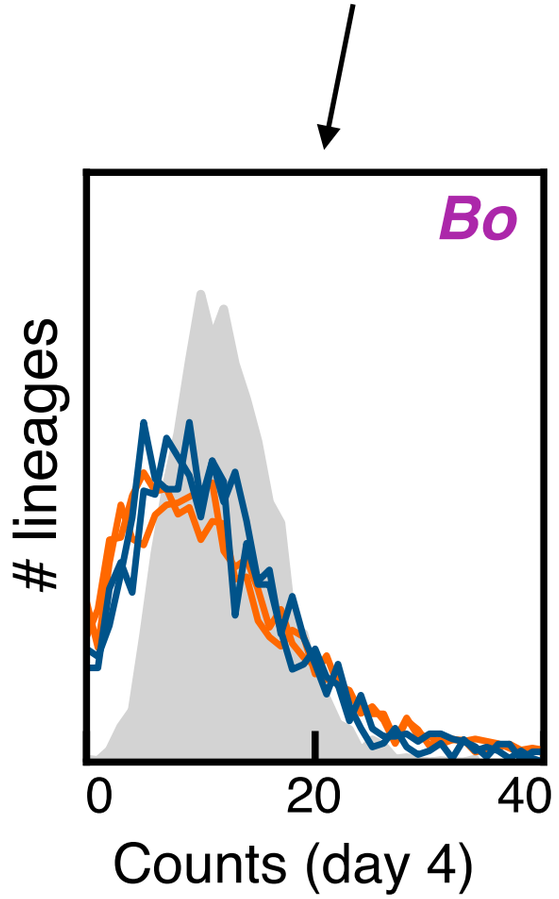
TnSeq Data: Wu et al (2015)



Question:
Natural selection vs *colonization bottlenecks*?

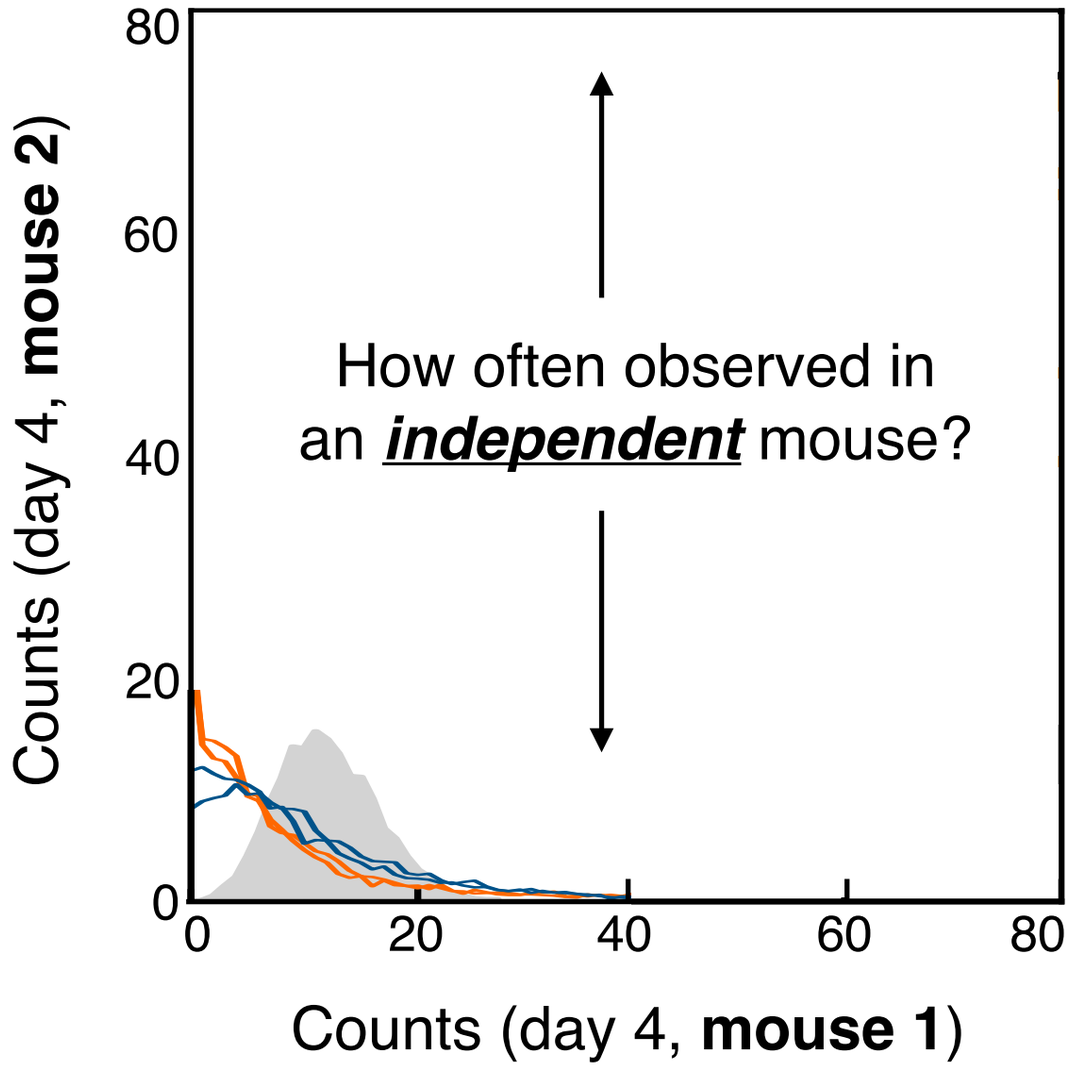




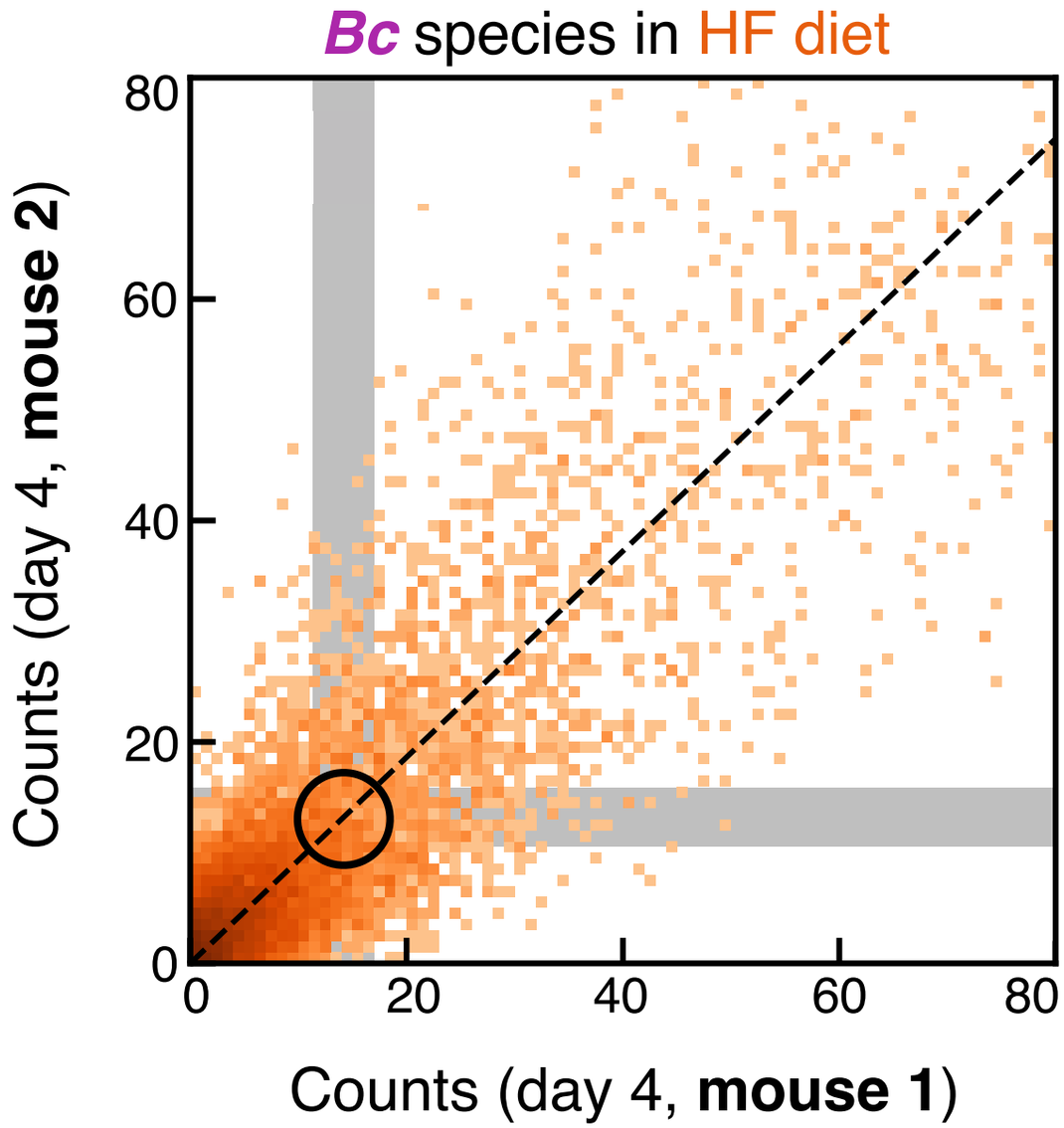


HF mice
LF mice
Sequencing noise alone

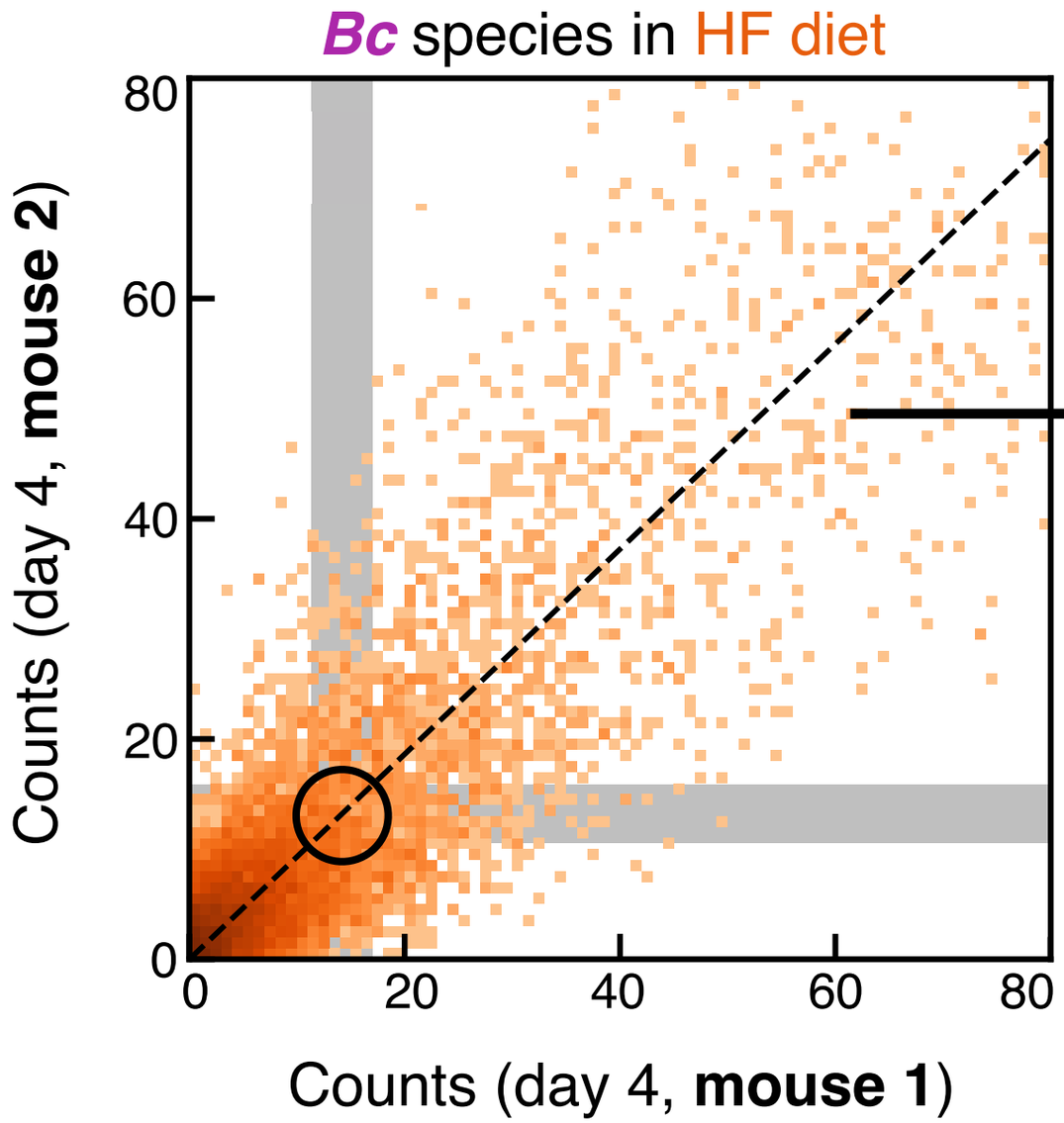
Fine-scale lineage dynamics reveal rapid adaptation *in vivo*



Fine-scale lineage dynamics reveal rapid adaptation *in vivo*



Fine-scale lineage dynamics reveal rapid adaptation *in vivo*



Positive selection on

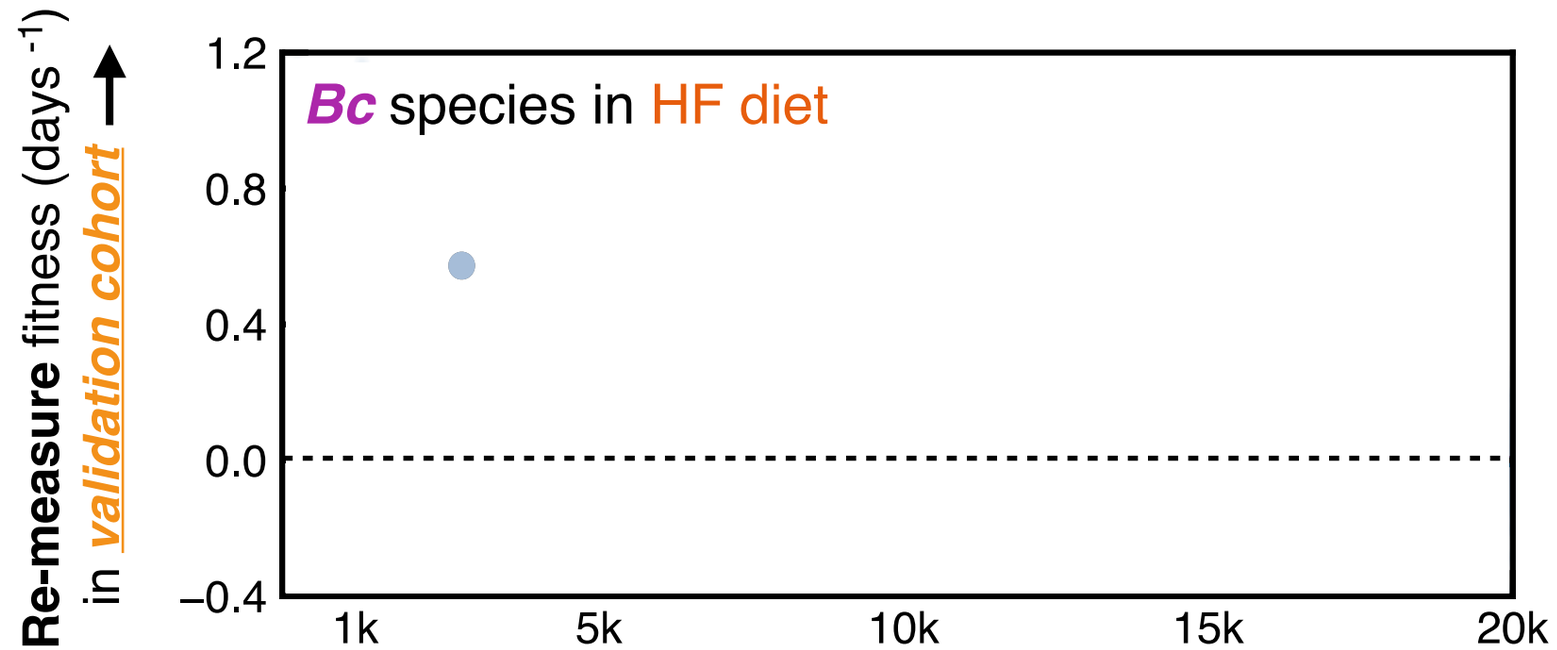
additional mut'ns

that accumulated

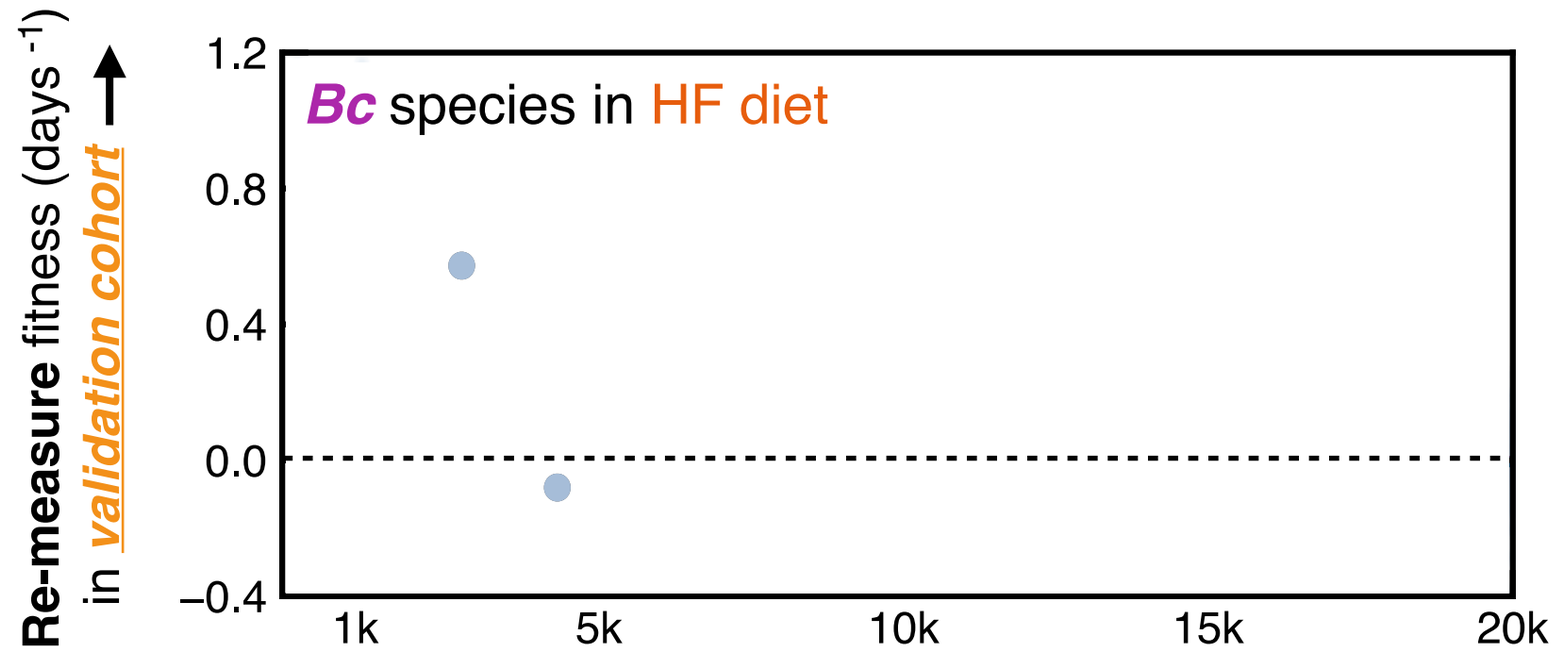
before colonization

Cross-validation reveals 1000's of strongly adaptive lineages

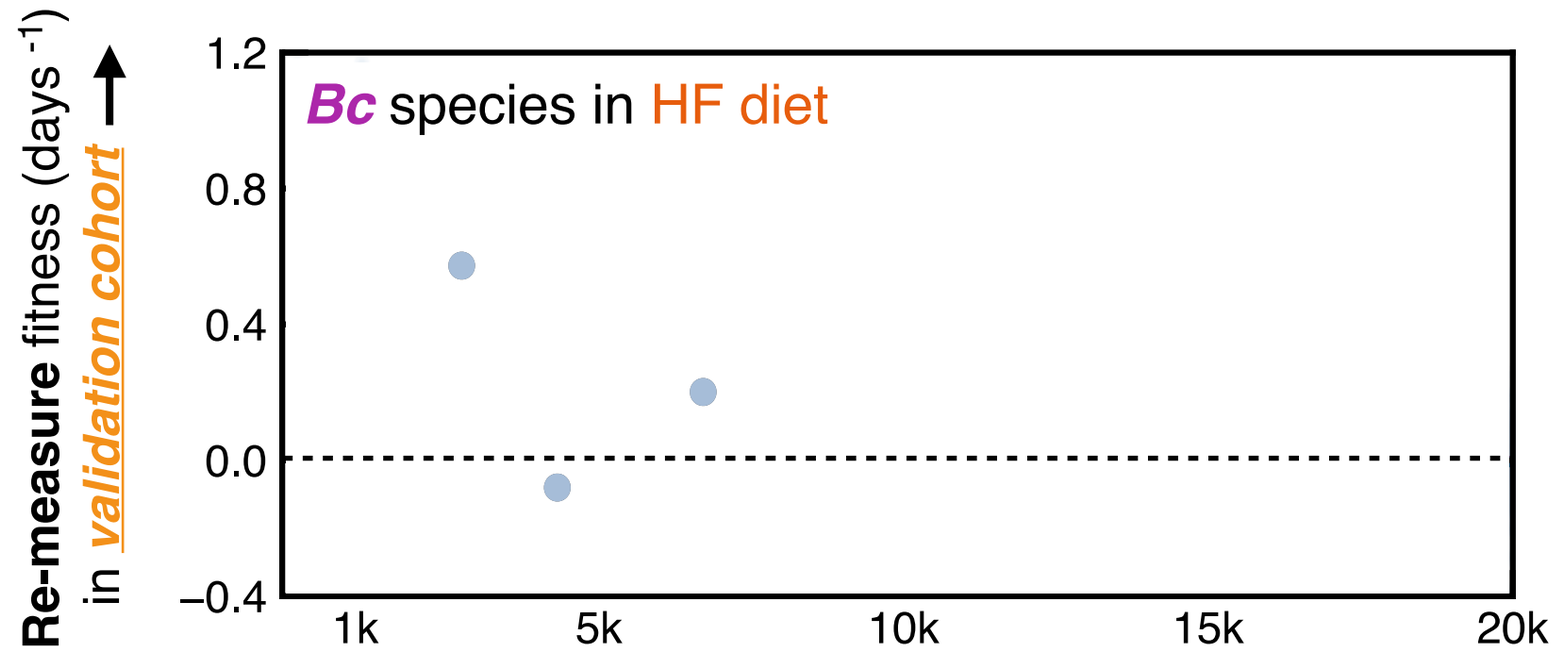
Cross-validation reveals 1000's of strongly adaptive lineages



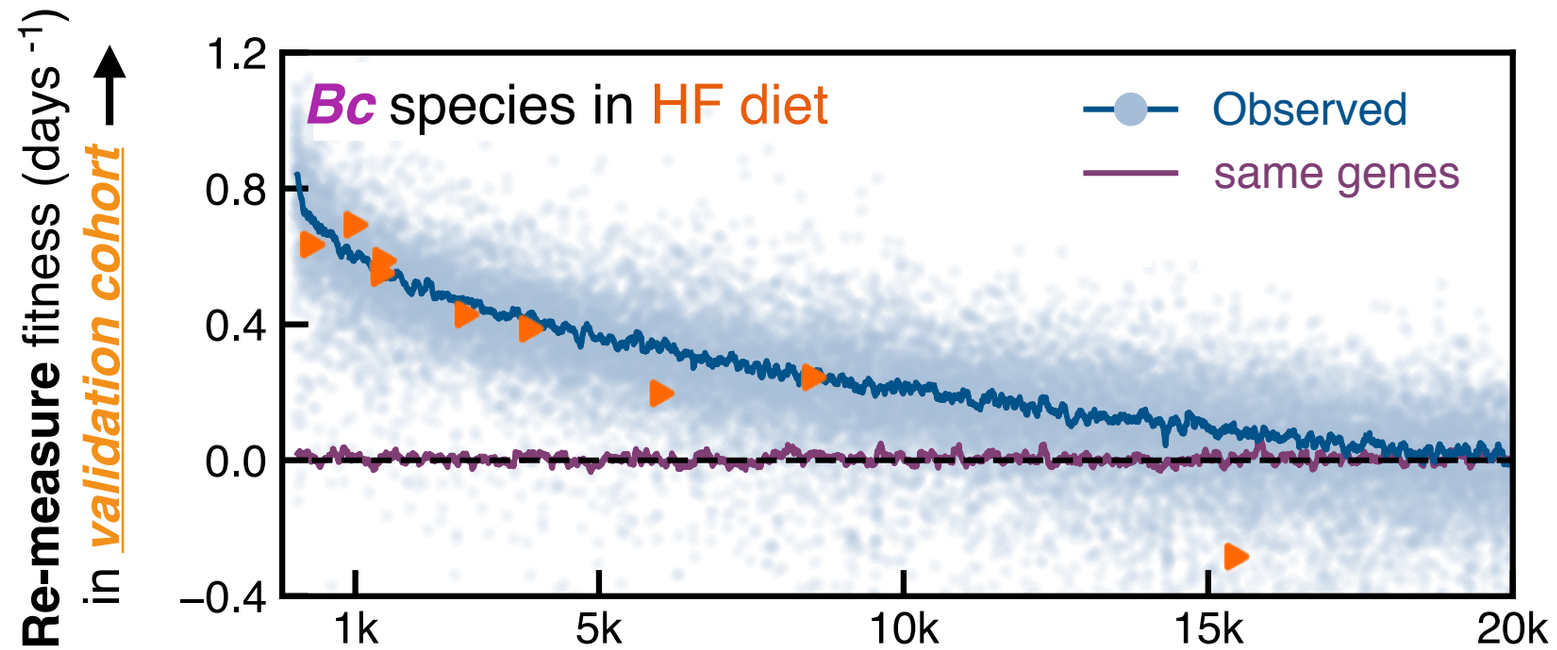
Cross-validation reveals 1000's of strongly adaptive lineages



Cross-validation reveals 1000's of strongly adaptive lineages

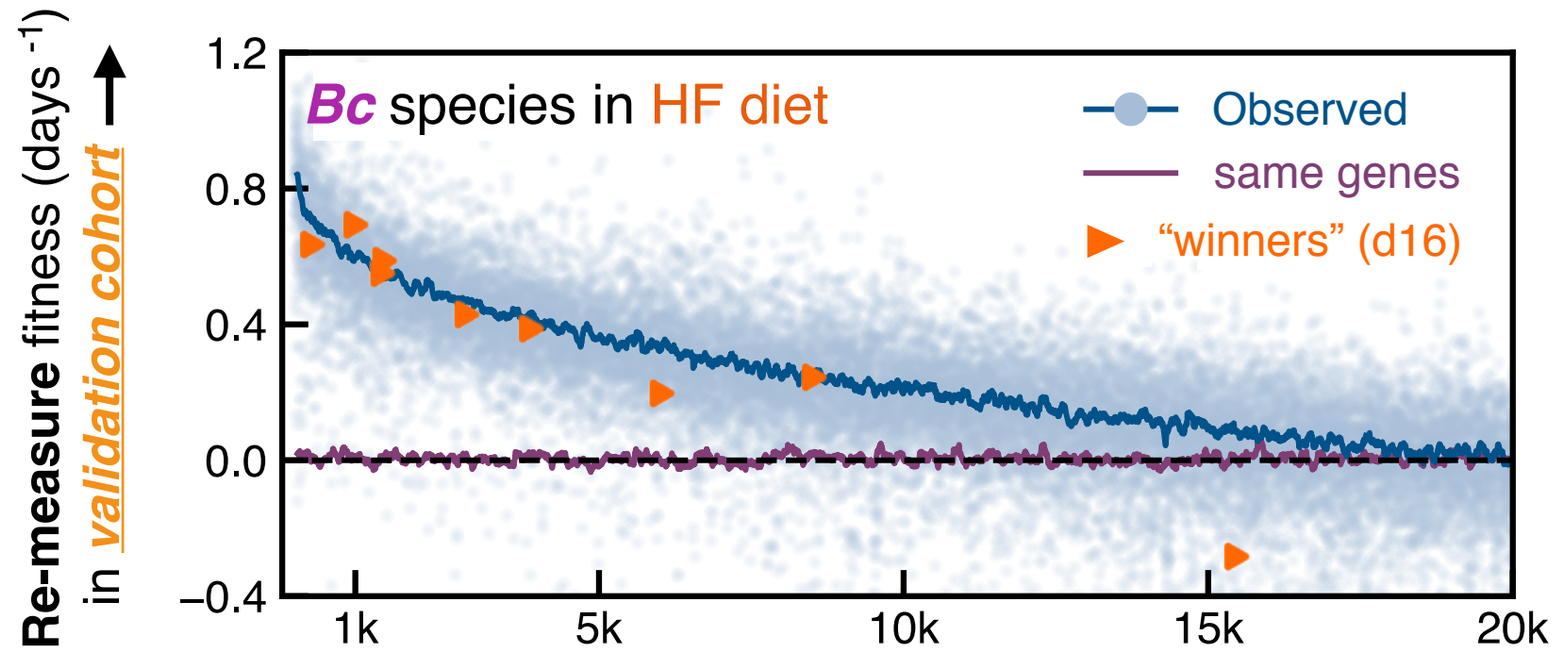


Cross-validation reveals 1000's of strongly adaptive lineages



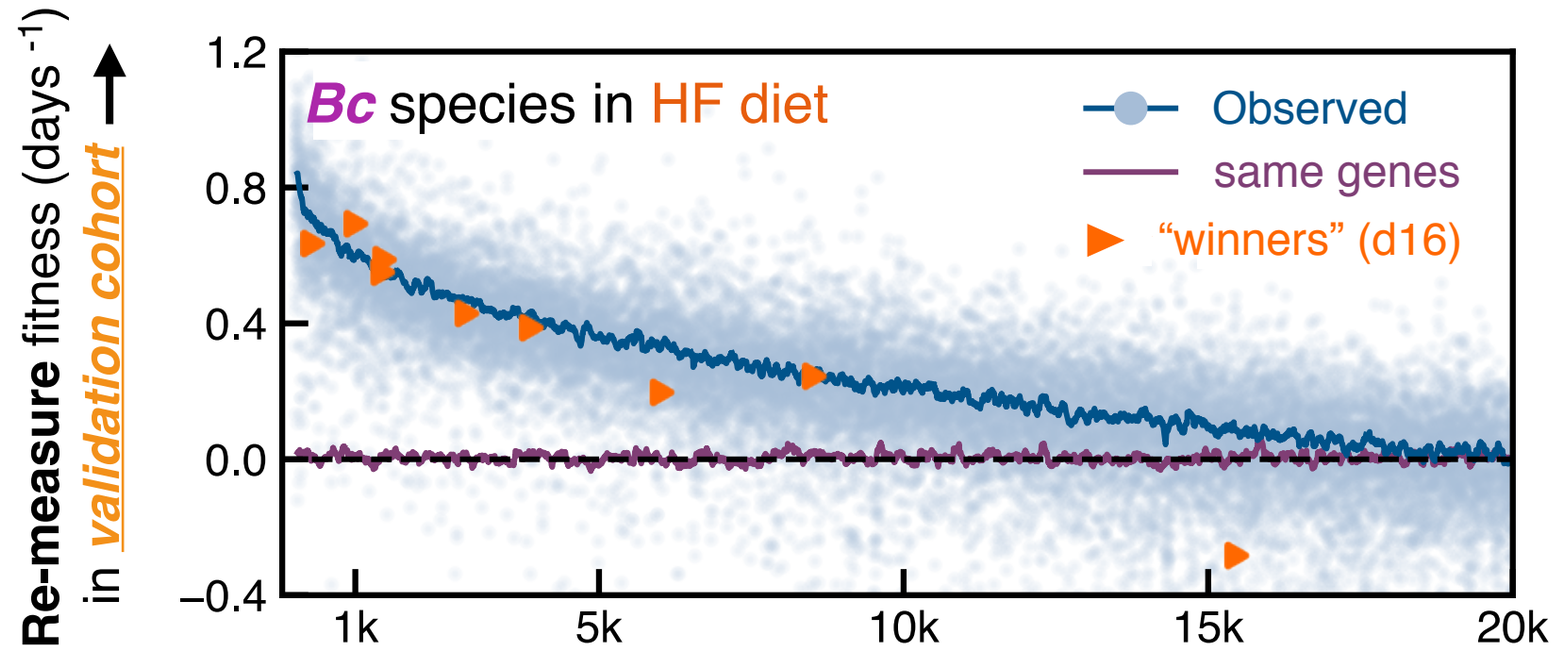
Rank lineages by fitness in ***discovery cohort*** →

Cross-validation reveals 1000's of strongly adaptive lineages

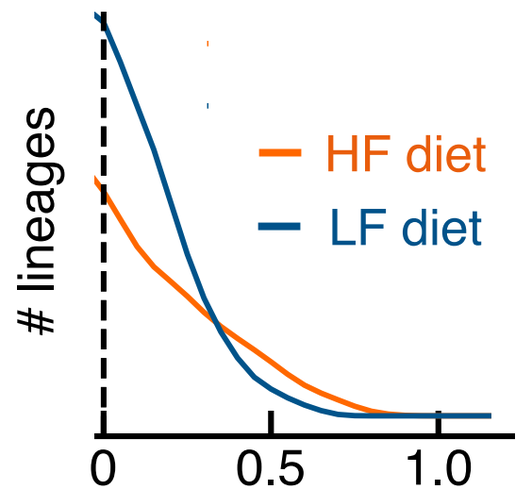


Rank lineages by fitness in ***discovery cohort*** →

Cross-validation reveals 1000's of strongly adaptive lineages

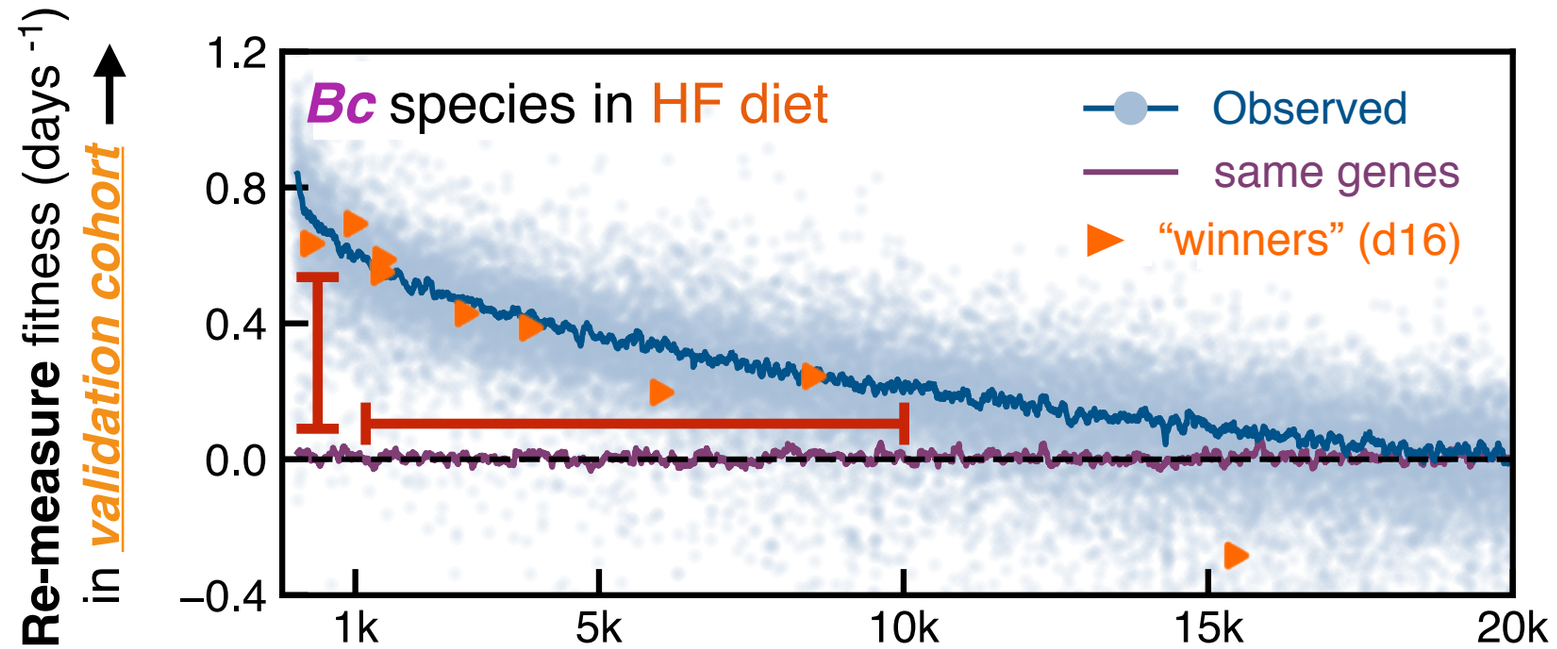


Can invert to infer "**DFE**"

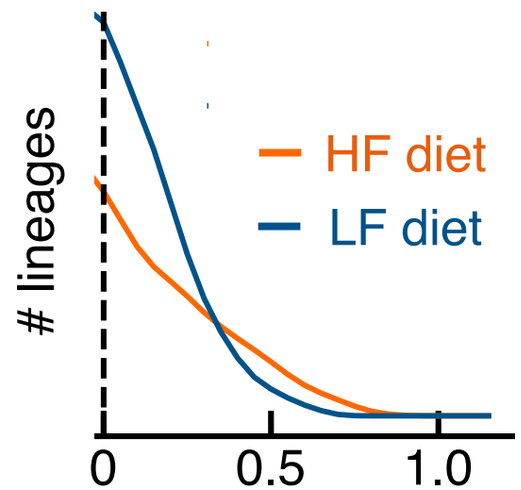


Rank lineages by fitness in ***discovery cohort***

Cross-validation reveals 1000's of strongly adaptive lineages

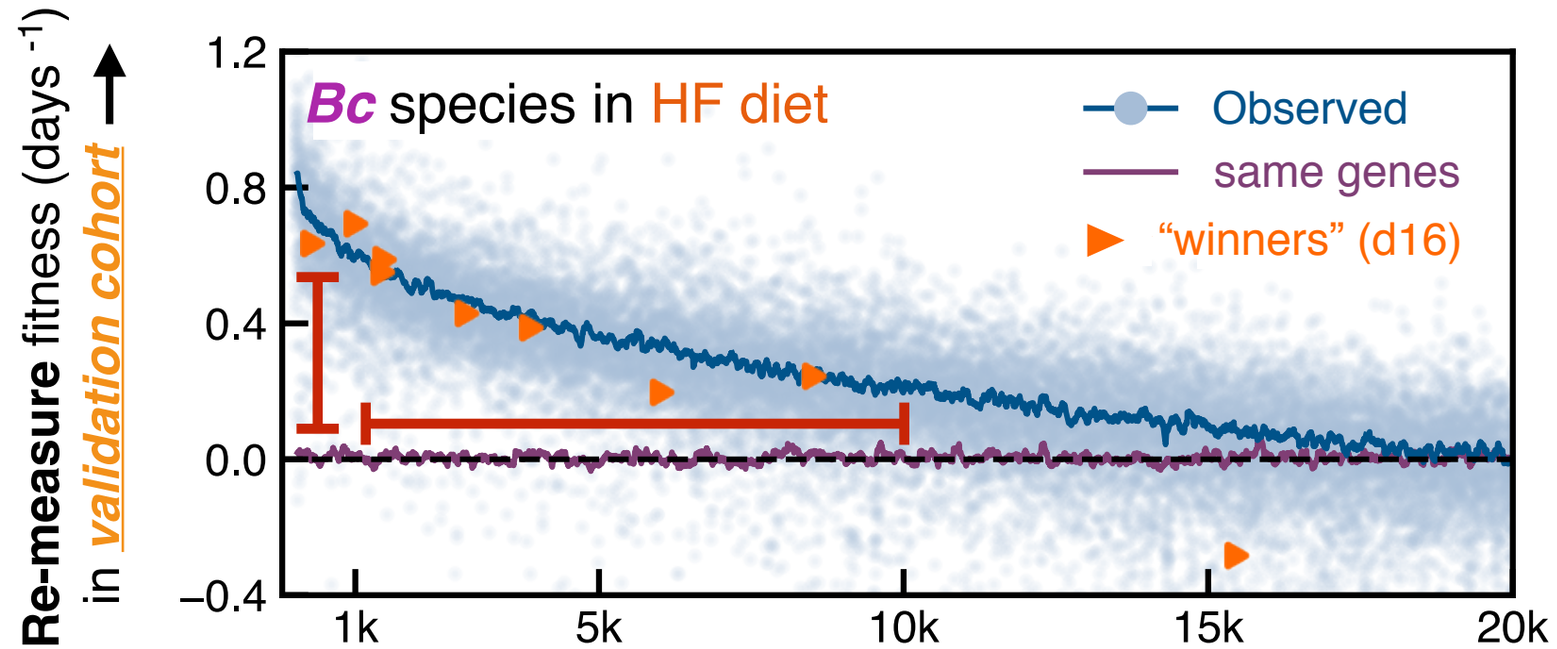


Can invert to infer "**DFE**"



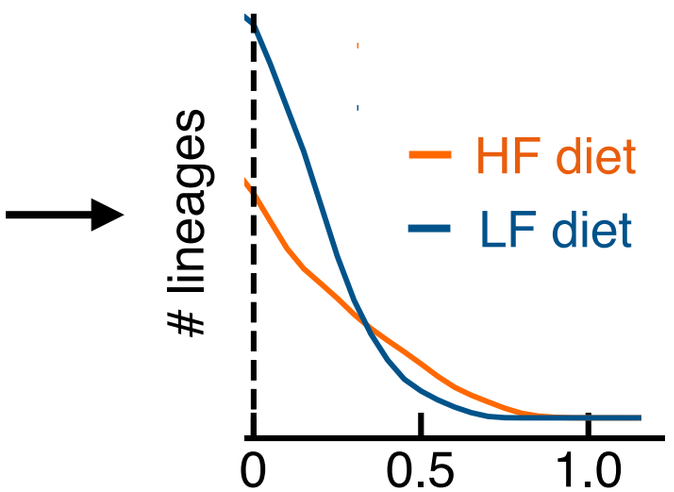
Rank lineages by fitness in ***discovery cohort***

Cross-validation reveals 1000's of strongly adaptive lineages



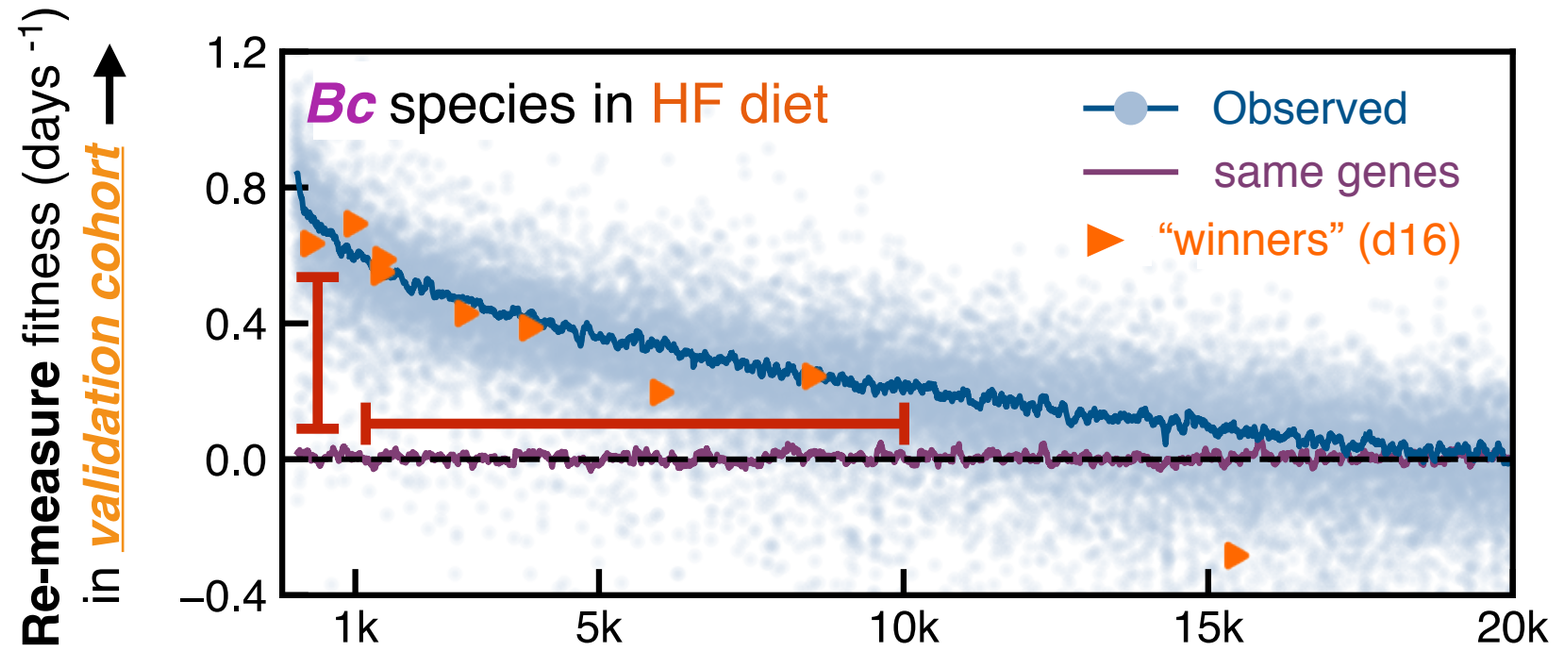
Rank lineages by fitness in ***discovery cohort*** →

Can invert to infer "**DFE**"

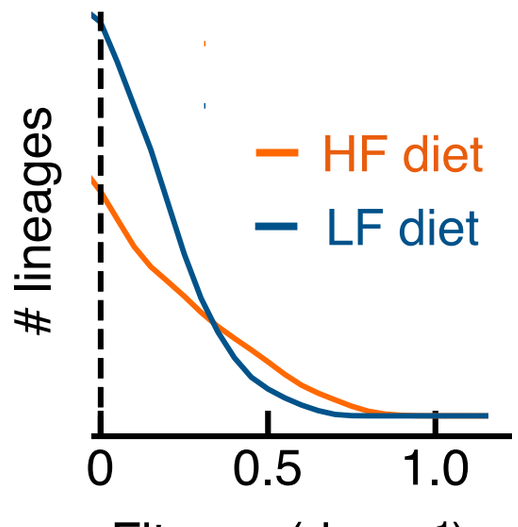


Winners emerge from competition between 1000's of adaptive variants

Cross-validation reveals 1000's of strongly adaptive lineages



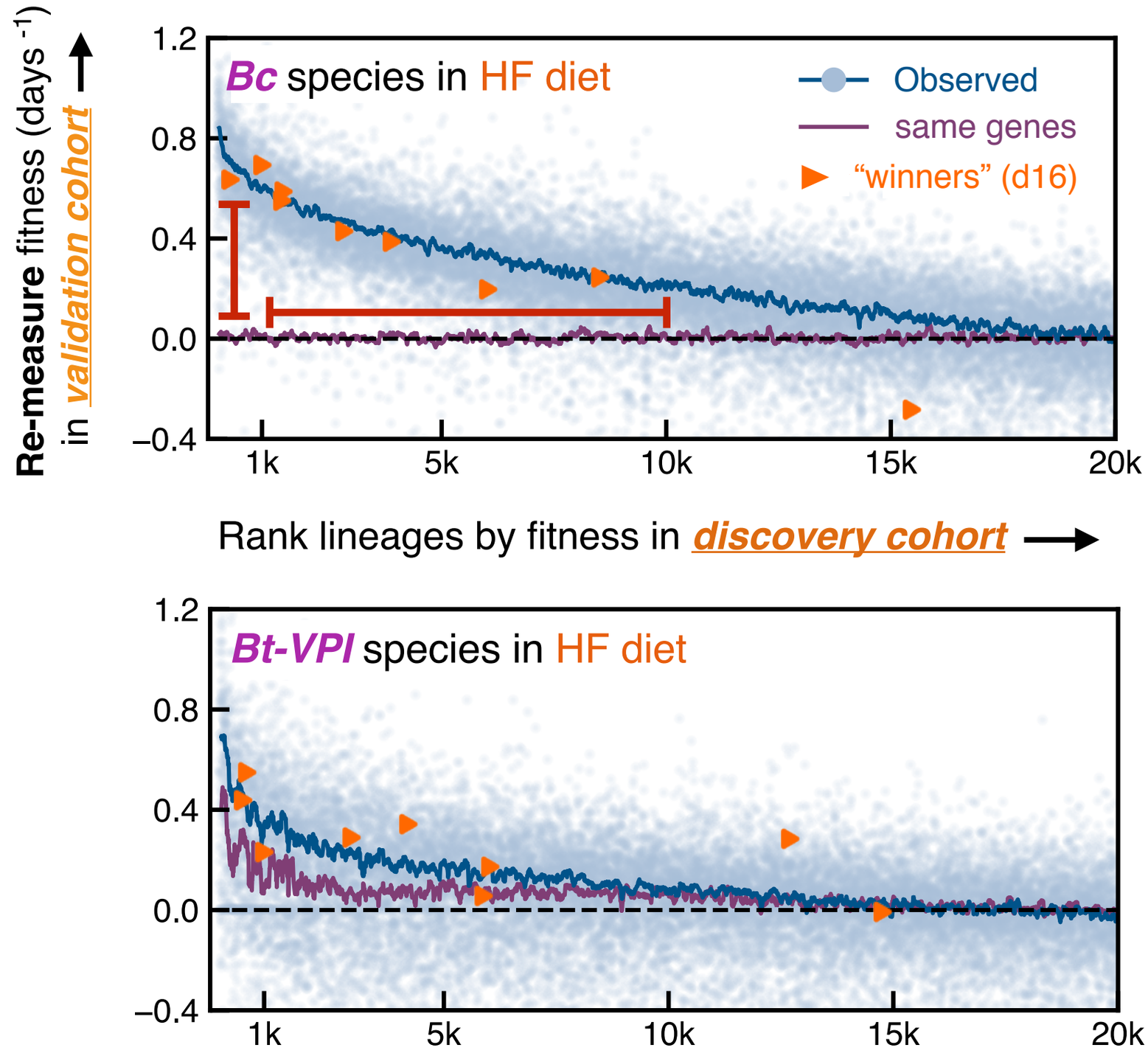
Can invert to infer "**DFE**"



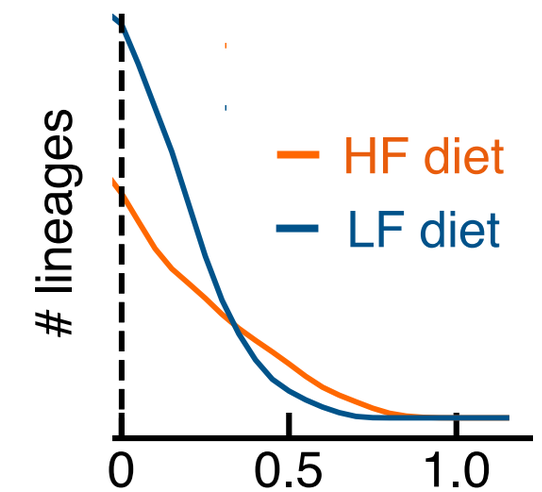
Winners emerge from competition between 1000's of adaptive variants

→ combination of ***luck (genetic "draft")*** & ***merit (fitness benefit)***

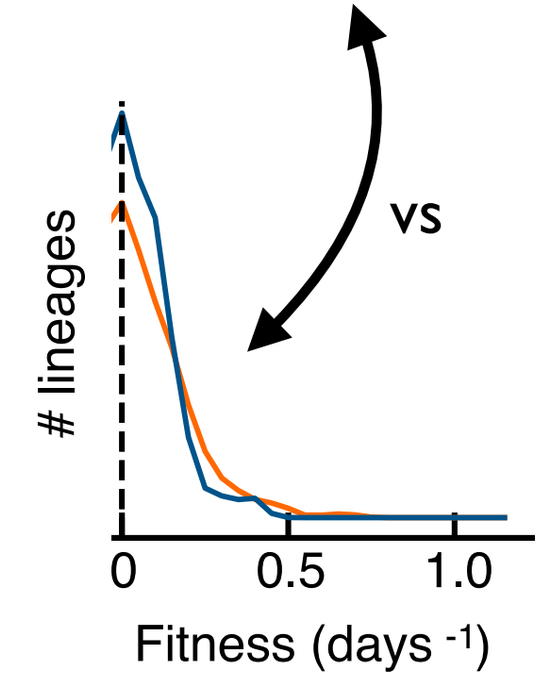
Cross-validation reveals 1000's of strongly adaptive lineages



Can invert to infer "**DFE**"

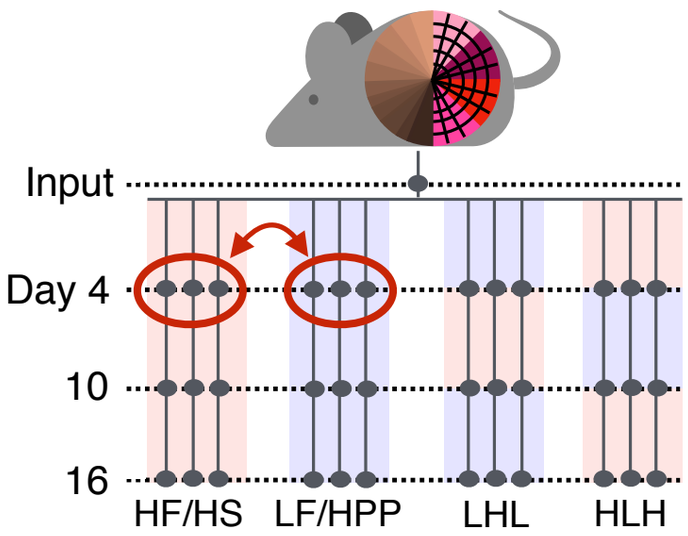


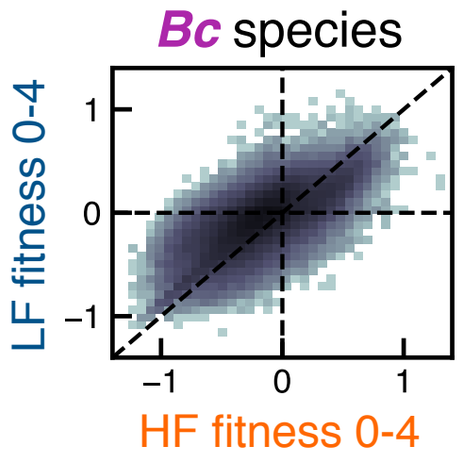
Rank lineages by fitness in ***discovery cohort***



Pleiotropic fitness tradeoffs across time and between diets

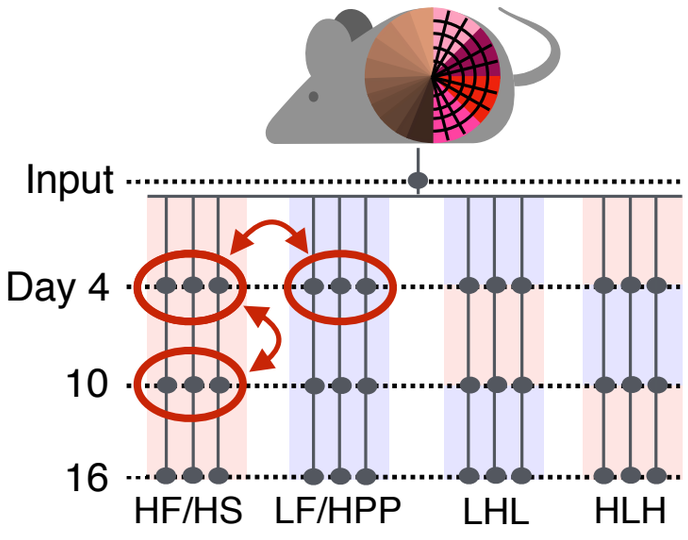
Can measure ***joint DFE***

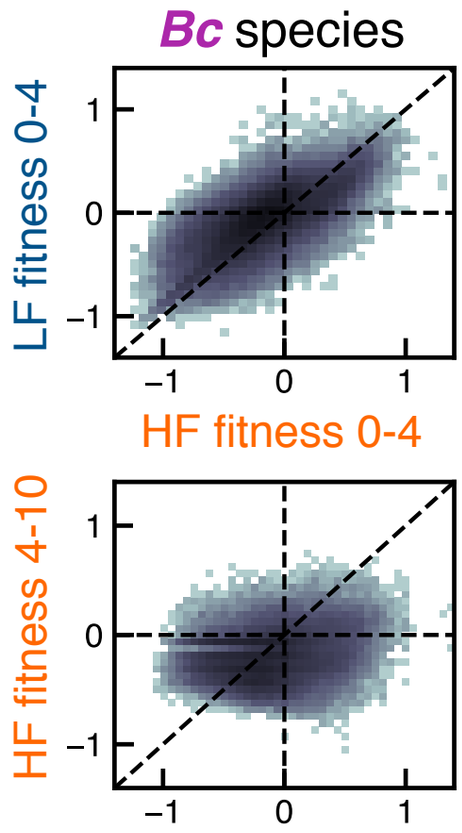




Pleiotropic fitness tradeoffs across time and between diets

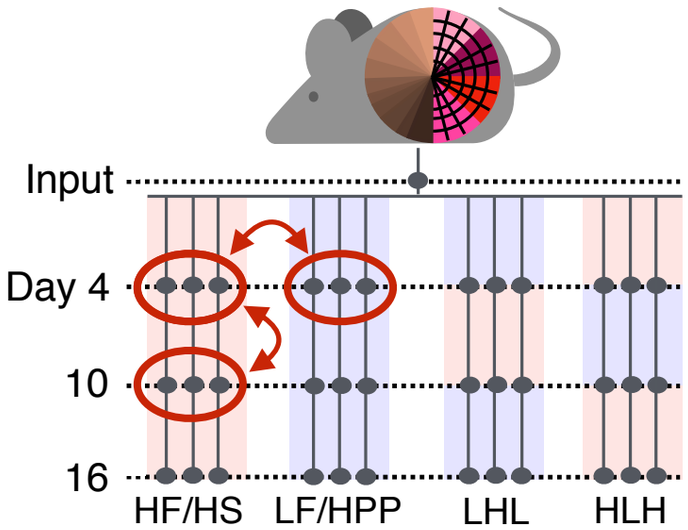
Can measure ***joint DFE***



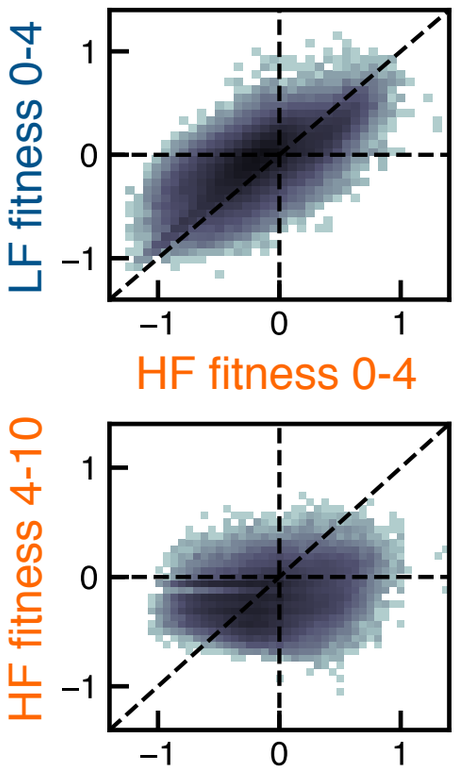


Pleiotropic fitness tradeoffs across time and between diets

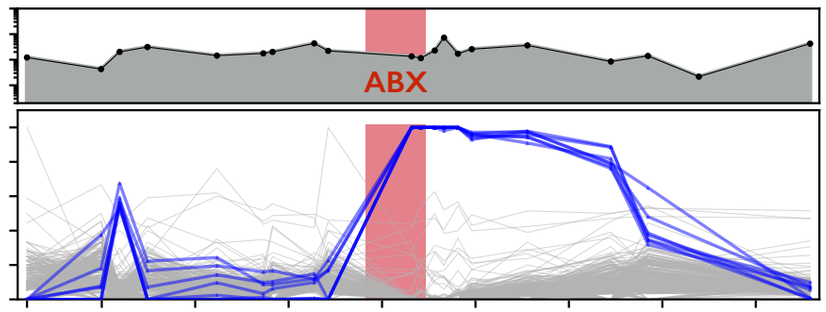
Can measure ***joint DFE***



Bc species

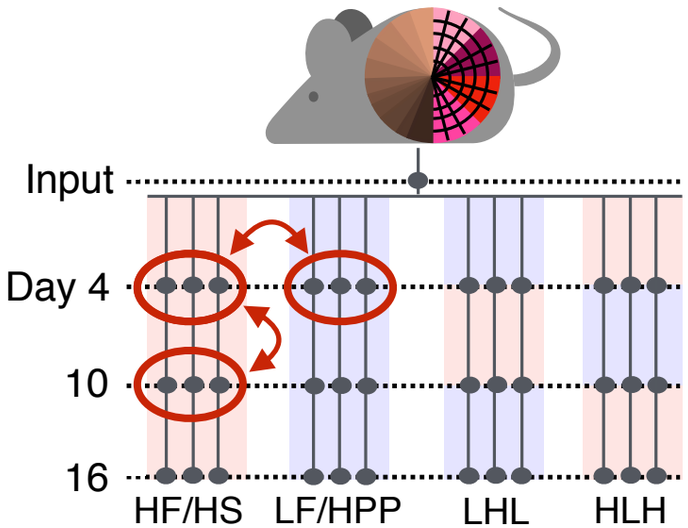


Selection pressures ***vary w/ time***

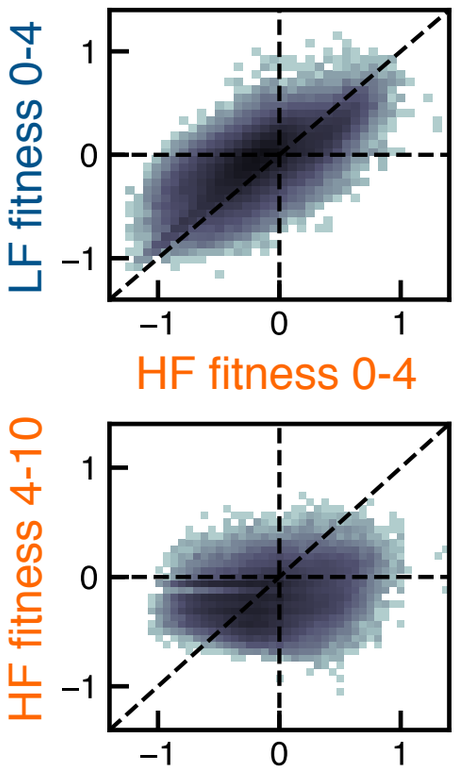


Pleiotropic fitness tradeoffs across time and between diets

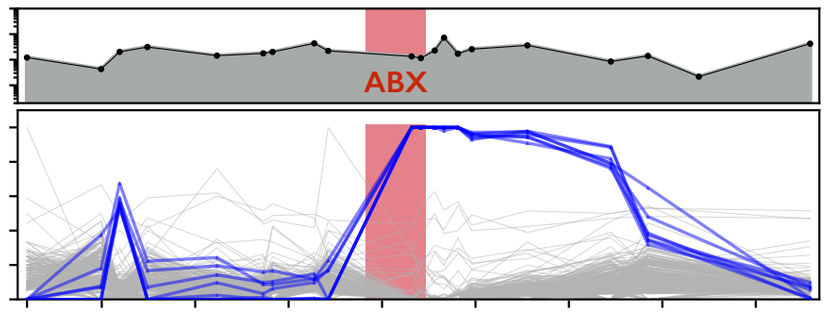
Can measure ***joint DFE***



Bc species



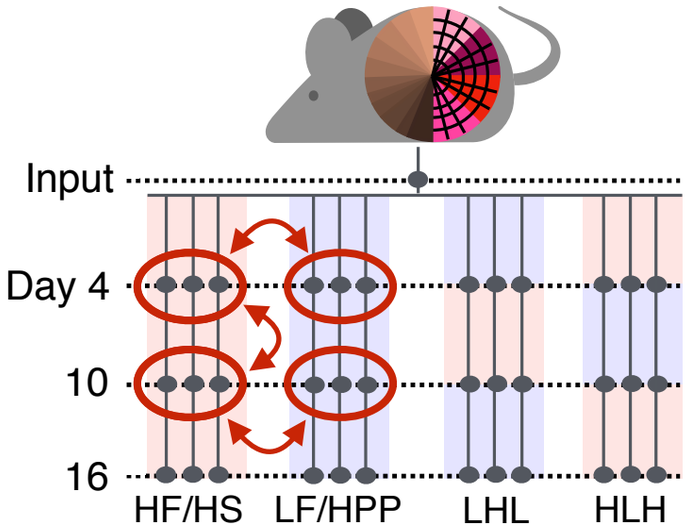
Selection pressures ***vary w/ time***



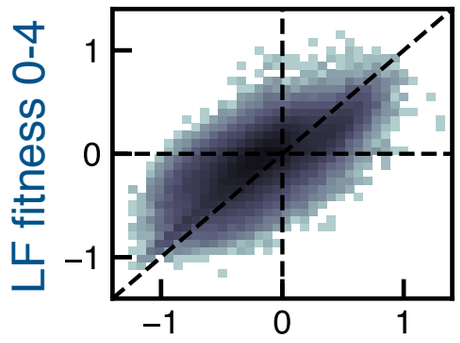
…but still consistent across hosts!

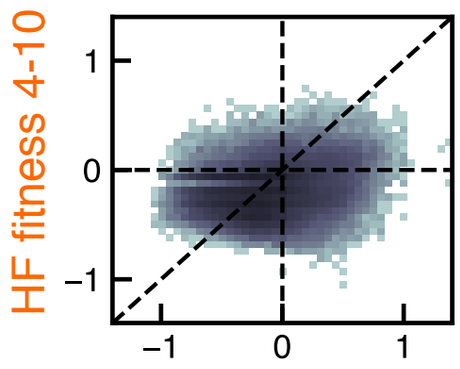
Pleiotropic fitness tradeoffs across time and between diets

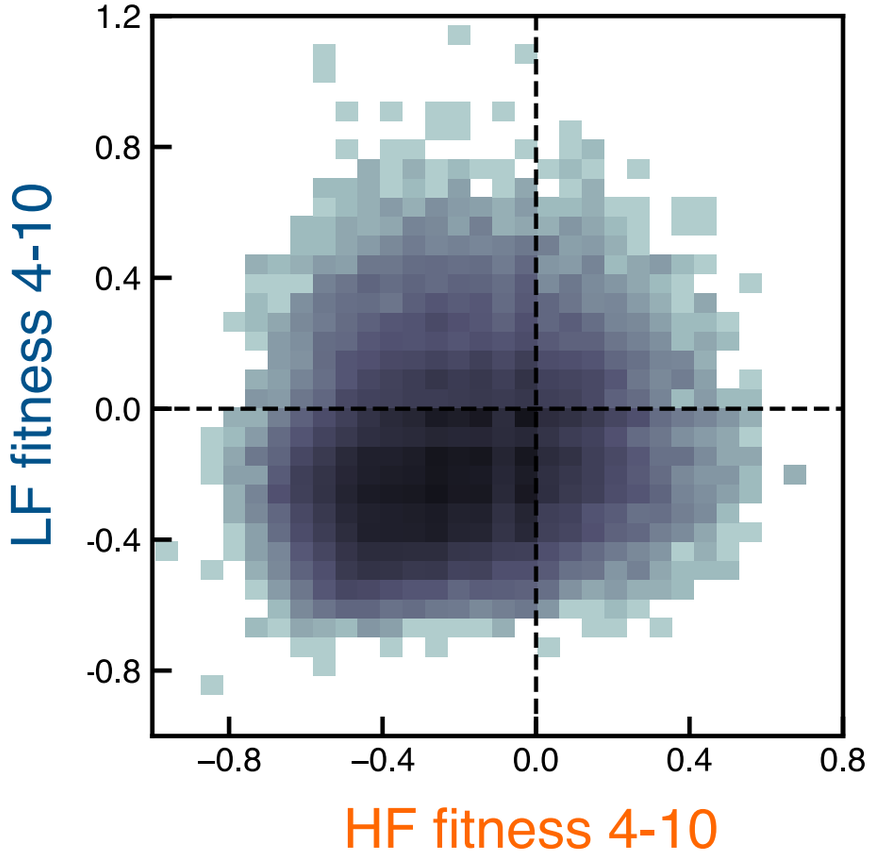
Can measure ***joint DFE***



Bc species

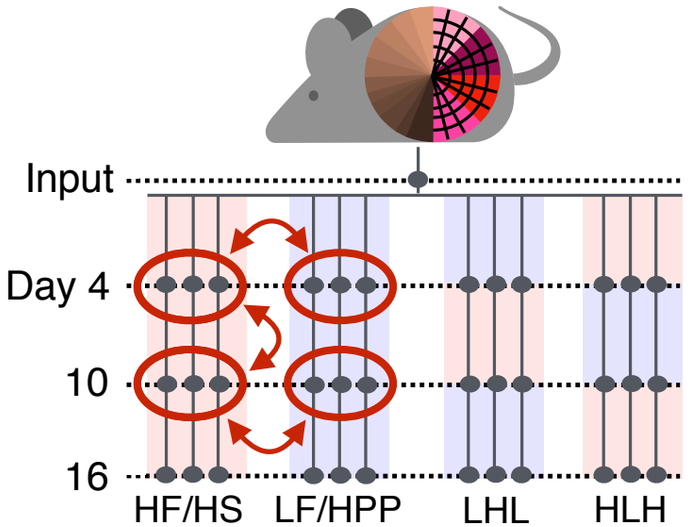


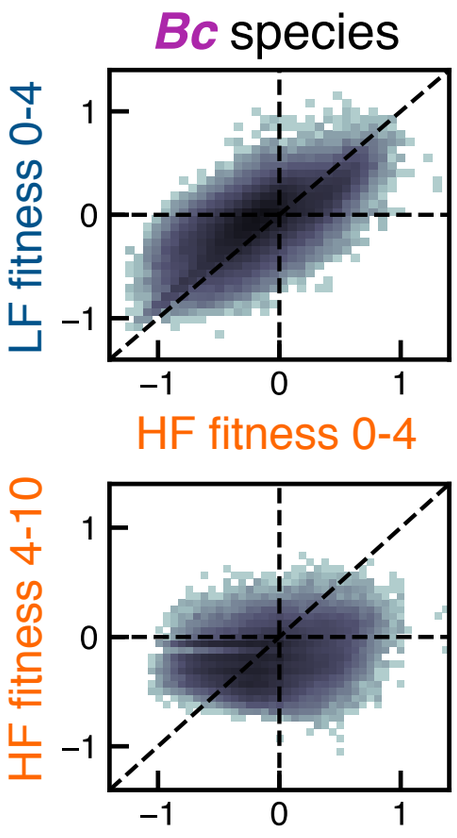


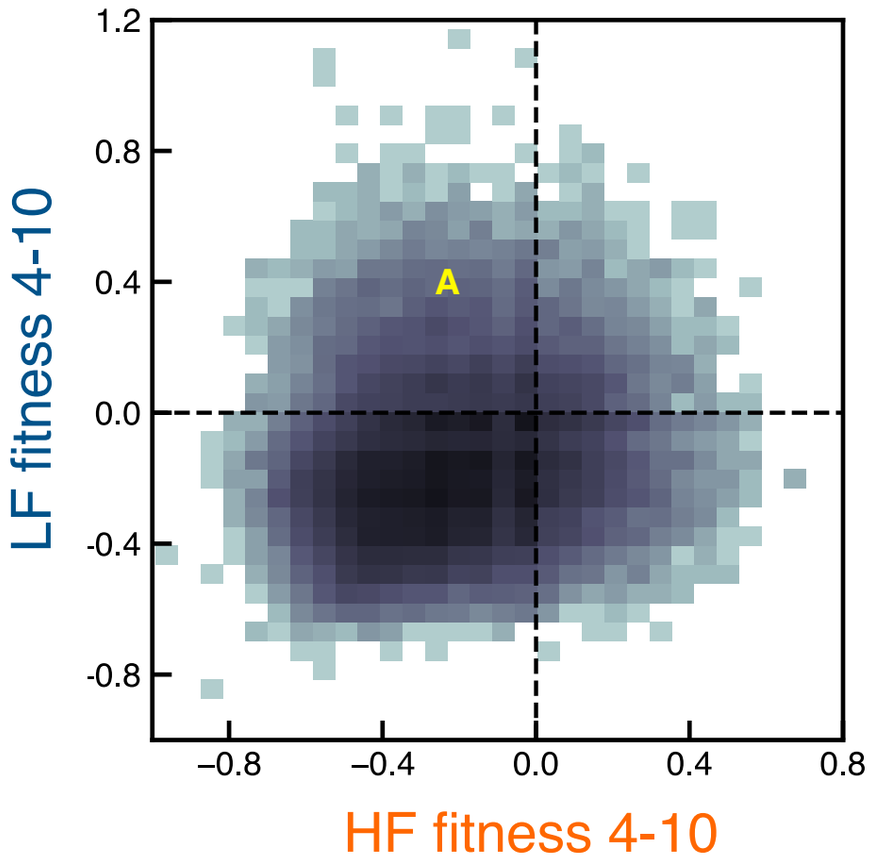


Pleiotropic fitness tradeoffs across time and between diets

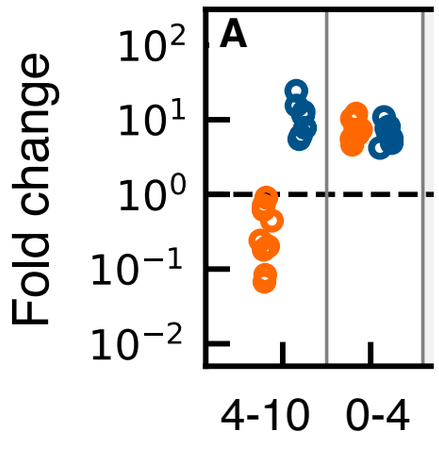
Can measure ***joint DFE***





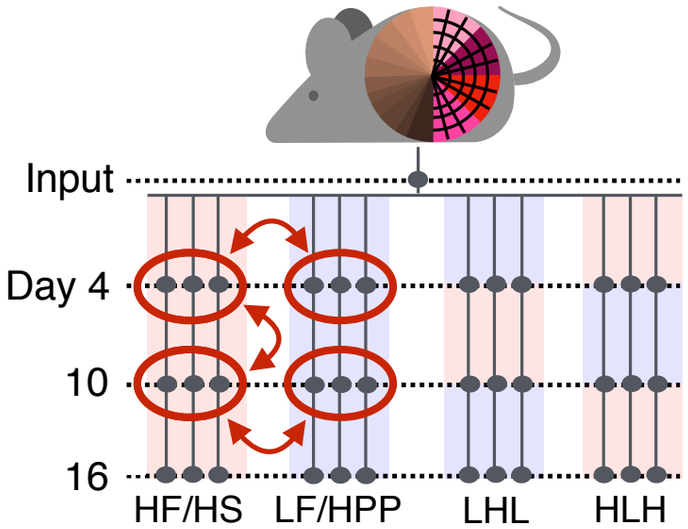


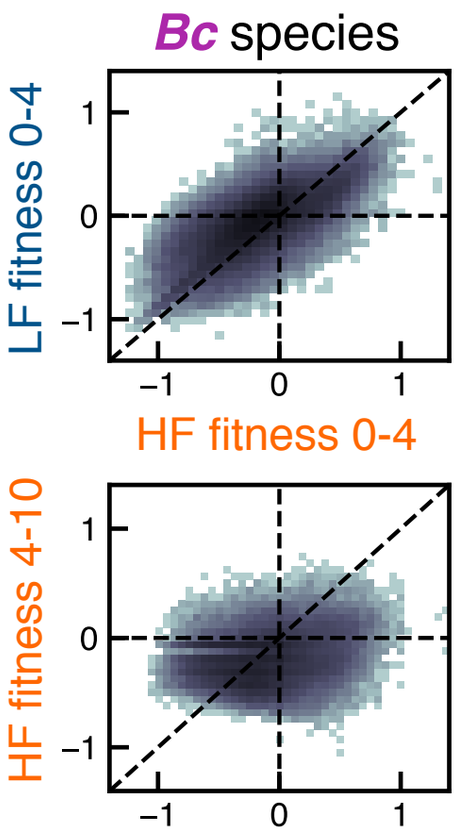
Strong tradeoffs for individual lineages:

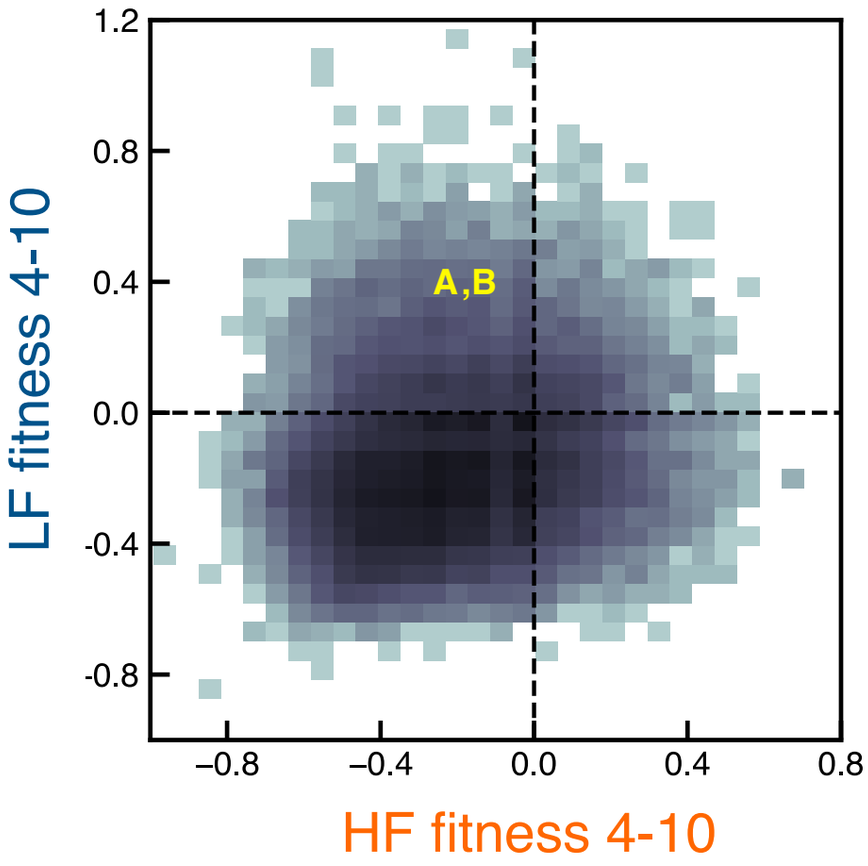


Pleiotropic fitness tradeoffs across time and between diets

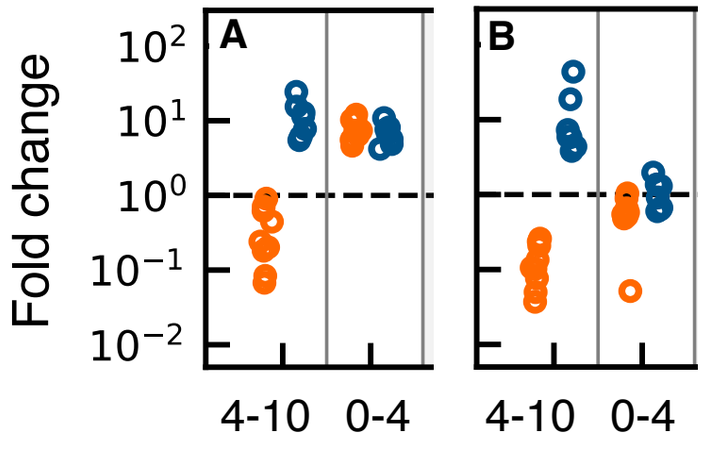
Can measure ***joint DFE***





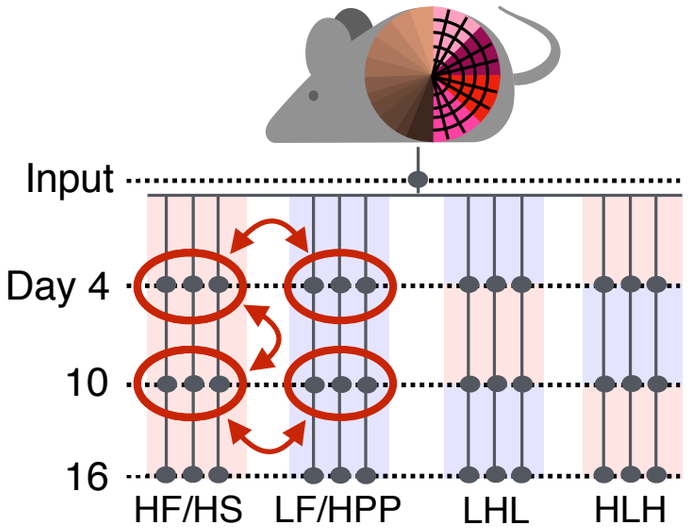


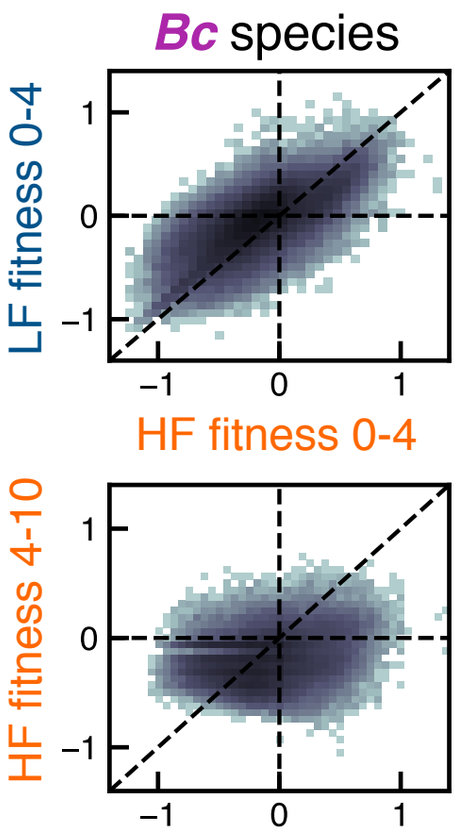
Strong tradeoffs for individual lineages:

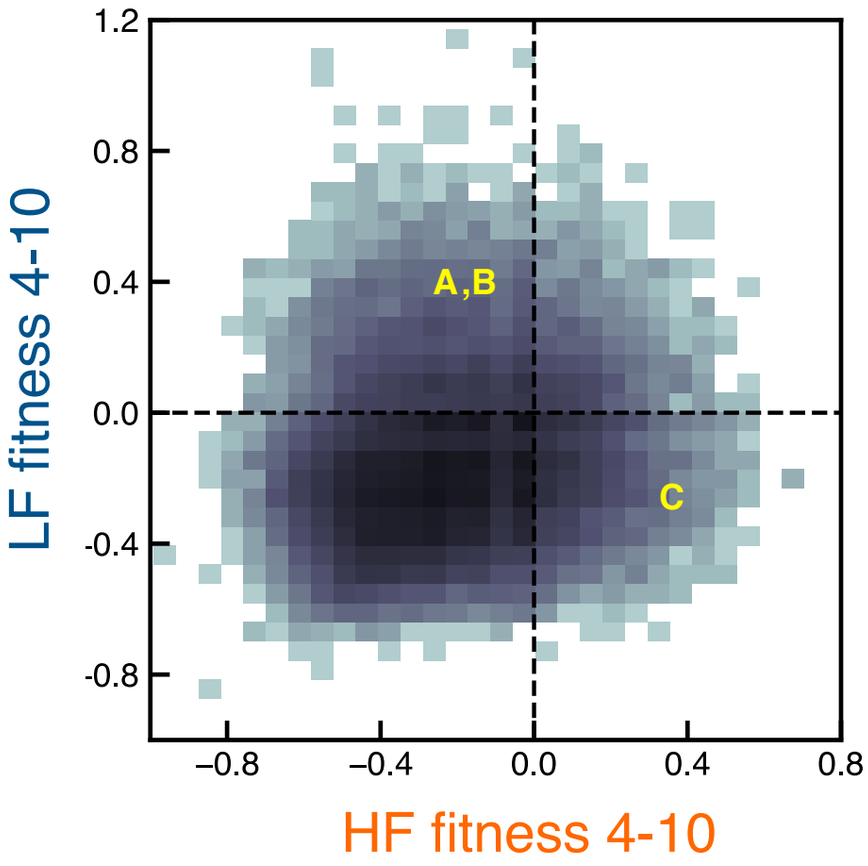


Pleiotropic fitness tradeoffs across time and between diets

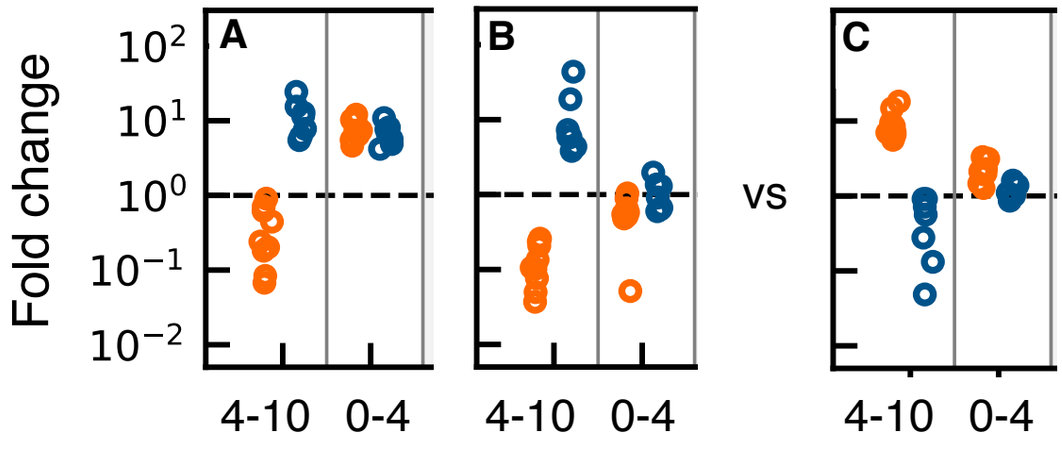
Can measure ***joint DFE***





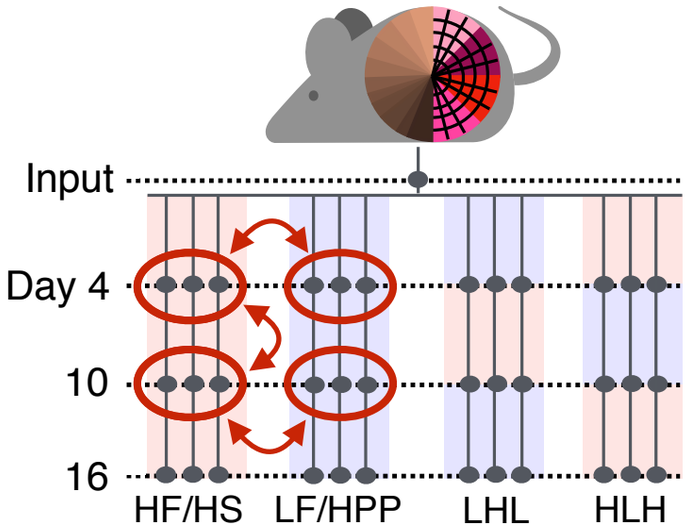


Strong tradeoffs for individual lineages:

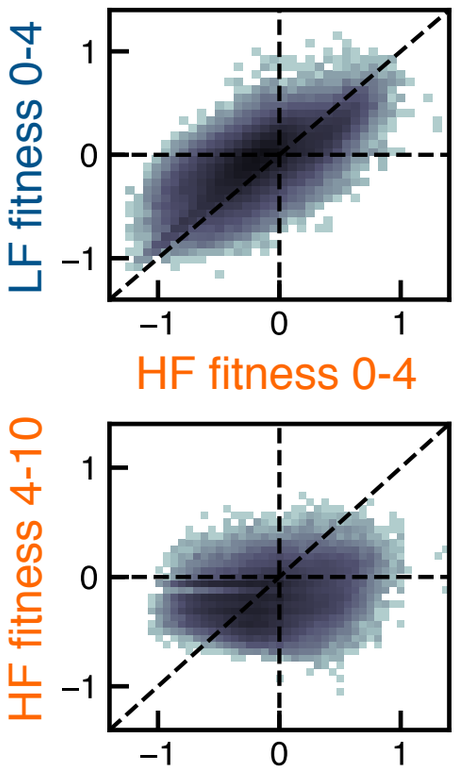


Pleiotropic fitness tradeoffs across time and between diets

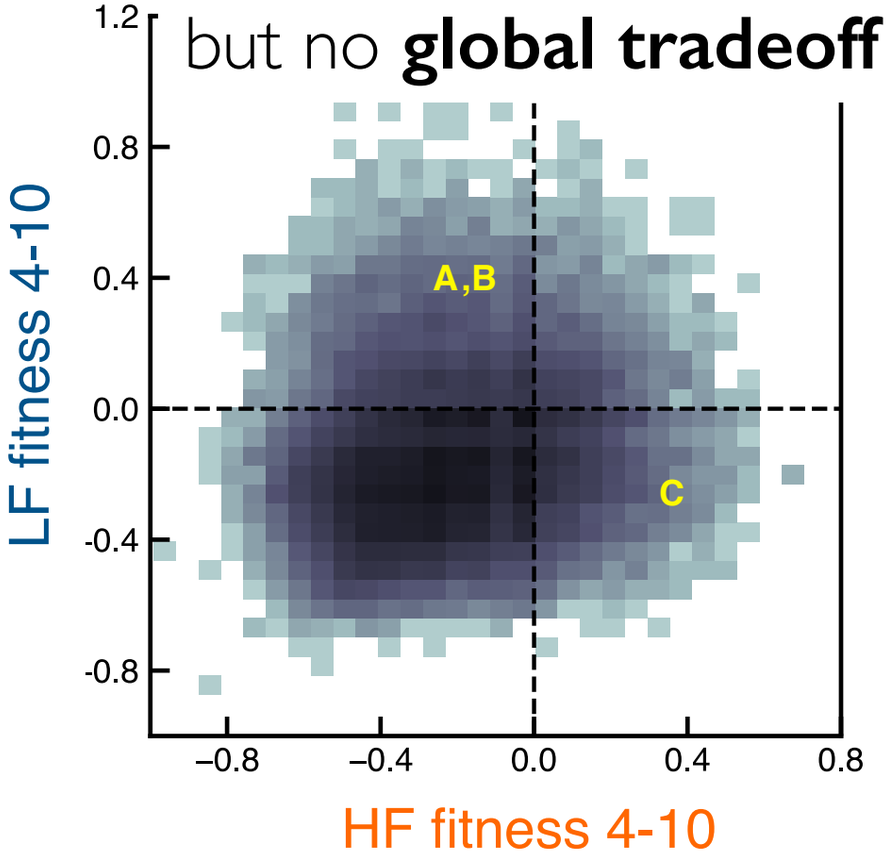
Can measure ***joint DFE***



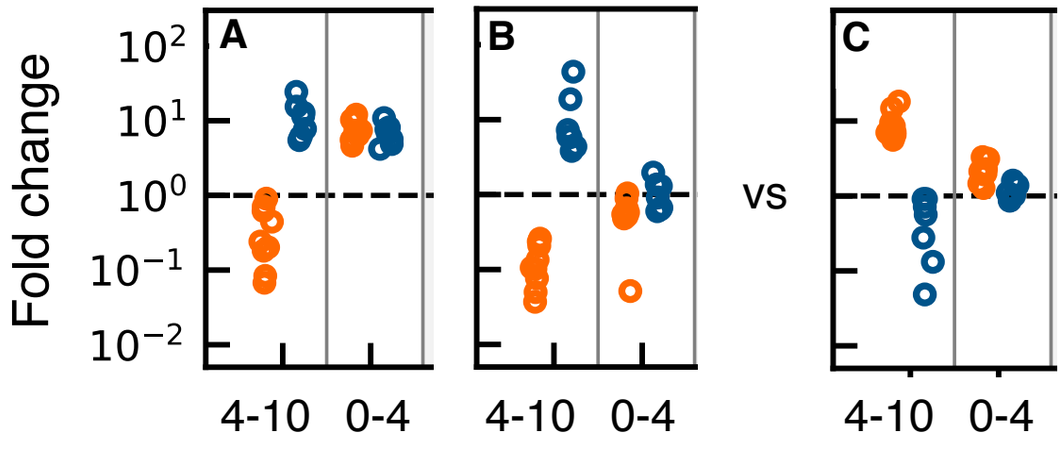
Bc species



but no **global tradeoff**

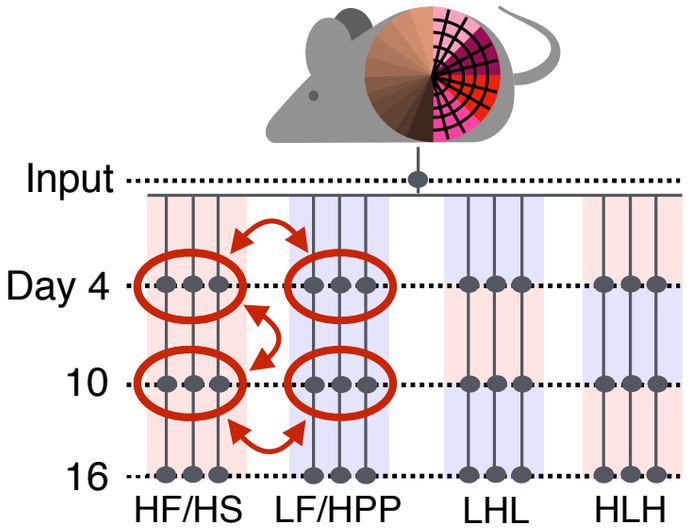


Strong tradeoffs for individual lineages:

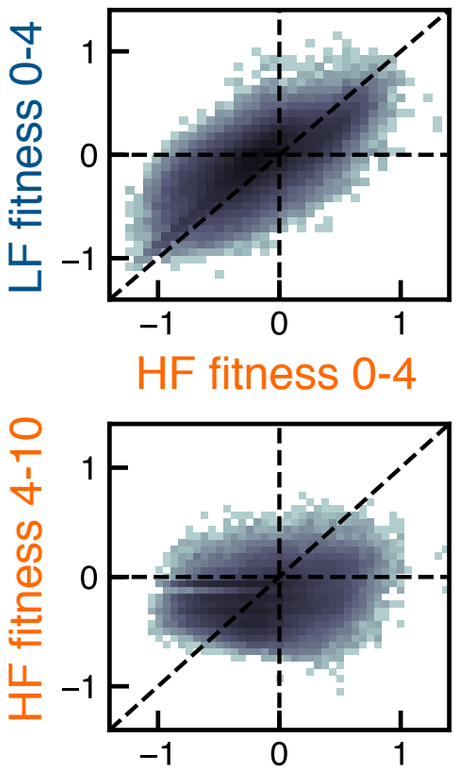


Pleiotropic fitness tradeoffs across time and between diets

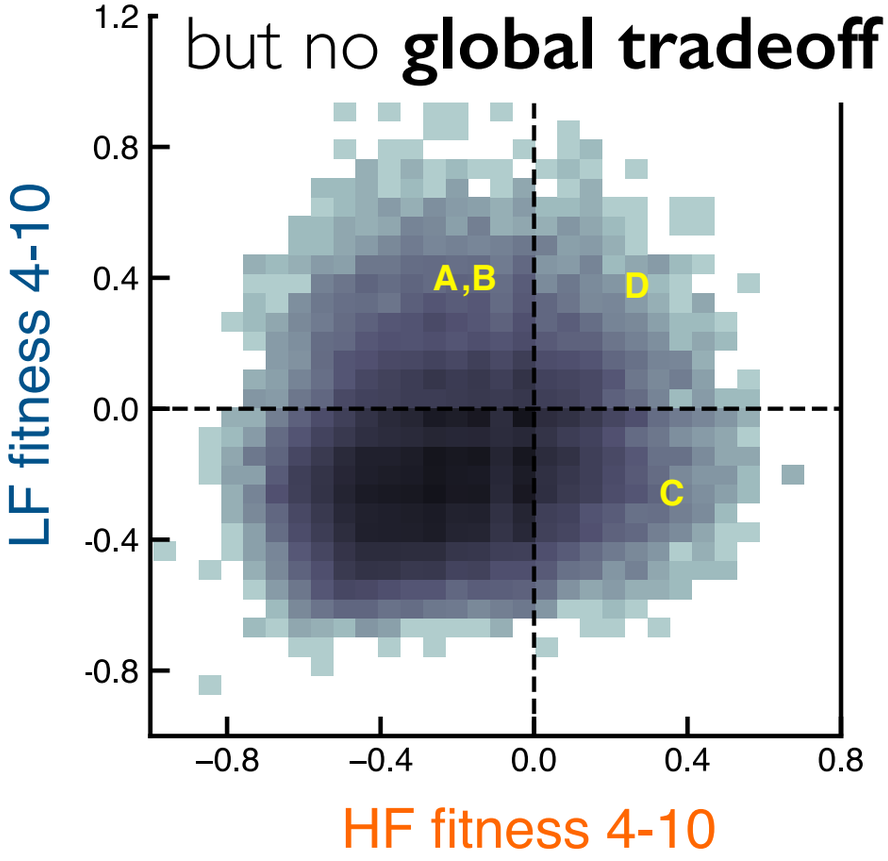
Can measure ***joint DFE***



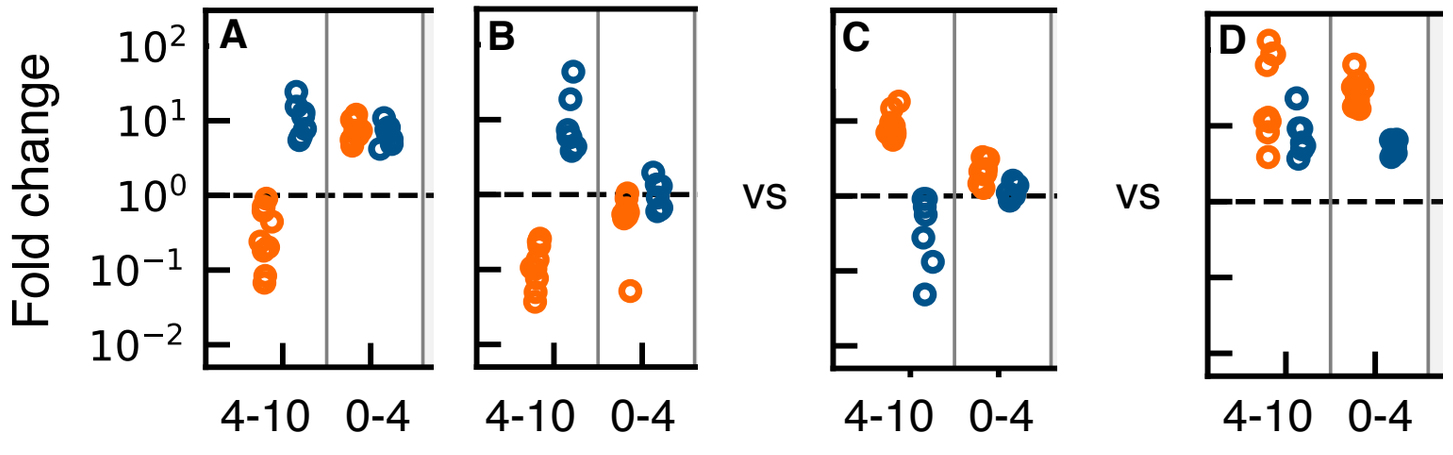
Bc species



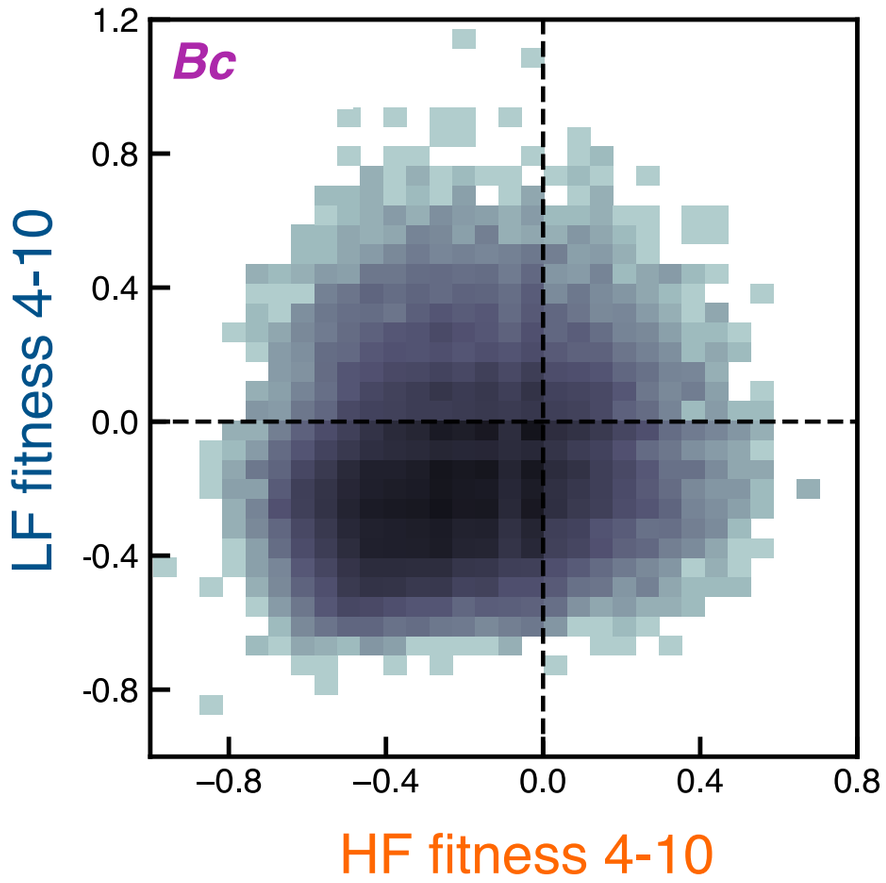
but no **global tradeoff**



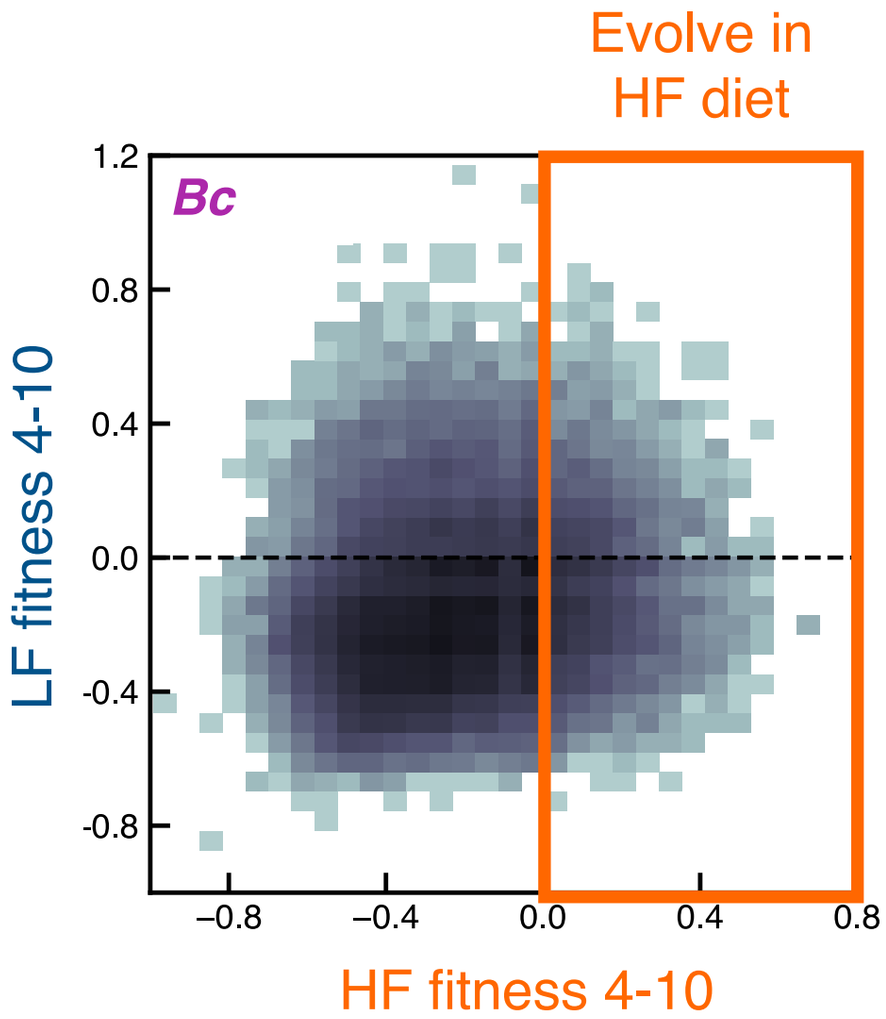
Strong tradeoffs for individual lineages:



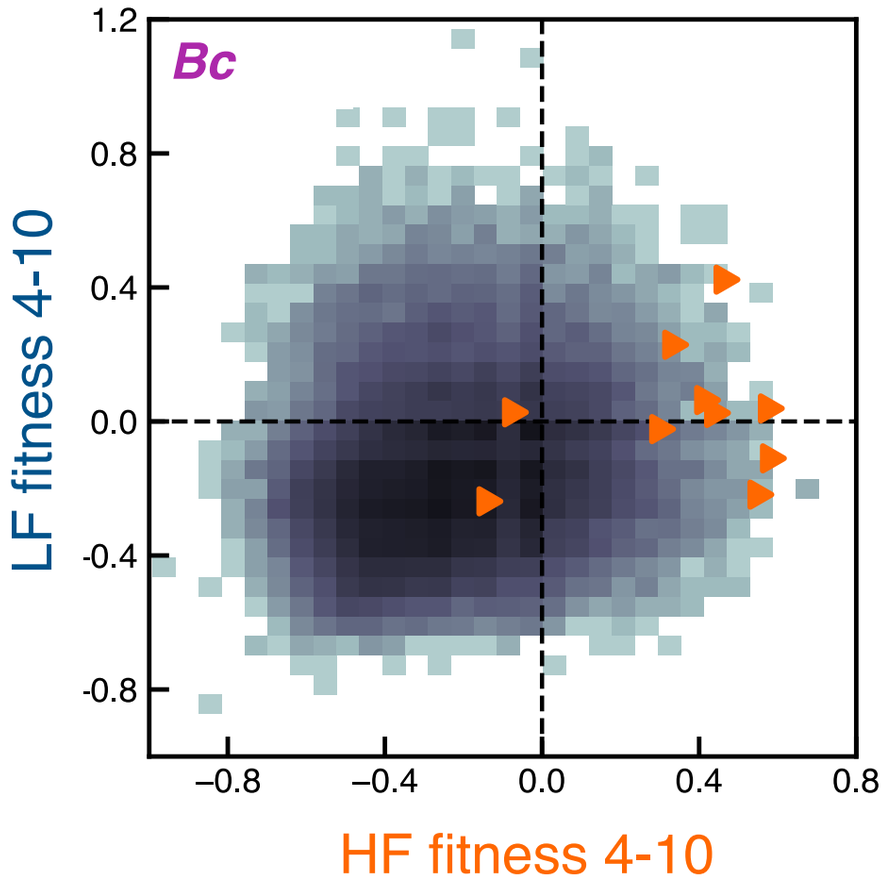
Long-term tradeoffs shaped by evolutionary dynamics



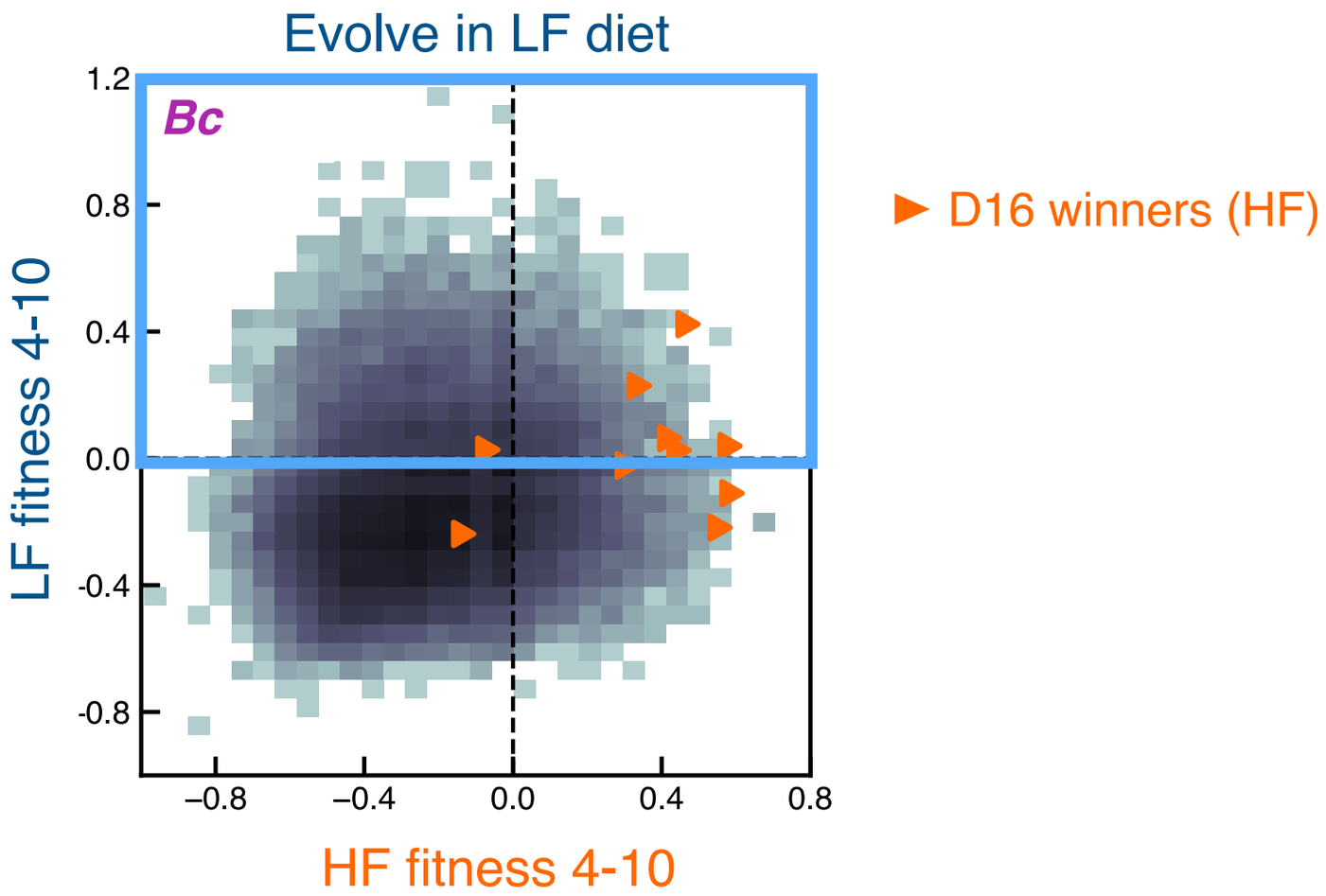
Long-term tradeoffs shaped by evolutionary dynamics



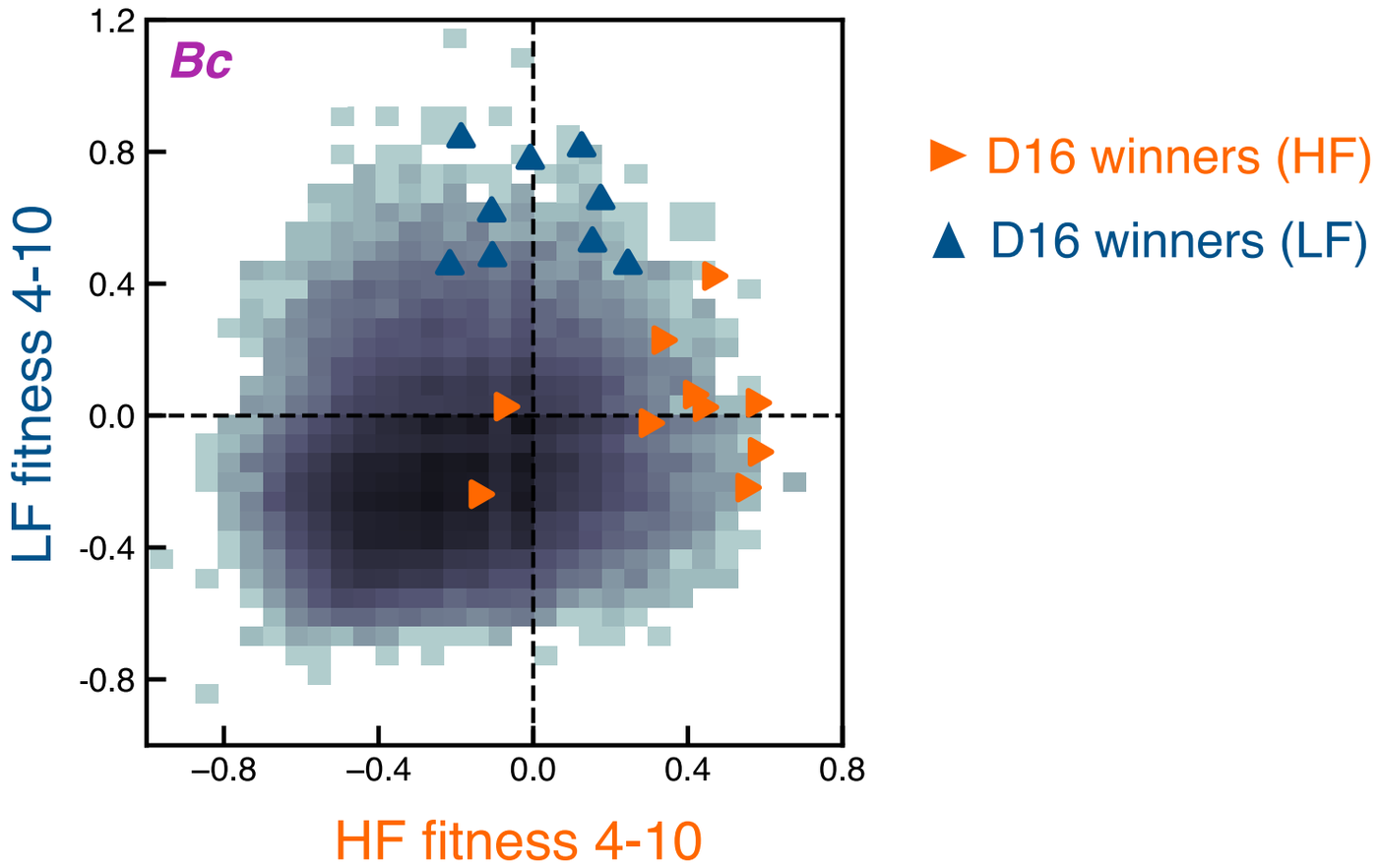
Long-term tradeoffs shaped by evolutionary dynamics



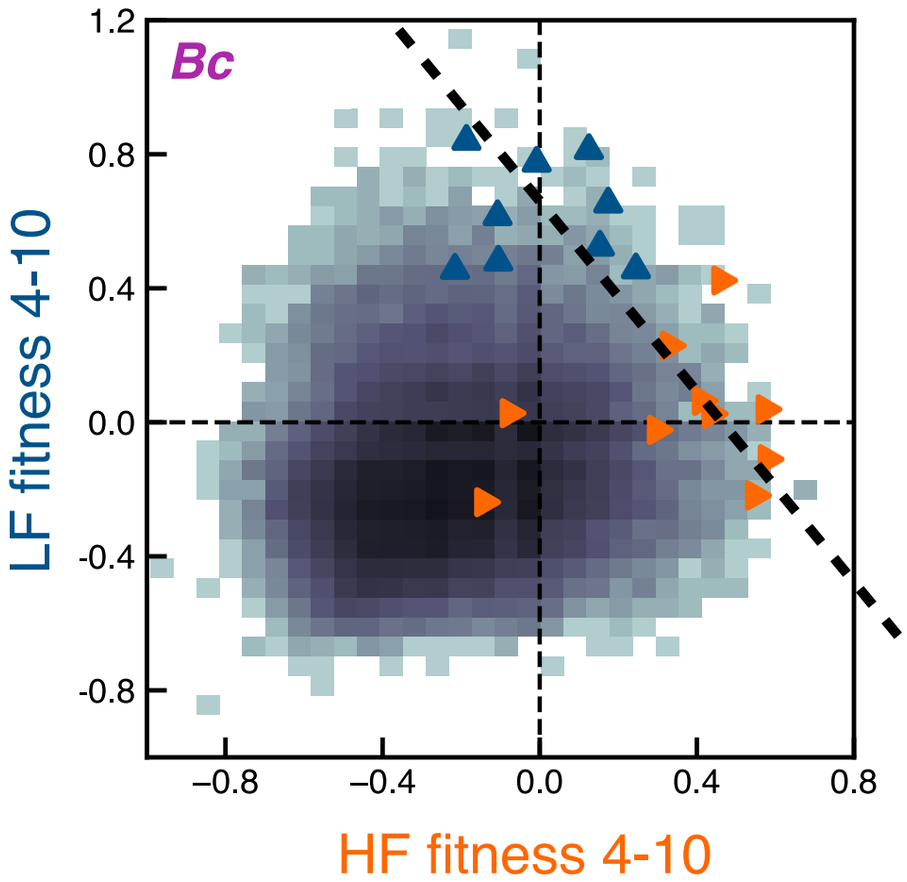
Long-term tradeoffs shaped by evolutionary dynamics



Long-term tradeoffs shaped by evolutionary dynamics



Long-term tradeoffs shaped by evolutionary dynamics



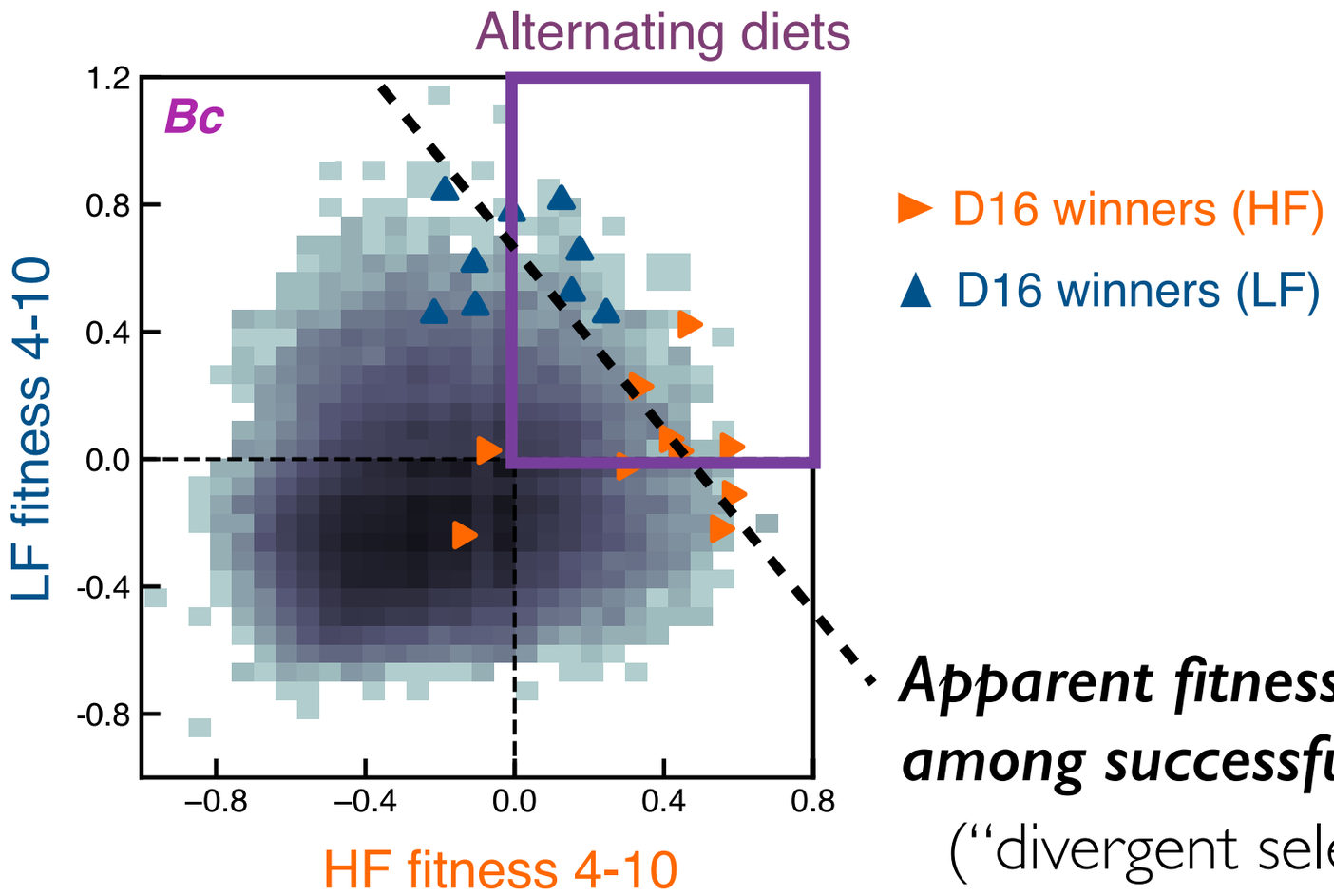
► D16 winners (HF)

▲ D16 winners (LF)

Apparent fitness tradeoffs among successful variants

("divergent selection")

Long-term tradeoffs shaped by evolutionary dynamics



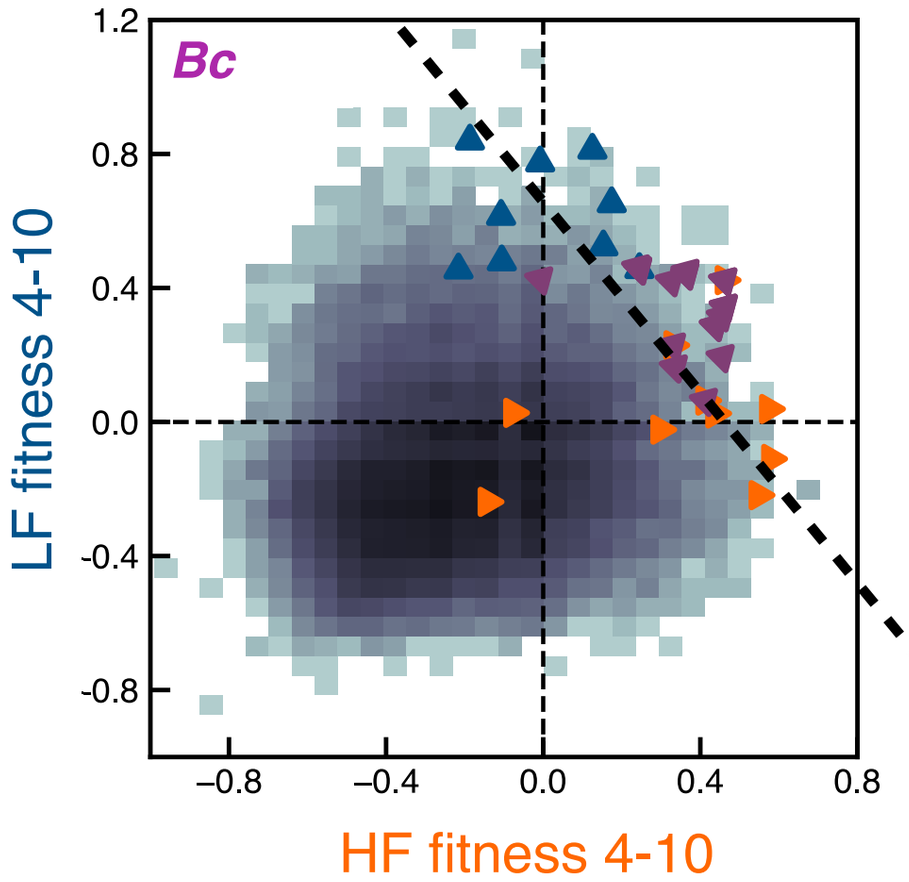
► D16 winners (HF)

▲ D16 winners (LF)

Apparent fitness tradeoffs among successful variants

("divergent selection")

Long-term tradeoffs shaped by evolutionary dynamics



► D16 winners (HF)

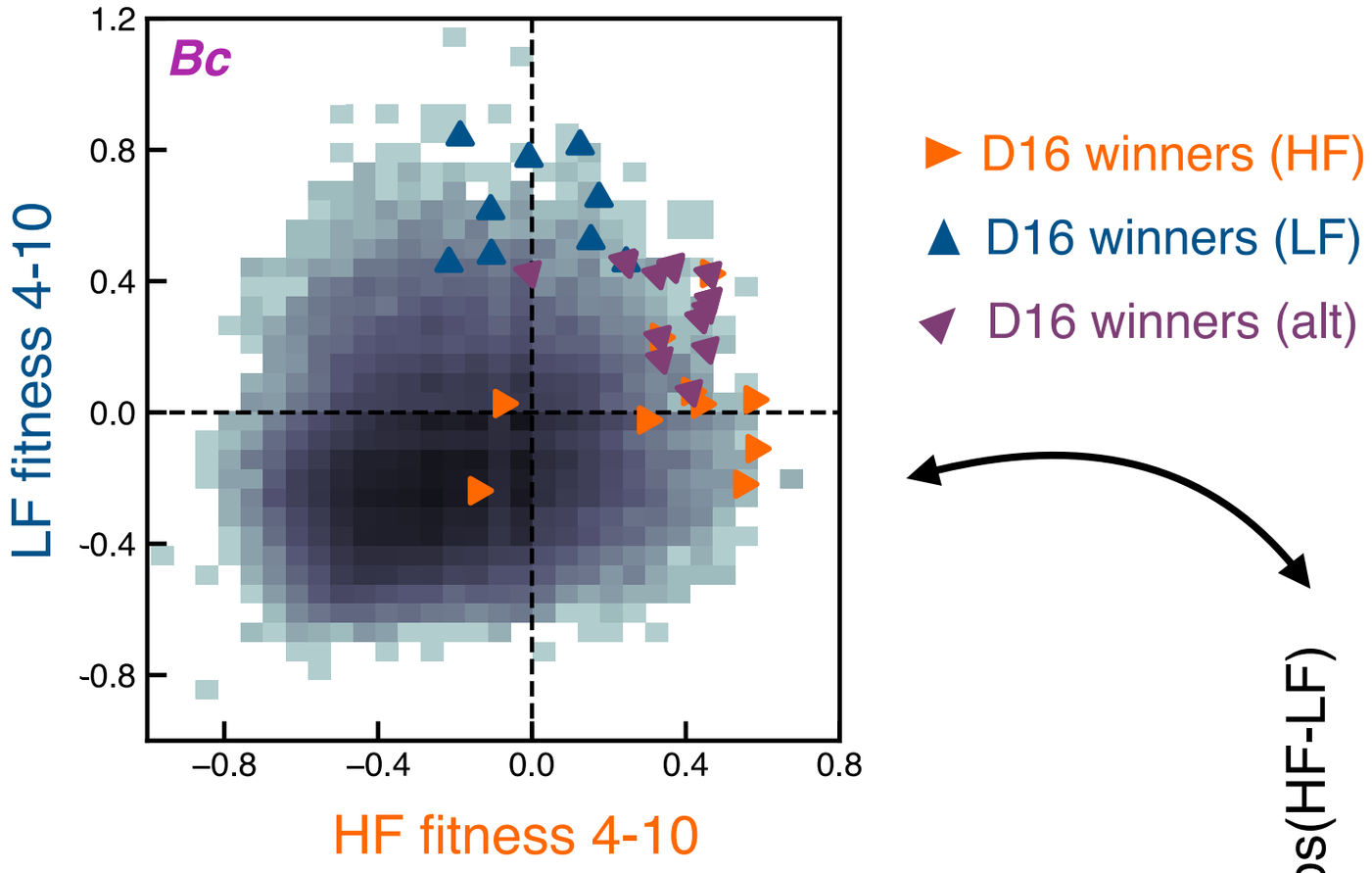
▲ D16 winners (LF)

◀ D16 winners (alt)

Apparent fitness tradeoffs among successful variants

("divergent selection")

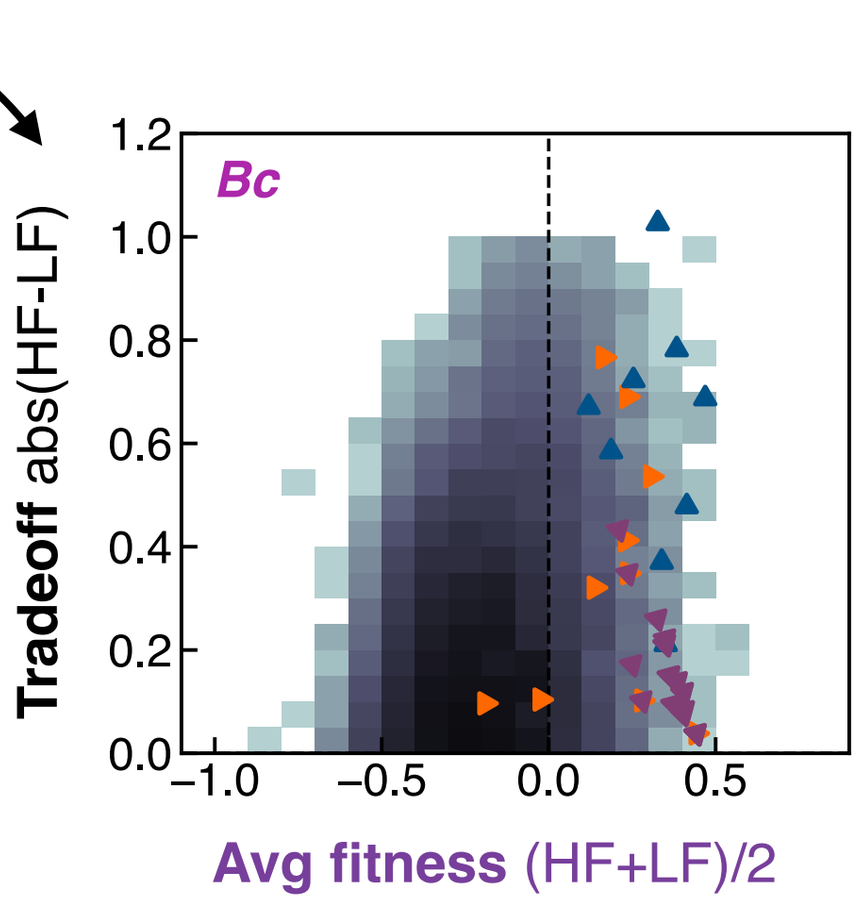
Long-term tradeoffs shaped by evolutionary dynamics



D16 winners (HF)

D16 winners (LF)

D16 winners (alt)



Fitness tradeoffs in other environments contain ***signature of evolutionary history***

Thanks!

Evolutionary dynamics in the human gut microbiome:

Garud*, **BHG***, et al, *PLoS Bio* 2019

Nandita Garud (UCLA)

Katie Pollard (UCSF)

Oskar Hallatschek (UC Berkeley)

Longitudinal ABX study

Roodgar*, **BHG*** *Gen Res* 2021

Morteza Roodgar

Mike Snyder (Stanford)

Good Lab @ Stanford

Daniel Wong (Applied Physics)

Zhiru Liu (Applied Physics)

Anastasia Lyulina (Biology)

James Ferrare (Biophysics)

Olivia Ghosh (Physics)

Sophie Walton (Biohysics)

Serena Debesai (STEM Fellow)

Preprint: Wong & BHG *biorxiv* 2022.05.13.491573
"Quantifying the adaptive landscape of commensal gut bacteria using high resolution lineage tracking"

Funding:
Alfred P. Sloan Foundation,
Chan Zuckerberg Biohub