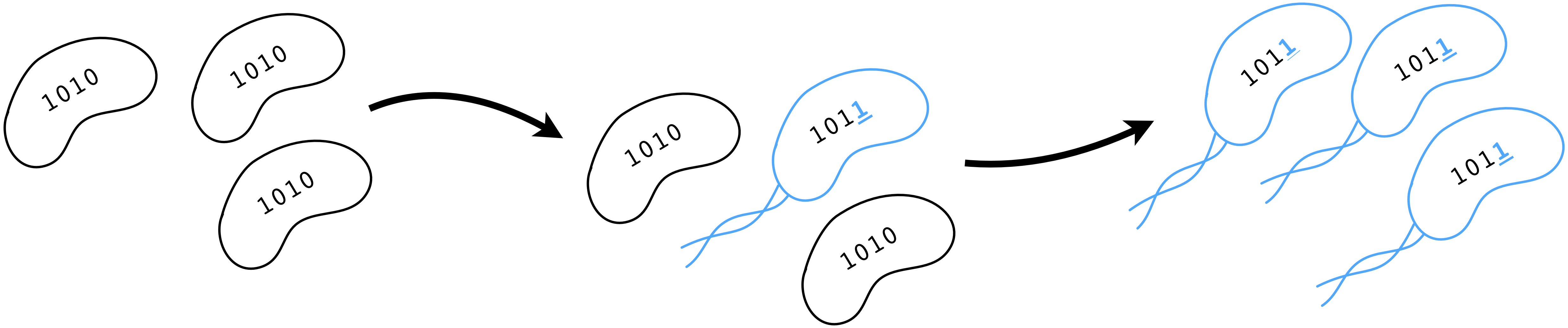
Evolutionary dynamics & ecological diversification in rapidly adapting populations

Benjamin Good

Miller Fellow, UC Berkeley

UCSB QBio Seminar, 2/15/18

Evolution as a stochastic dynamical process



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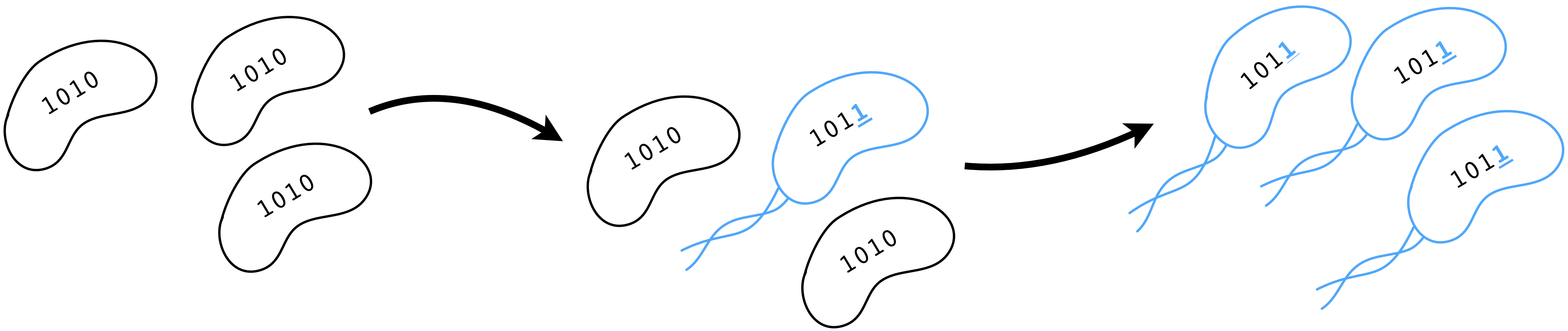
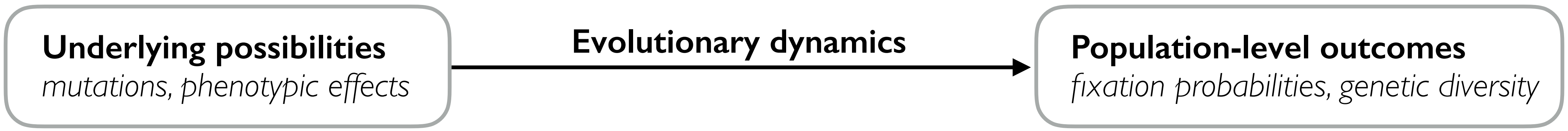


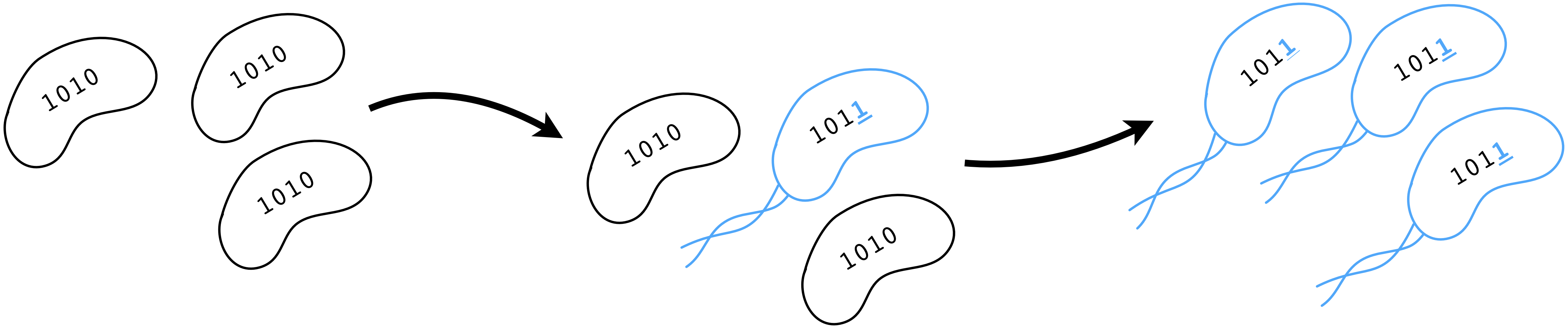


Underlying possibilities
mutations, phenotypic effects

Evolutionary dynamics

Population-level outcomes
fixation probabilities, genetic diversity

Evolution as a stochastic dynamical process



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Evolutionary dynamics
(general principles?)

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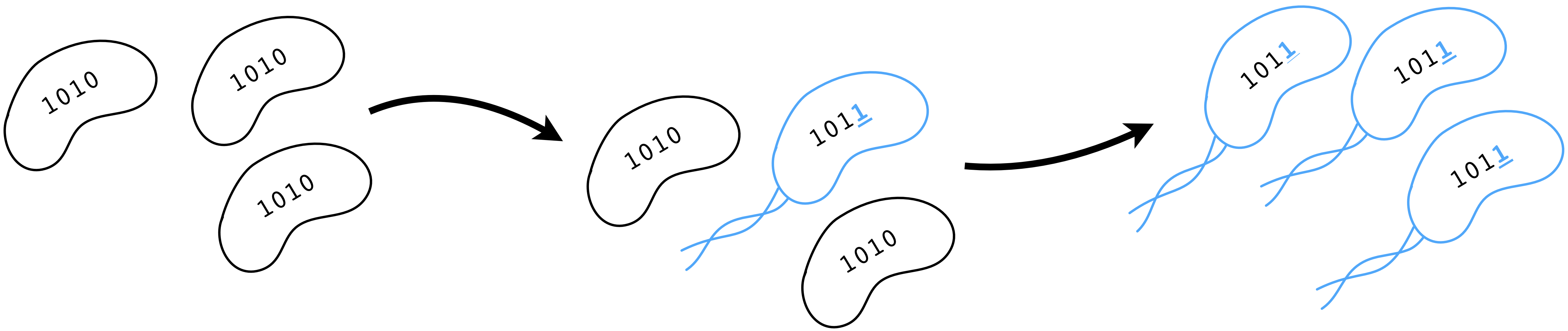

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Can we understand this process in a quantitative way, to make predictions ?

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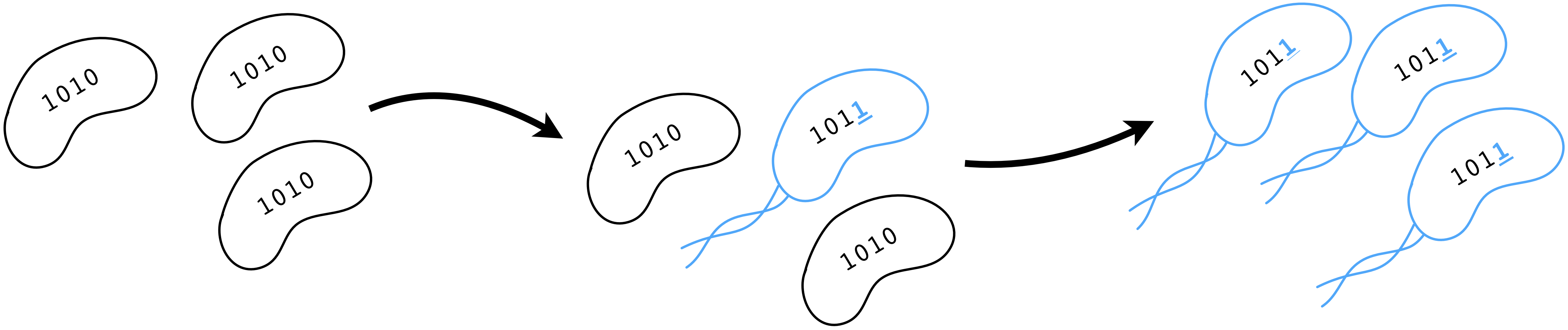

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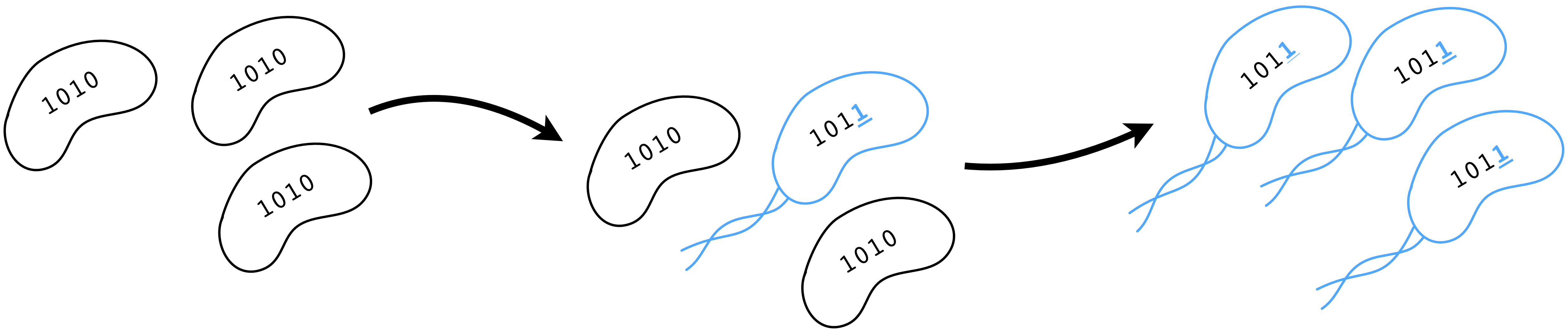
Can we understand this process in a quantitative way, to make ~~predictions~~ ?

short-term predictions

for microbes, cancer cells,
immune repertoires, etc.

Evolution as a stochastic dynamical process



Underlying possibilities
mutations, phenotypic effects
(probe w/ gene editing)

Evolutionary dynamics →
(general principles?)

Population-level outcomes
fixation probabilities, genetic diversity
(observe w/ sequencing)

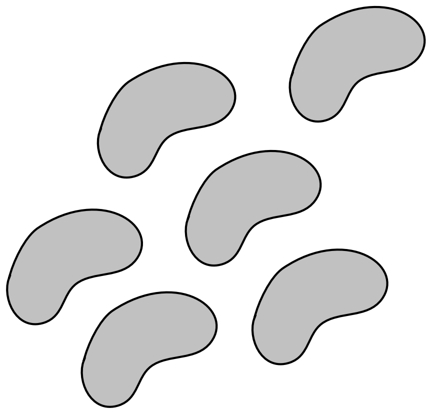
Can we understand this process in a quantitative way, to make ~~predictions~~ ?

short-term predictions

for microbes, cancer cells, immune repertoires, etc.

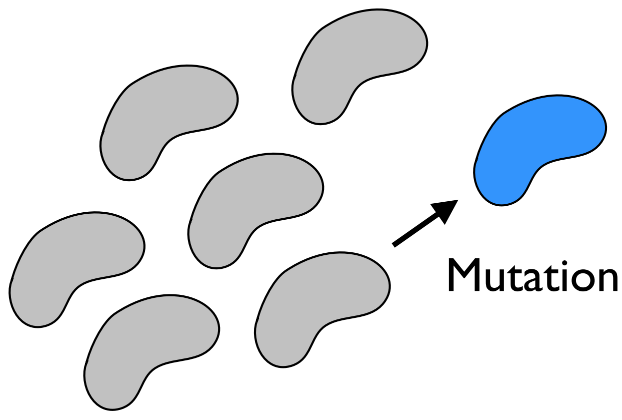
The simplest model of evolution

Population, size N



Generation 0

The simplest model of evolution



Population, size N

Mutation, μ

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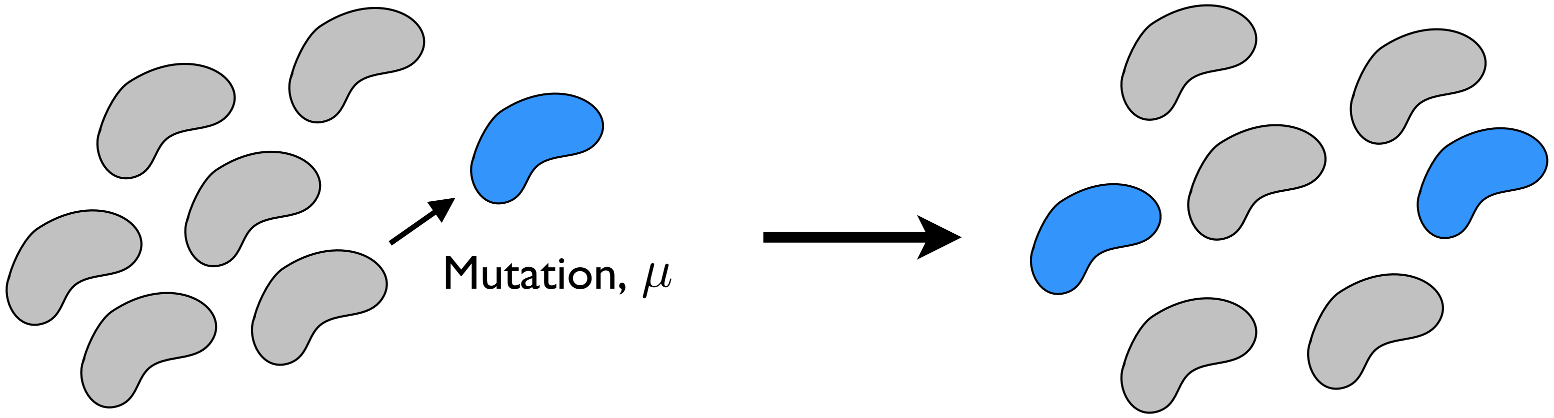

Population, size N

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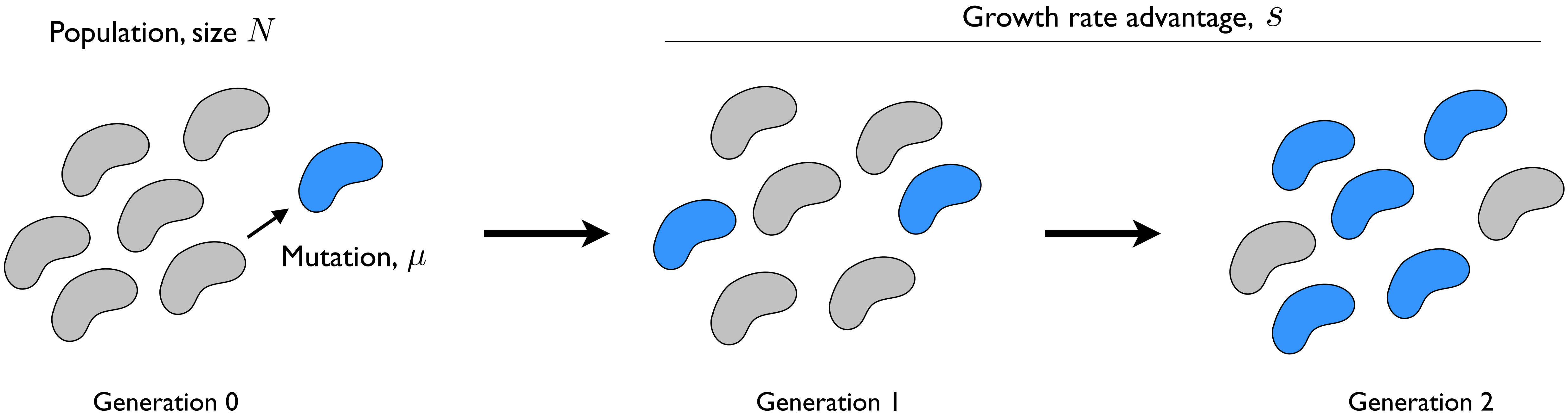
Generation 0

Generation 1

The simplest model of evolution



Population, size N

Growth rate advantage, s

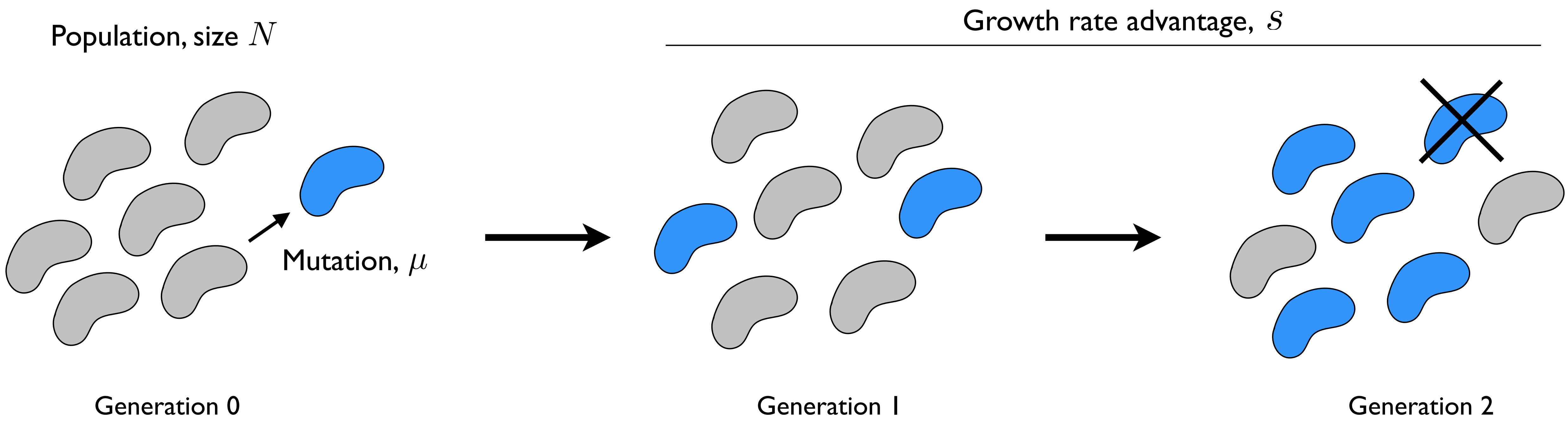
Mutation, μ

Generation 0

Generation 1

Generation 2

The simplest model of evolution



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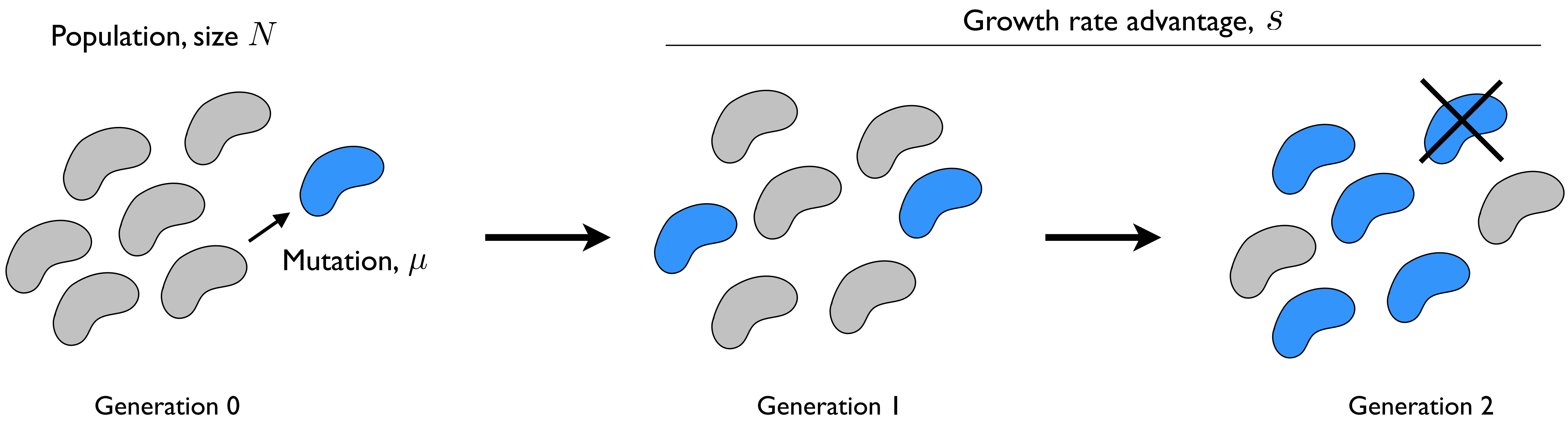

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Fraction mutant cells, f, grows as:

$$\frac{\partial f}{\partial t} \approx \underbrace{\mu(1-f)}_{\text{mutation}} + \underbrace{sf(1-f)}_{\text{selection}} + \underbrace{\sqrt{\frac{f(1-f)}{N}}\,\eta(t)}_{\substack{\text{genetic drift}\\ \textit{(birth-death noise)}}}$$

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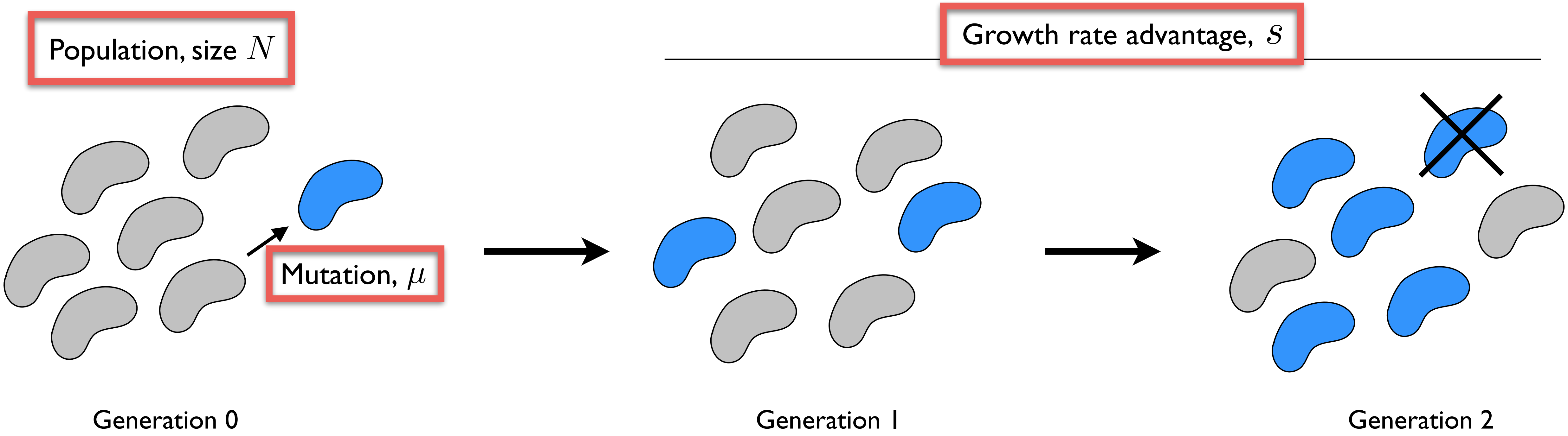

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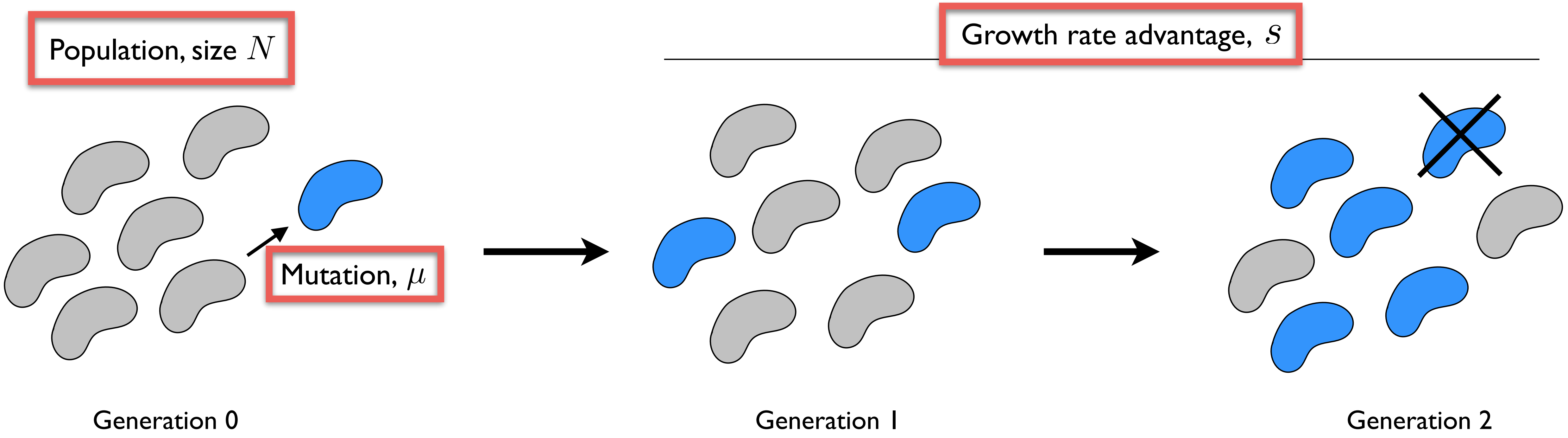
Measure

The simplest model of evolution



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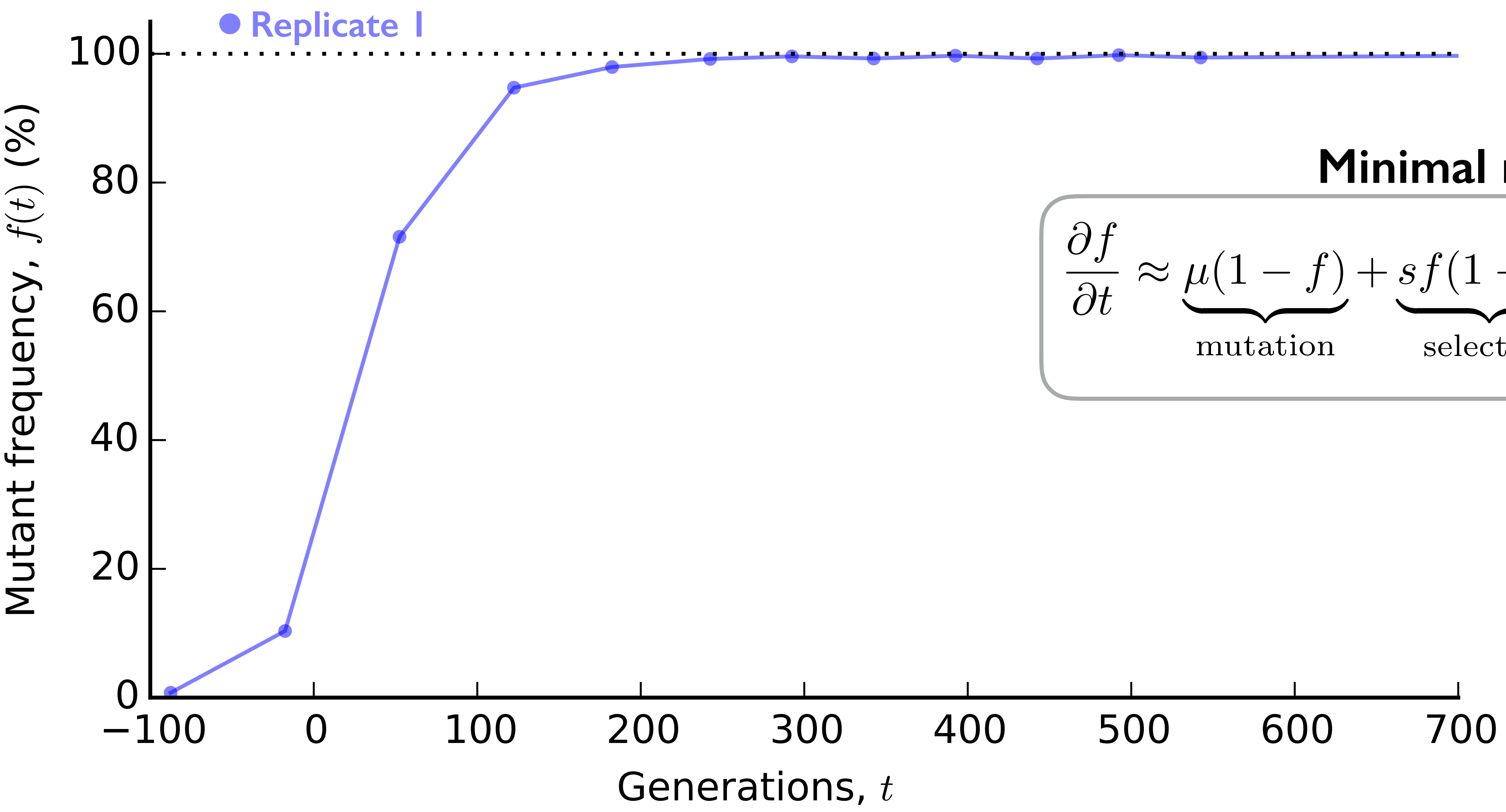
(birth-death noise)

Measure → ***Predict evolution!***

e.g. how long until $f = 100\%$ ("fixation") ?

A laboratory “test” of the simple model



Minimal model

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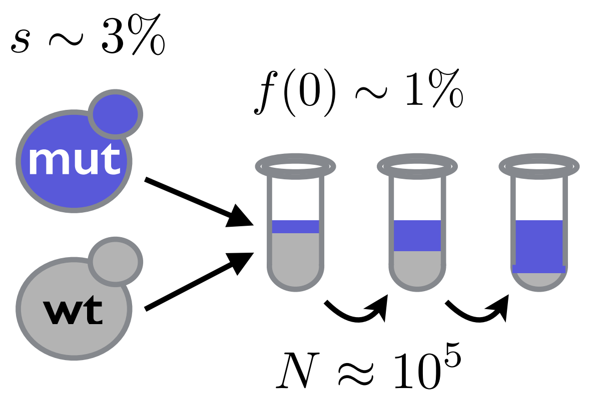

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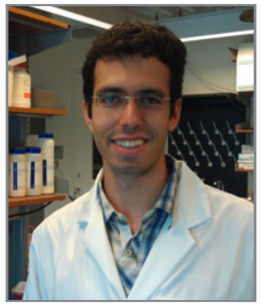
Measure frequency
w/ flow cytometry



Evgeni Frenkel

Data from Frenkel, Good, and Desai (2014)

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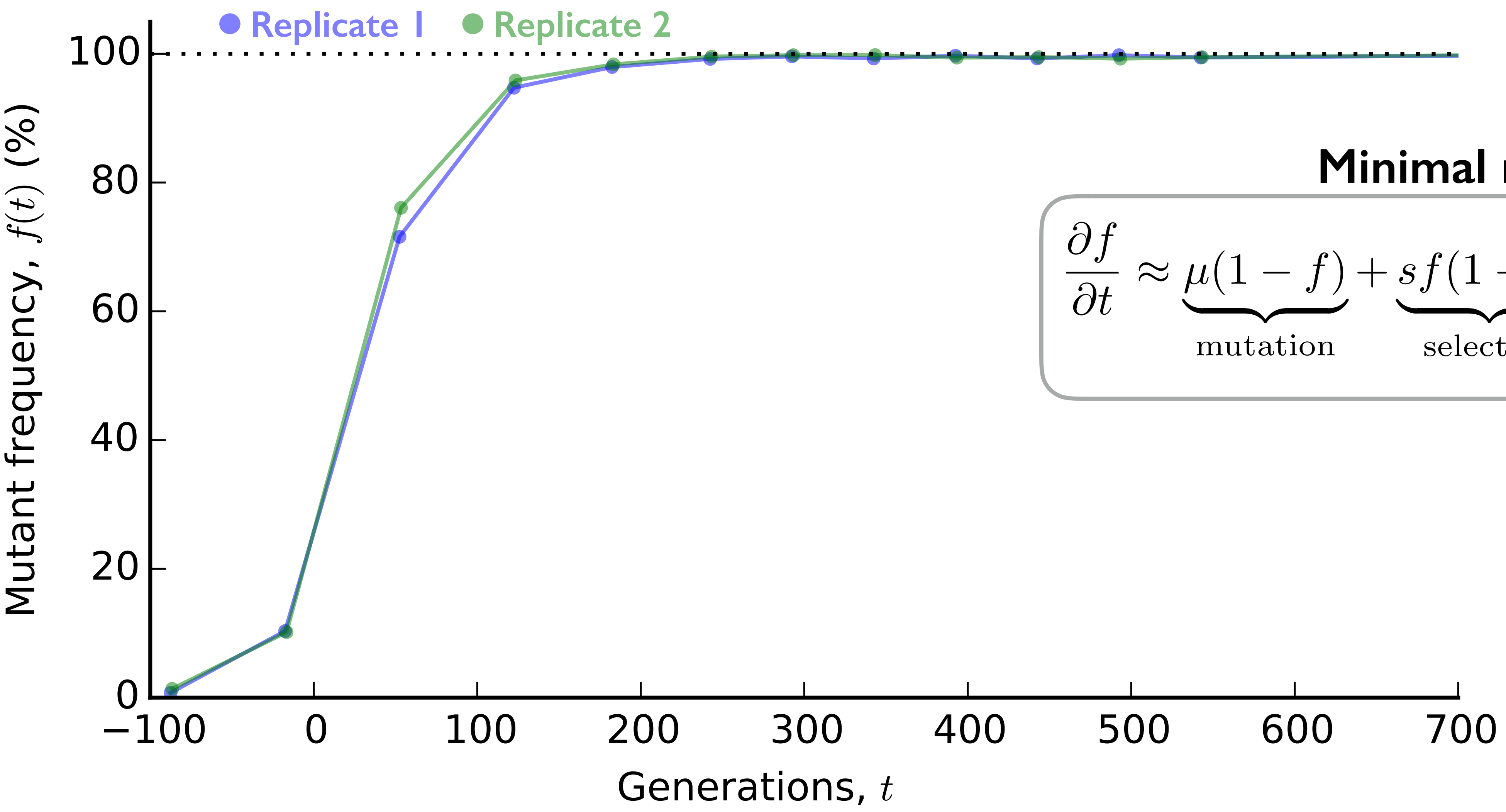

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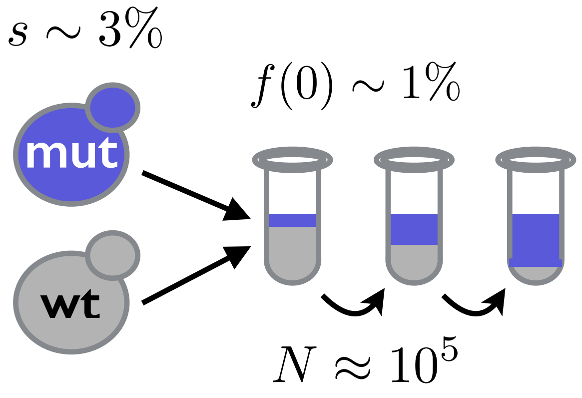

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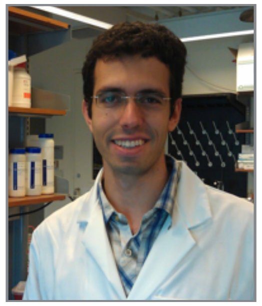

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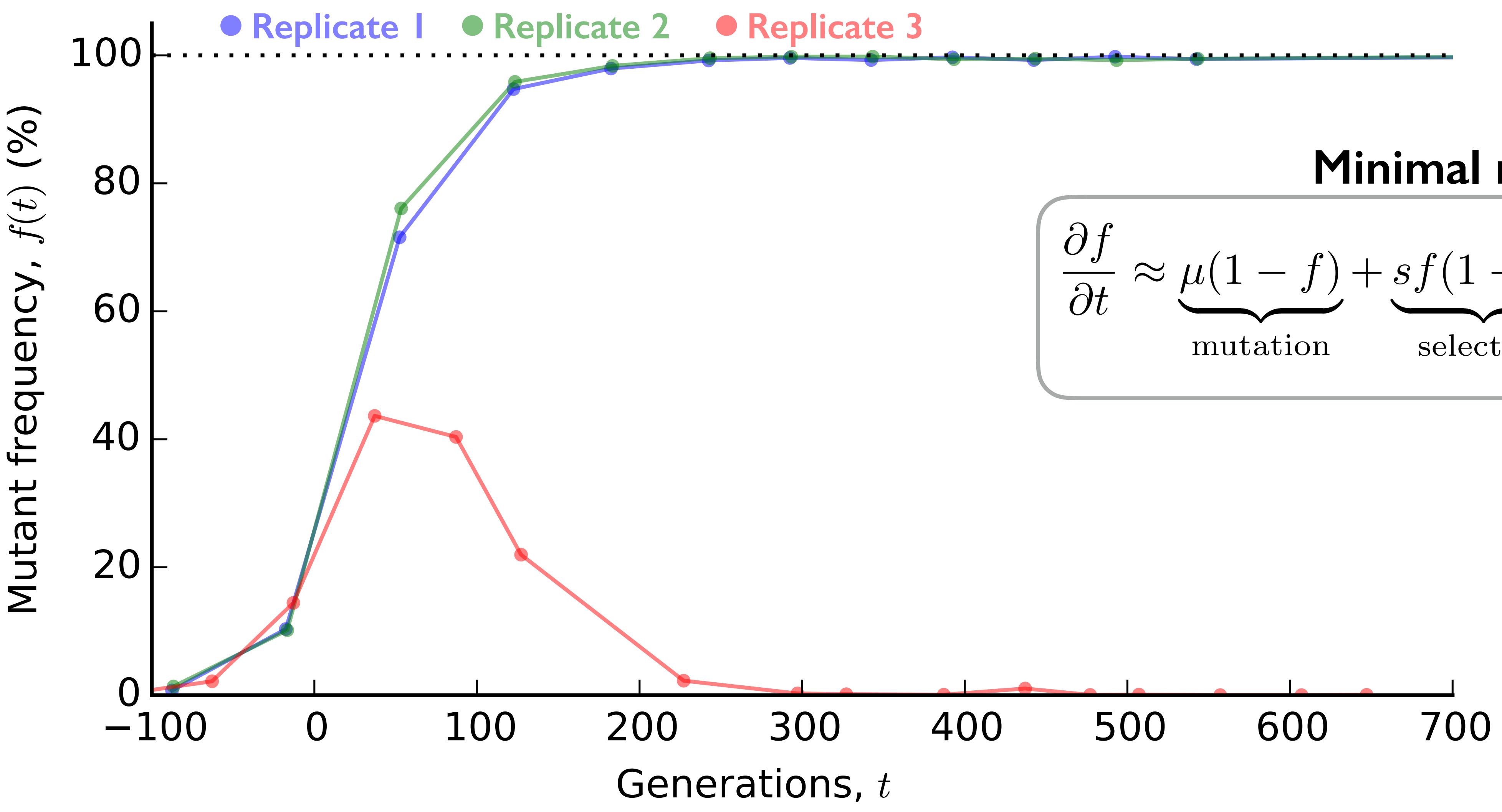

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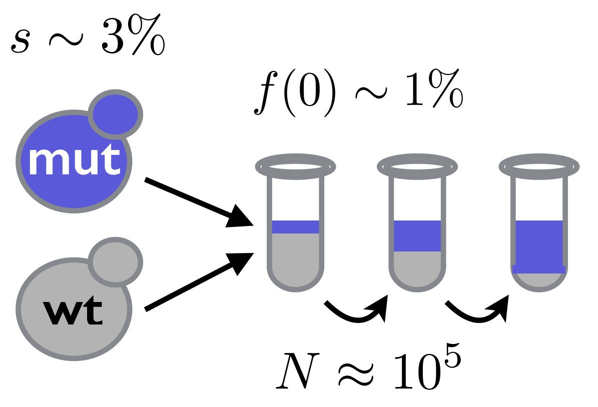

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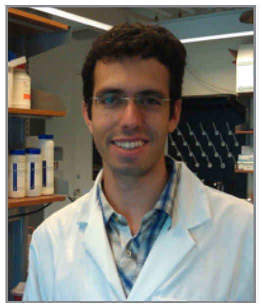

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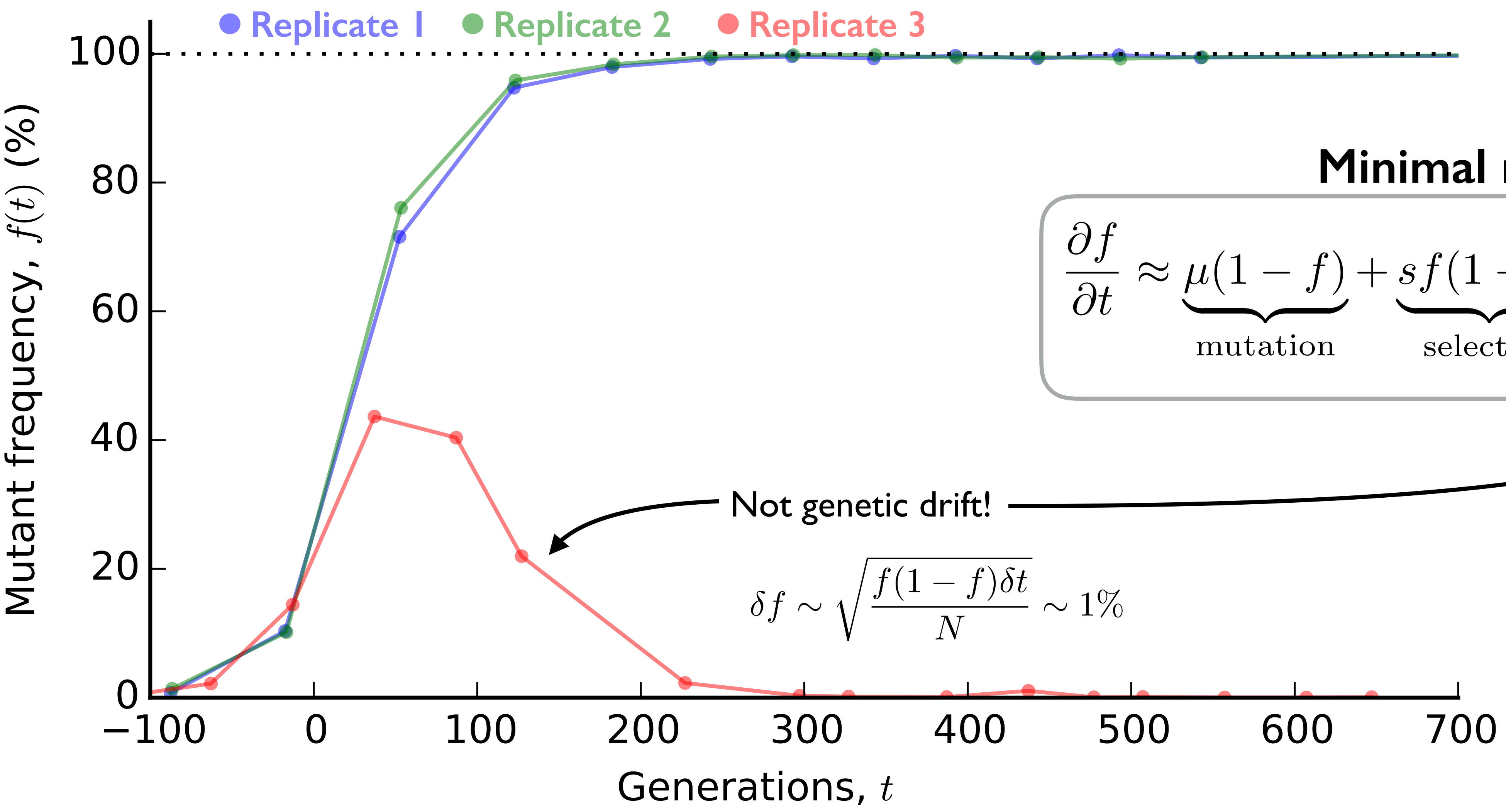

Not genetic drift!

$$\delta f \sim \sqrt{\frac{f(1-f)\delta t}{N}} \sim 1\%$$

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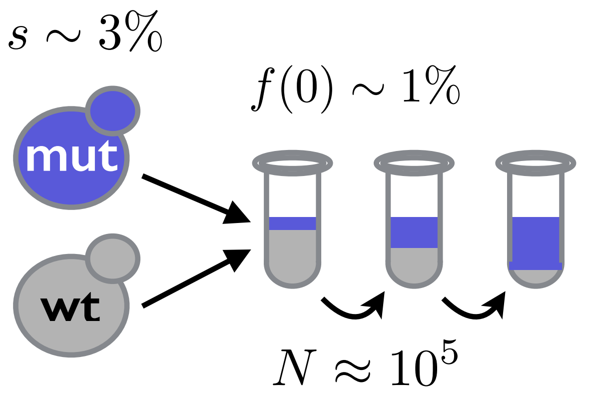

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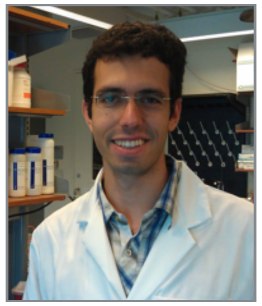

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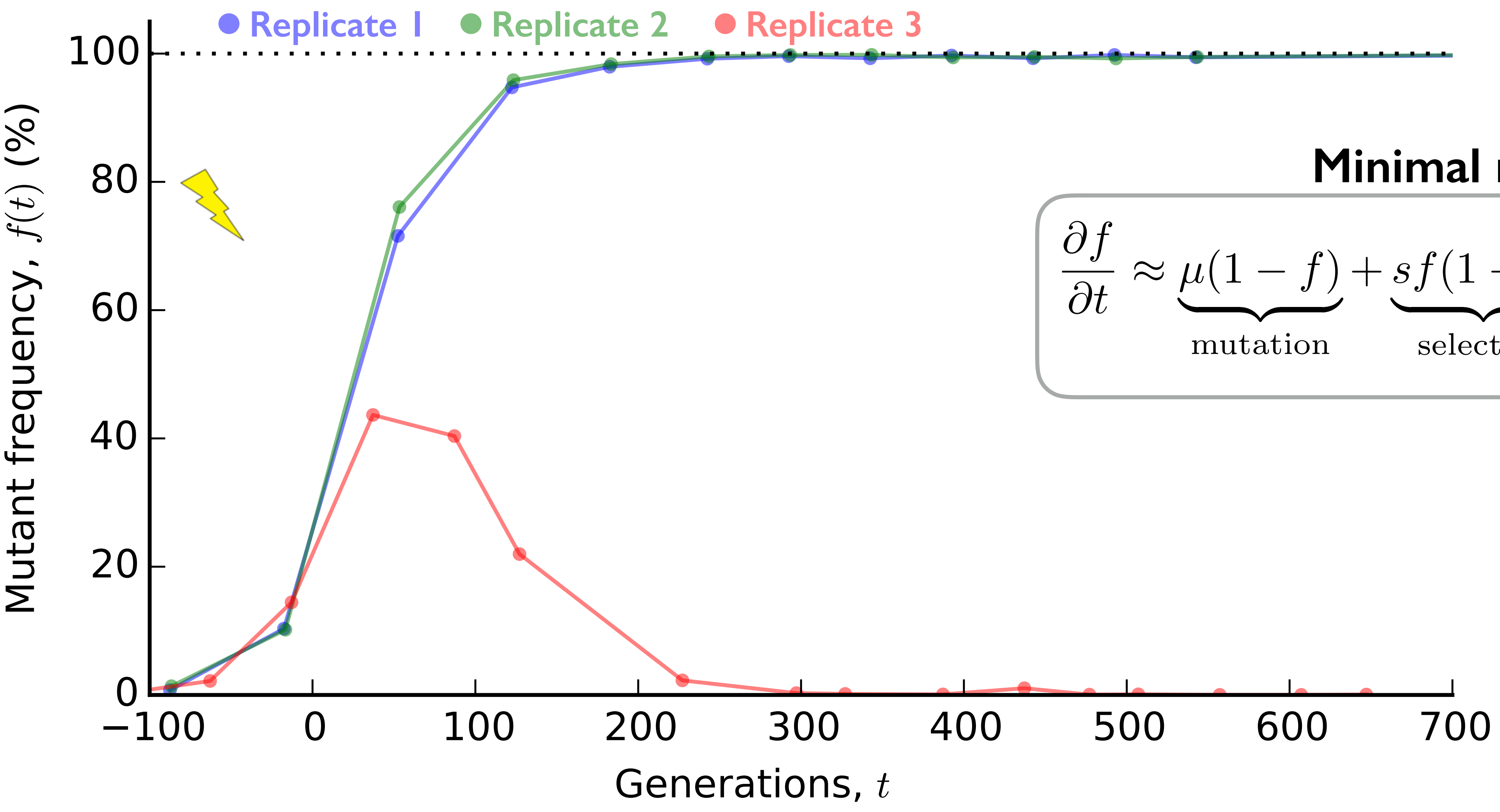

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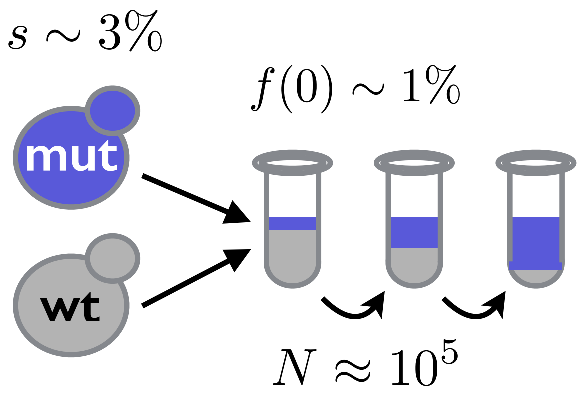

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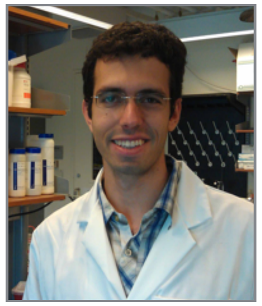

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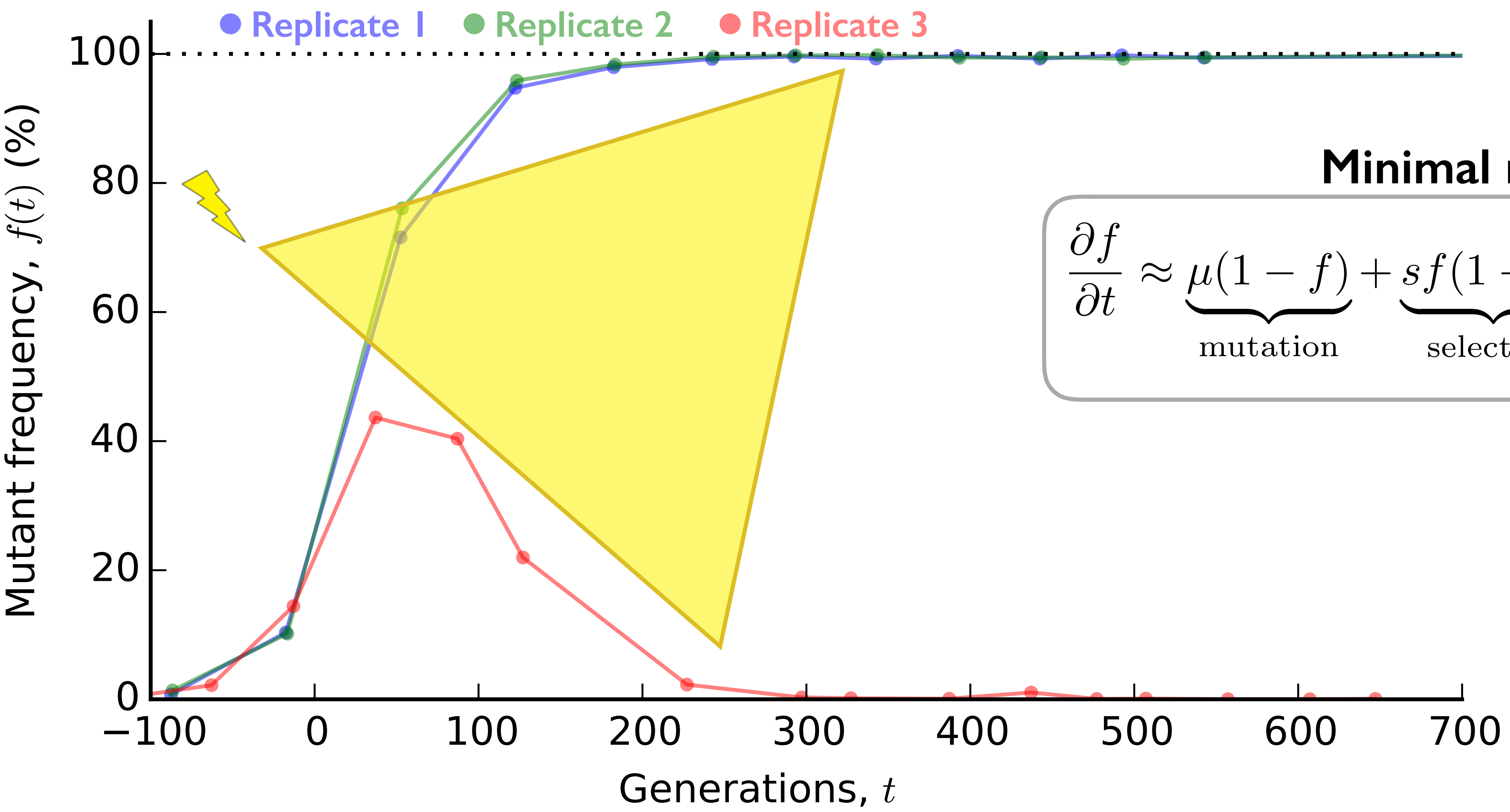

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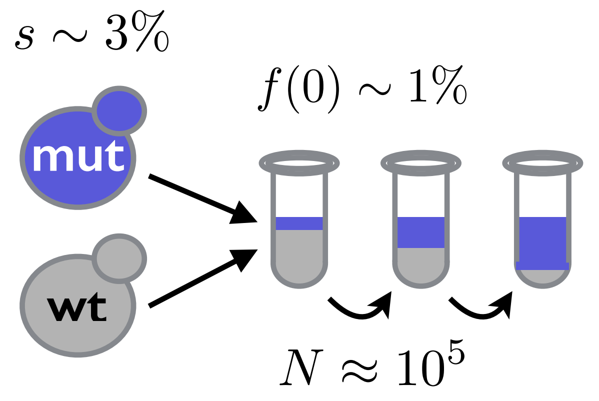

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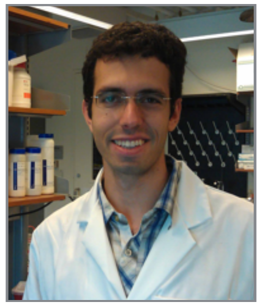

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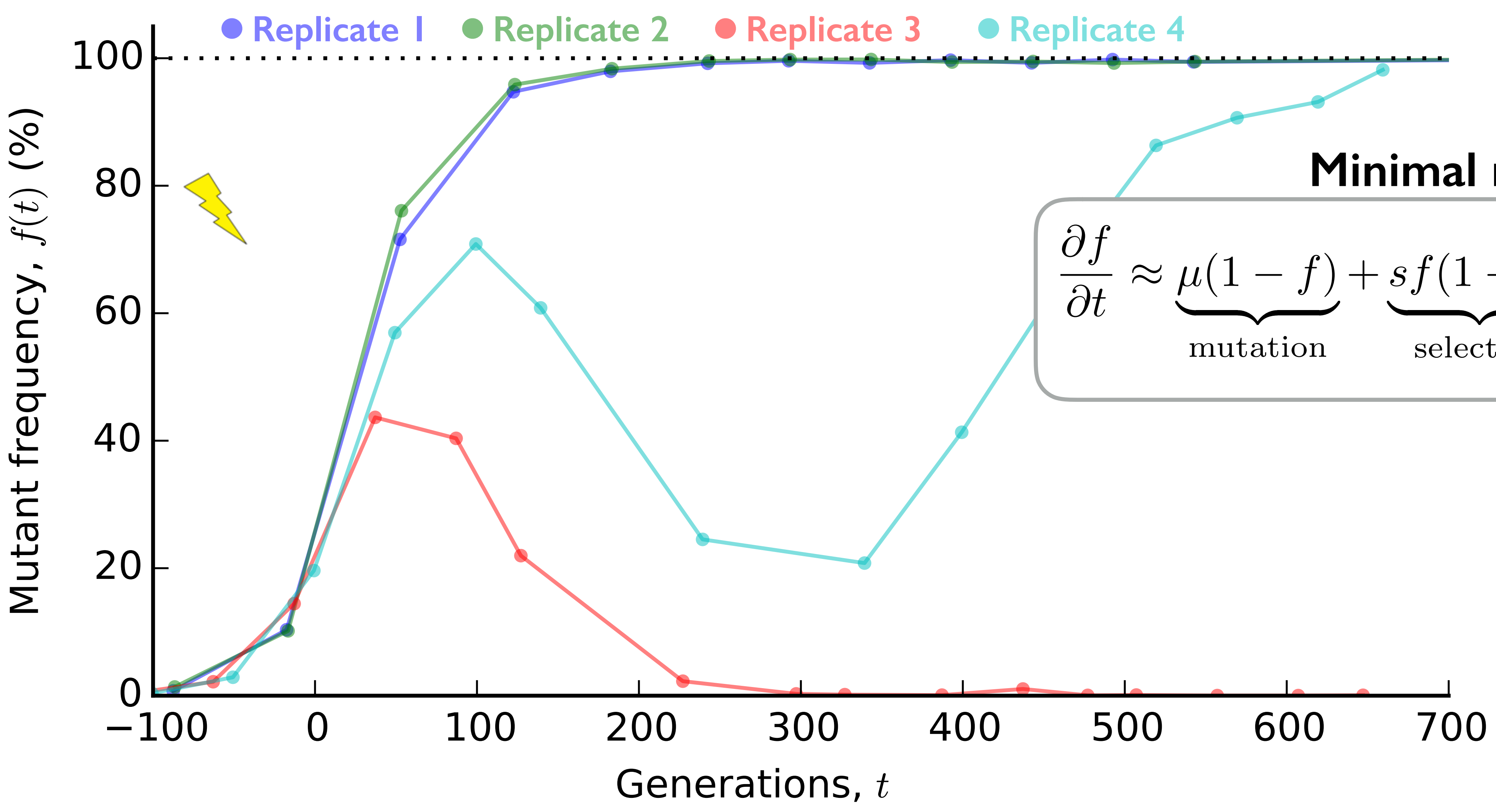

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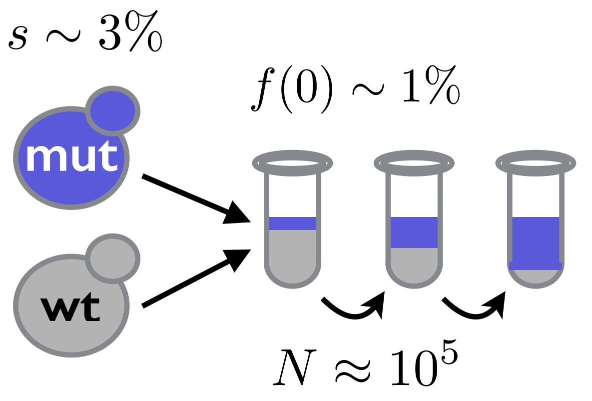

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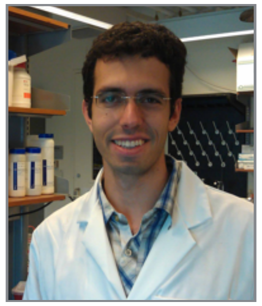

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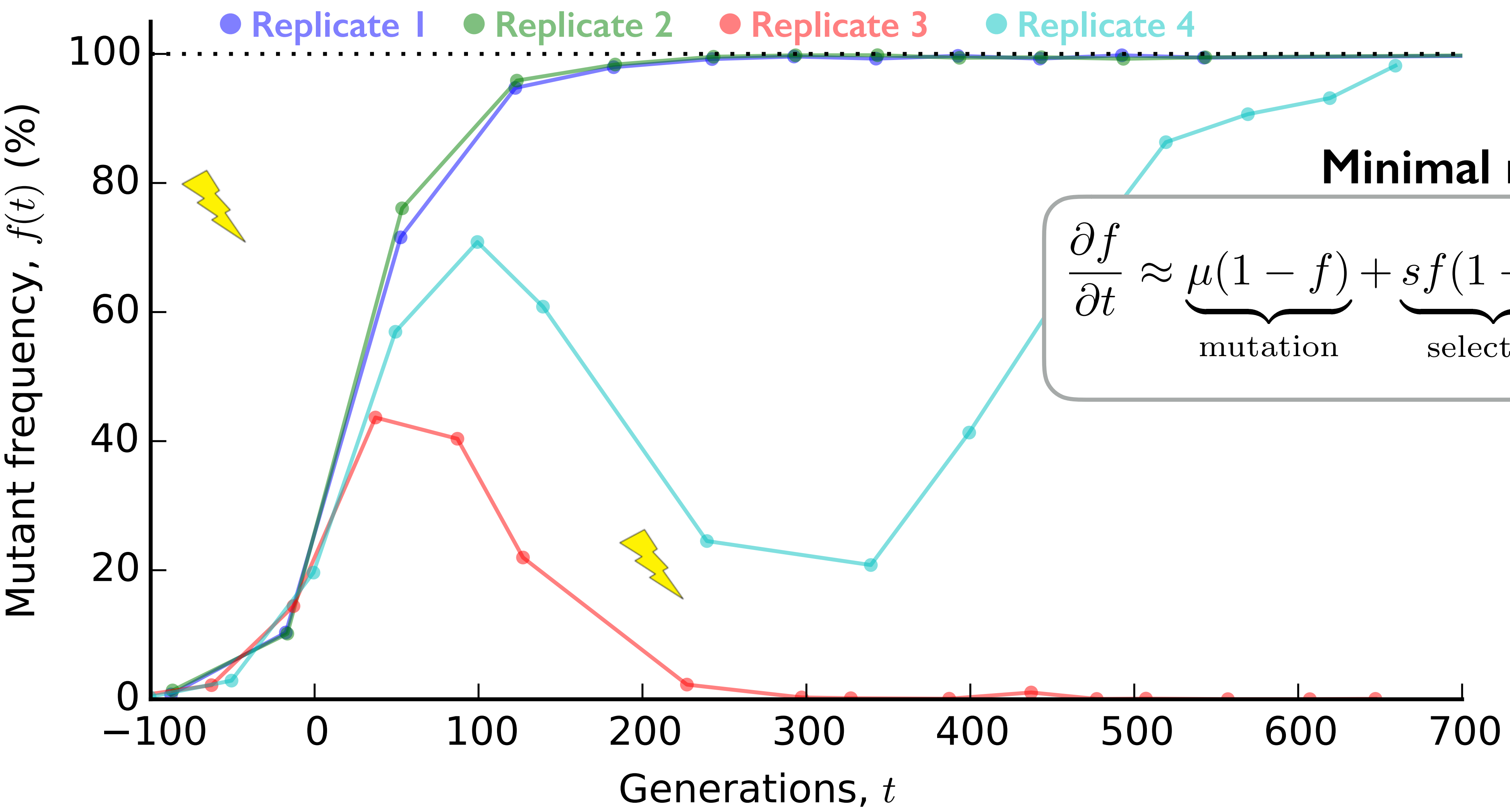

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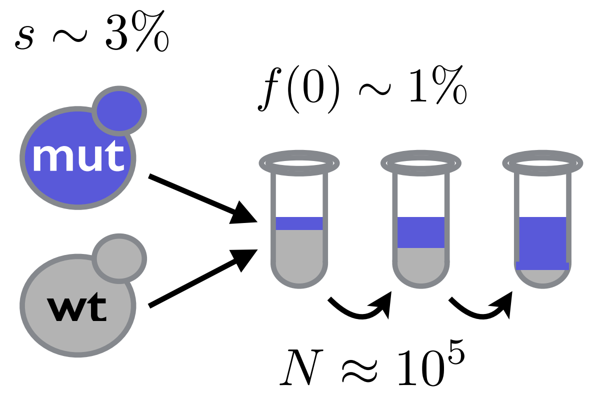

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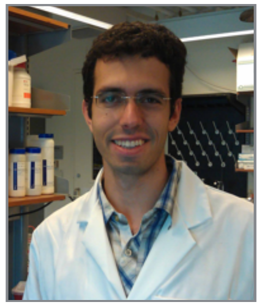

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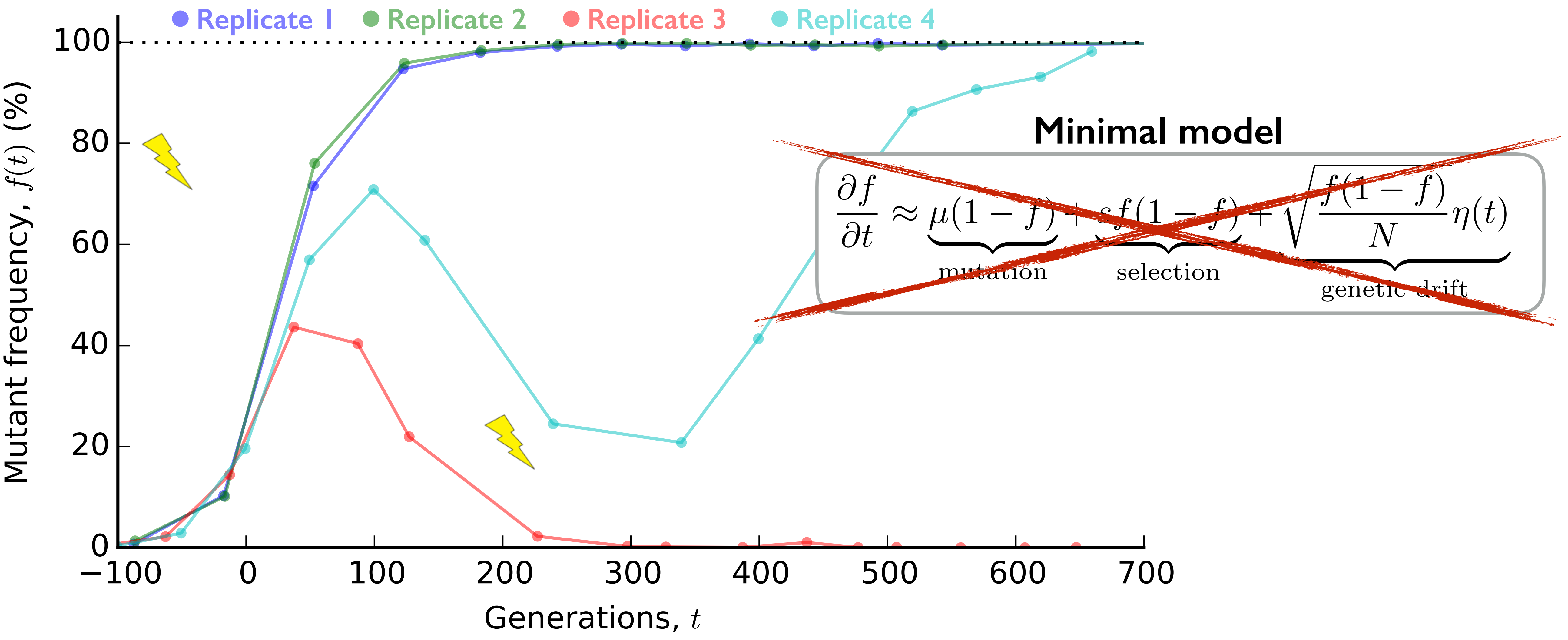

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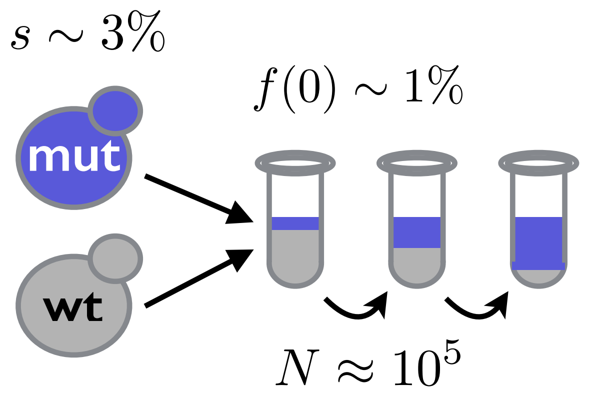

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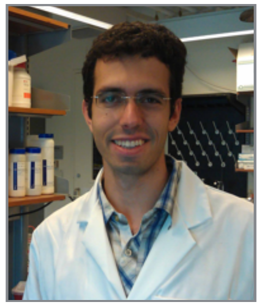

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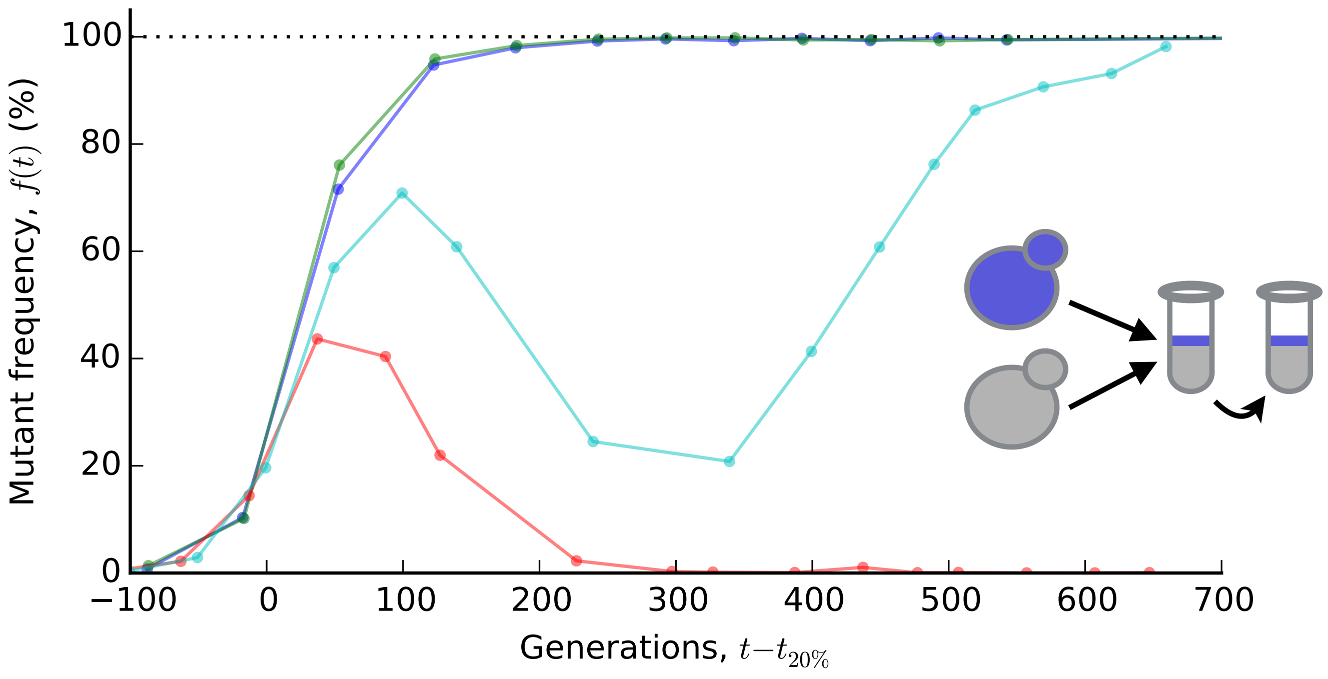
Key observations from laboratory evolution experiments



1. *Large microbial populations can adapt* ***extremely*** *rapidly*

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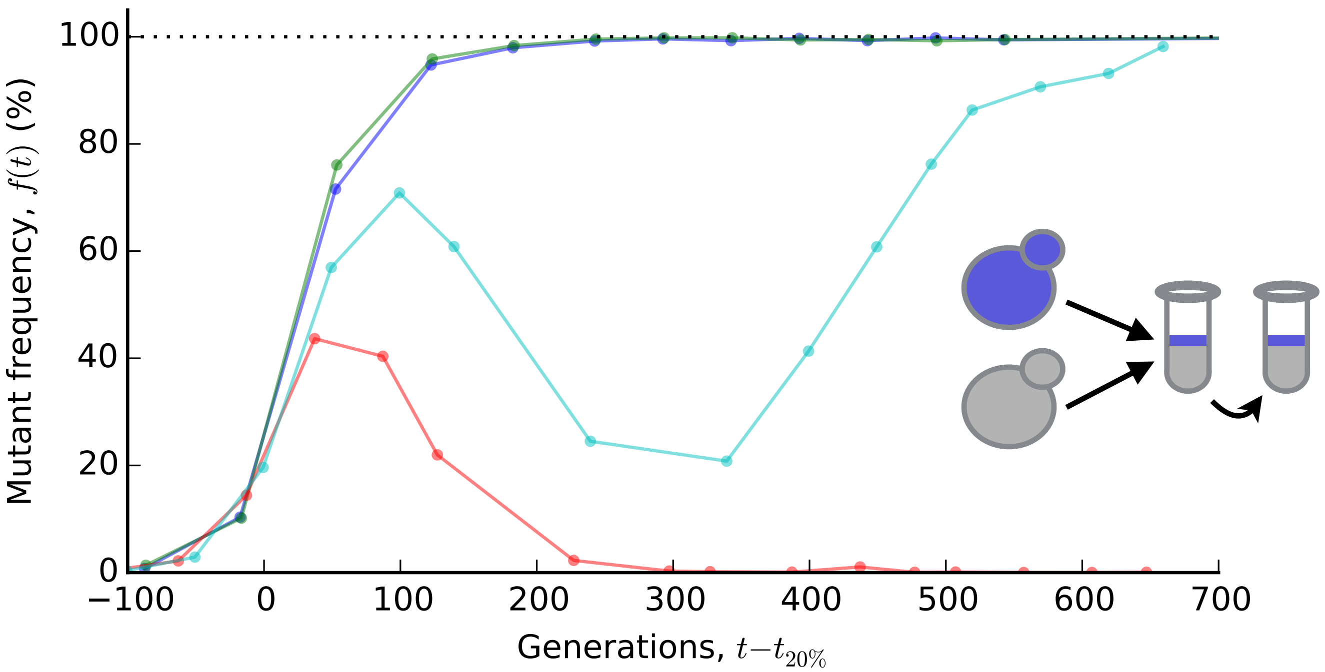

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↓

2. *Must account for* ***combinations*** *of mutations on same genome*

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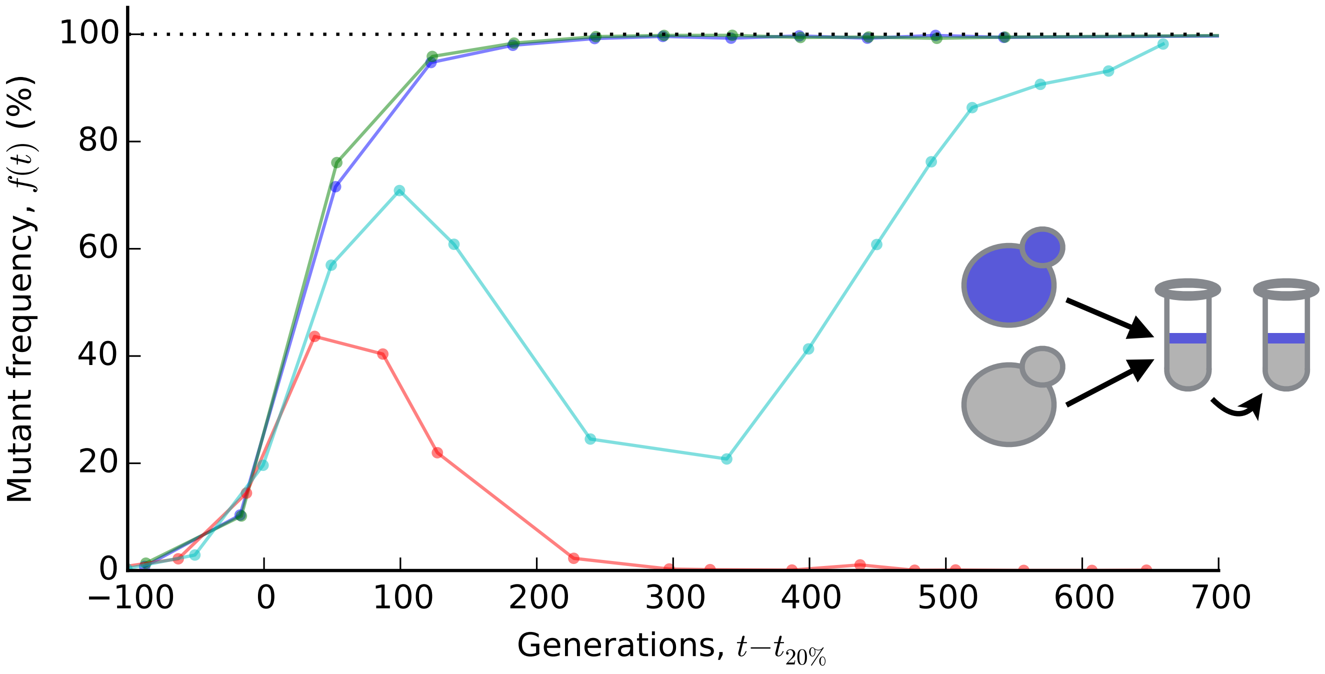

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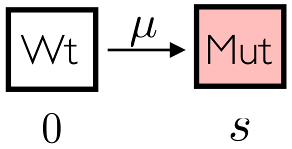
"genetic linkage"

Why does genetic linkage make this a hard problem?

Before:



(2 states)

Frequency of ***mutant***:

$$\frac{\partial f}{\partial t} = sf(1-f) + \ldots$$

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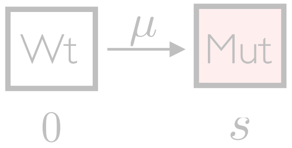

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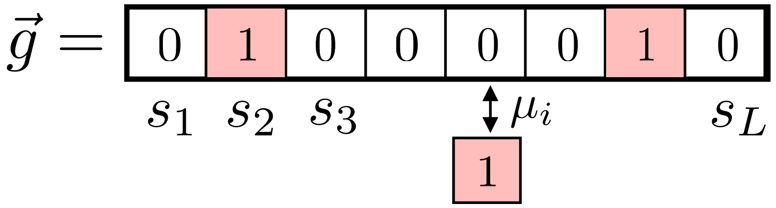
Linkage: *model full* genome (* 2^L *states)*



Frequencies of ***genotypes***:

$$\frac{\partial f(\vec{g})}{\partial t} = [X(\vec{g}) - \sum_{\vec{g}'} X(\vec{g}')f(\vec{g}')]f(\vec{g}) + \ldots$$

Why does genetic linkage make this a hard problem?

Before: $\underset{0}{\boxed{\text{Wt}}} \xrightarrow{\mu} \underset{s}{\boxed{\text{Mut}}}$ *(2 states)*

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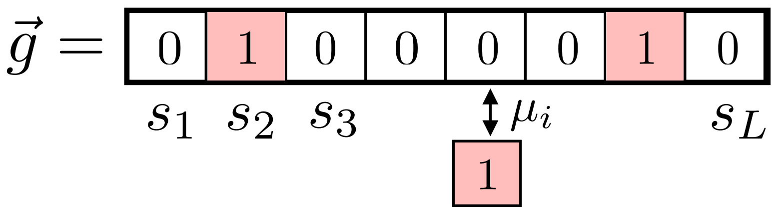

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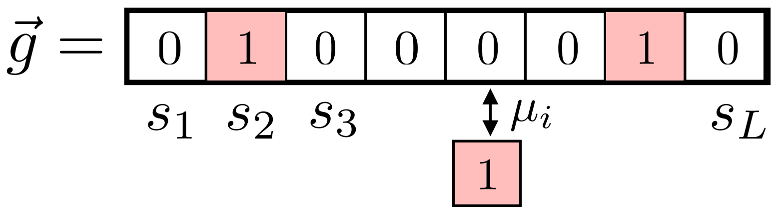

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$0 \qquad s$

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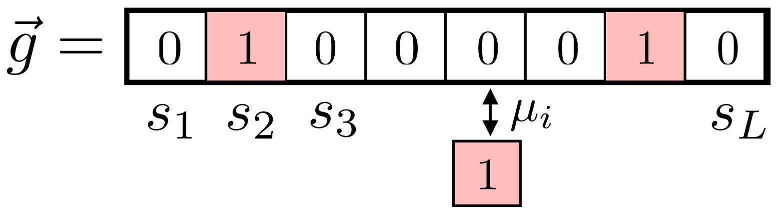
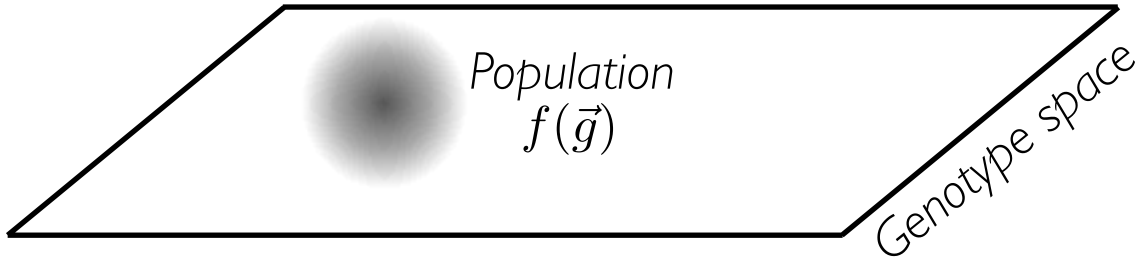


Frequencies of ***genotypes***:

$$\frac{\partial f(\vec{g})}{\partial t} = [X(\vec{g}) - \sum_{\vec{g}'} X(\vec{g}')f(\vec{g}')]f(\vec{g}) + \ldots$$

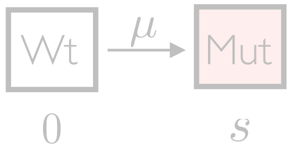
Fitness of ***genotype***: $X(\vec{g}) \approx \sum_{i=1}^{L} s_i g_i + \text{epistasis}$

1. ***Population size (N) is large, but # genotypes vastly larger!***



→ ***always "out-of-equilibrium"***

Why does genetic linkage make this a hard problem?

Before: 

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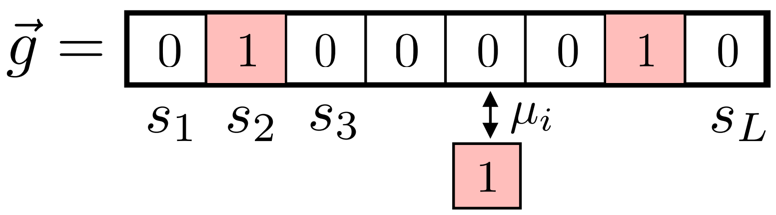

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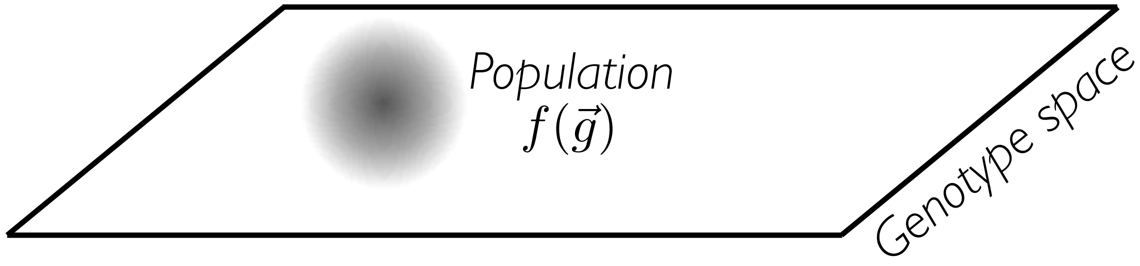

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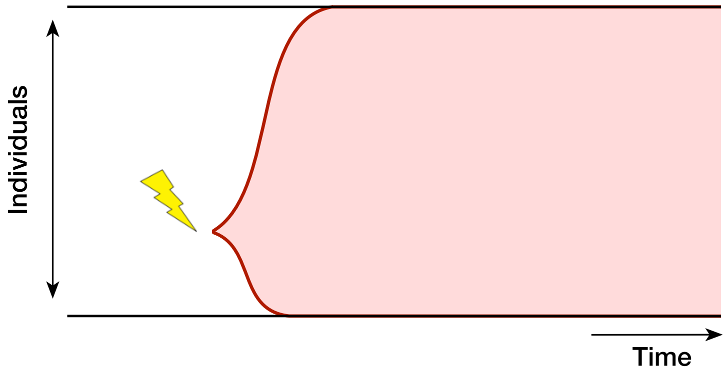
2. Individual mutations still take over!



→ ***noise matters @ pop'n level***

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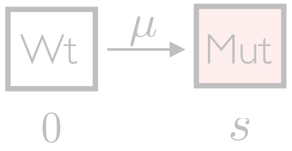

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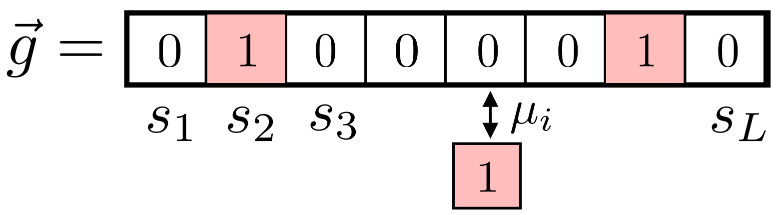

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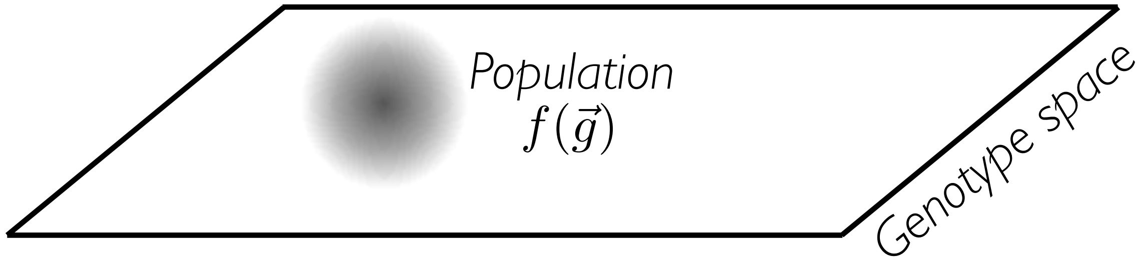

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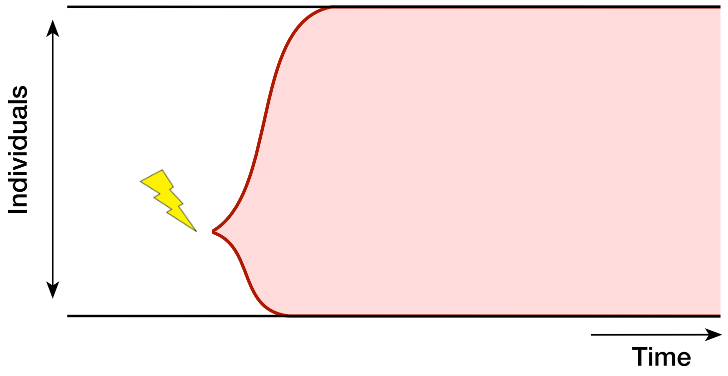
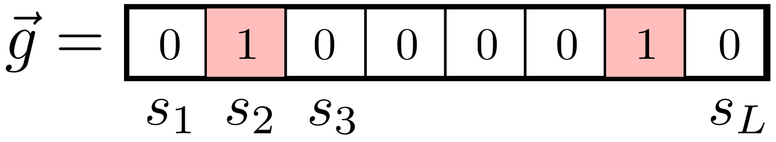


→ ***noise matters @ pop'n level***

---

3. Explosion of parameters!



→ ***which combinations matter? how might we measure them?***

How do we think about genetic linkage theoretically?

Good et al (2012); Good and Desai (2013; 2014; 2016)
see also Neher et al (2010); Hallatschek (2011); Fisher (2013)

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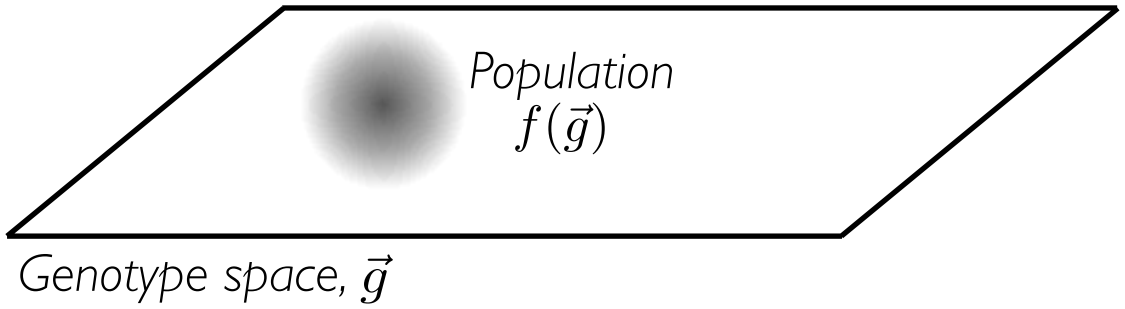

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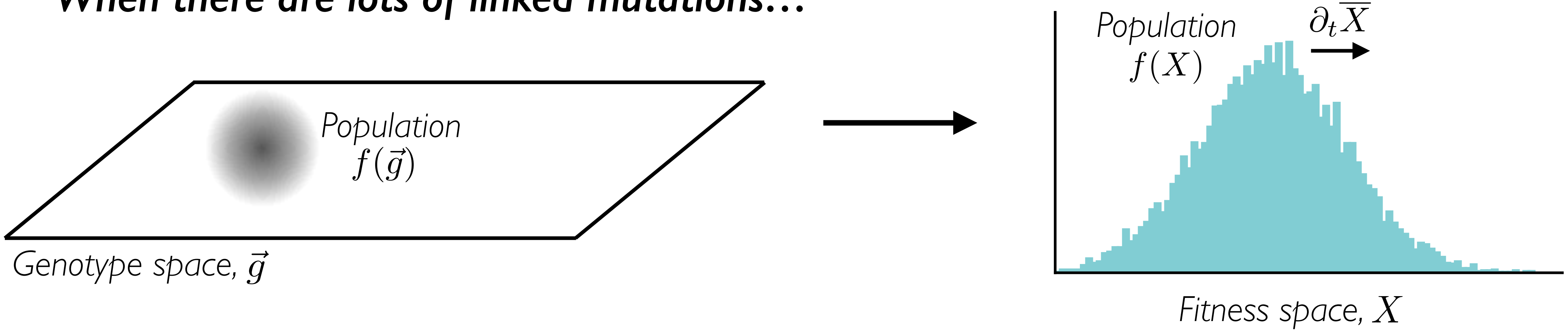

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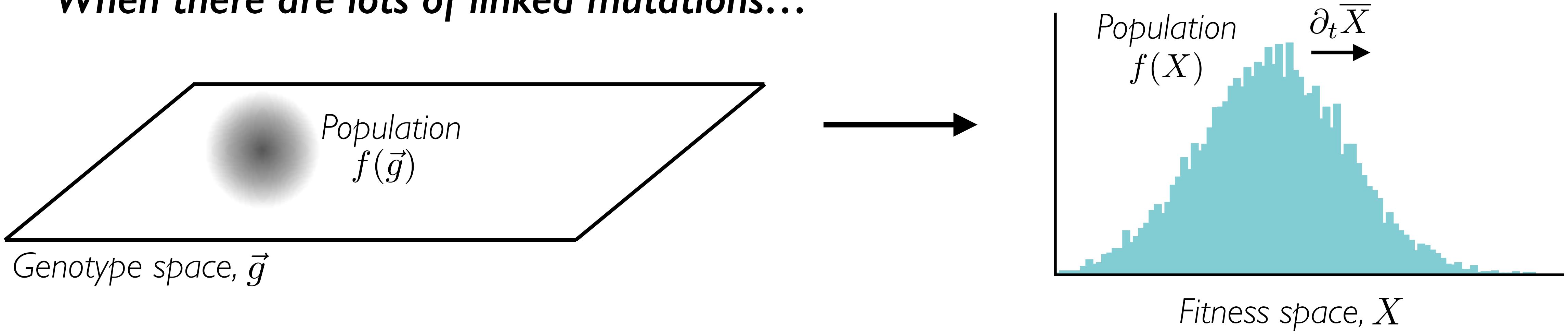

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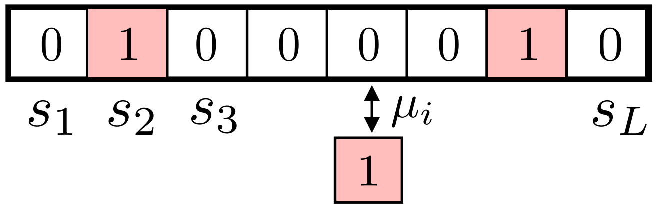

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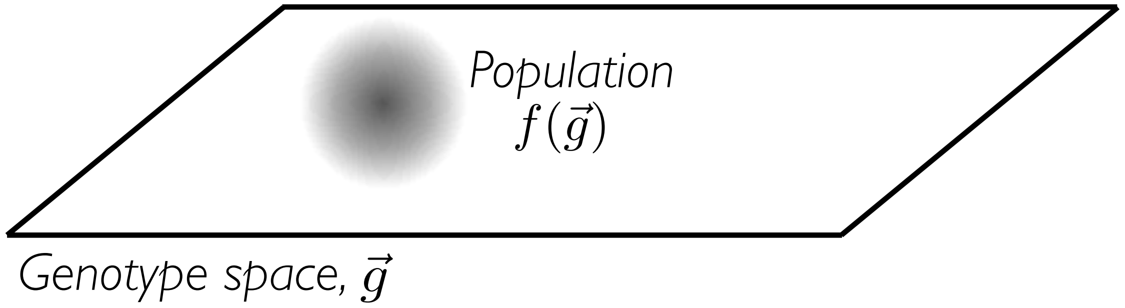

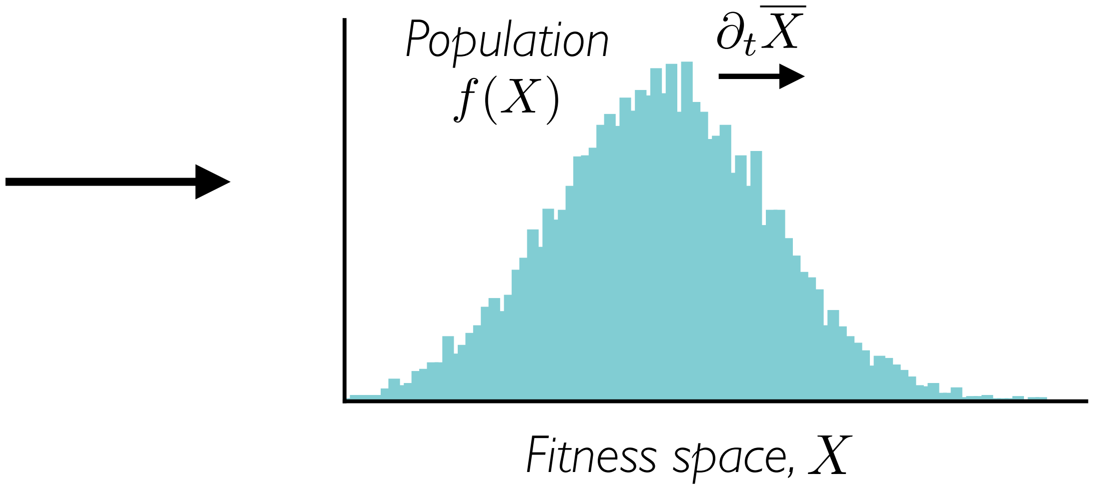

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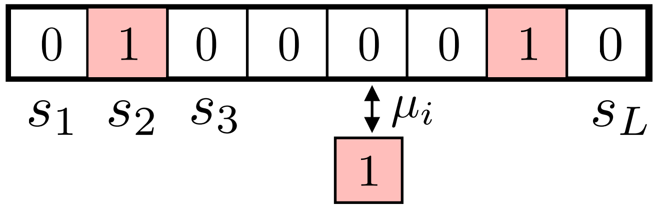
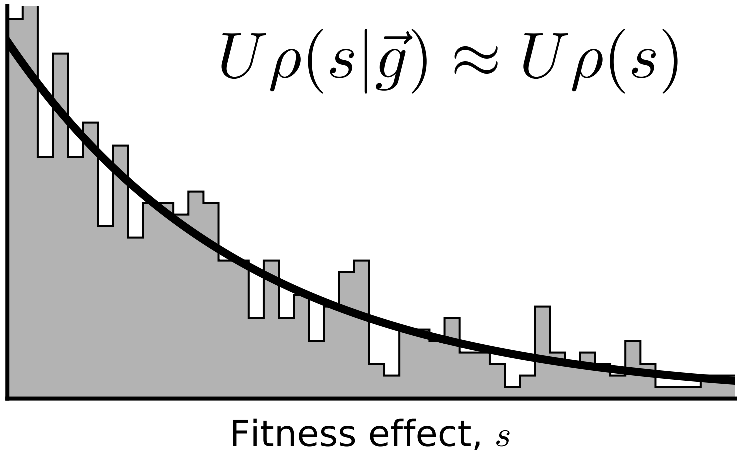


Now: $X \rightarrow X + s$

Statistical distribution of fitness effects (DFE),



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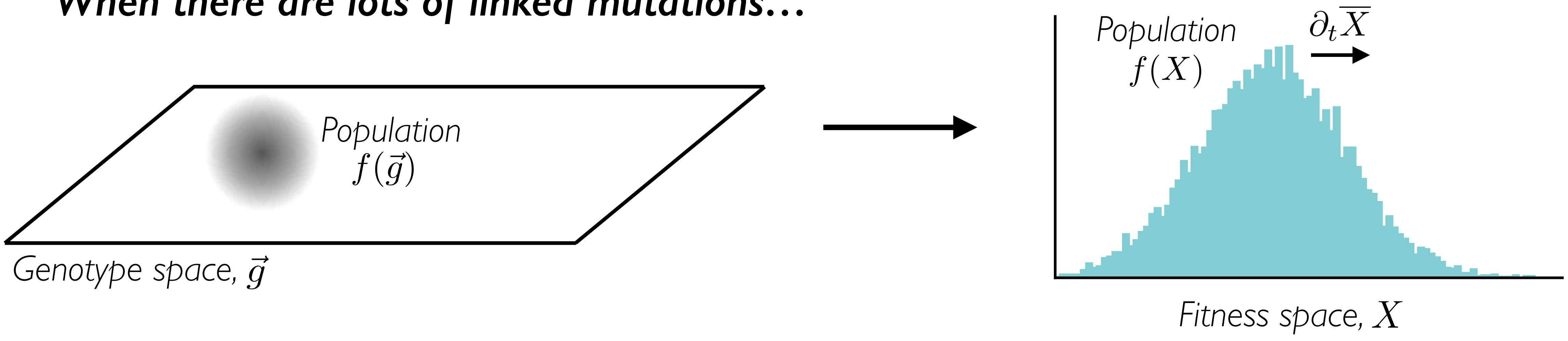

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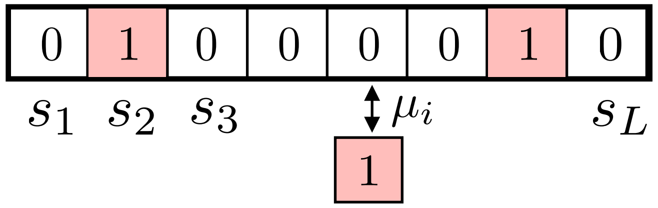

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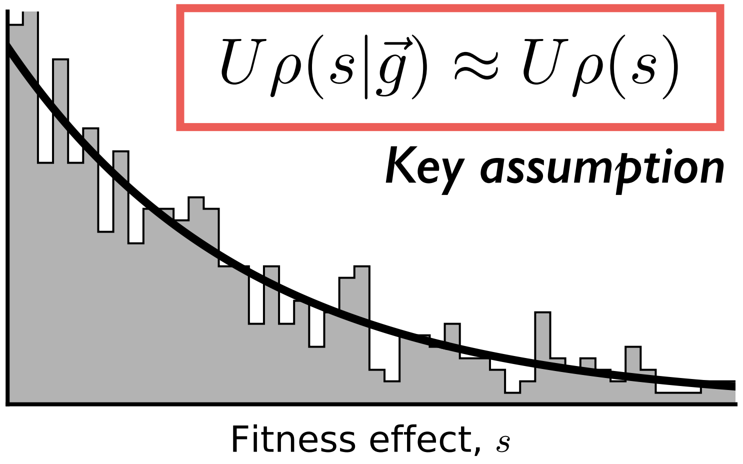

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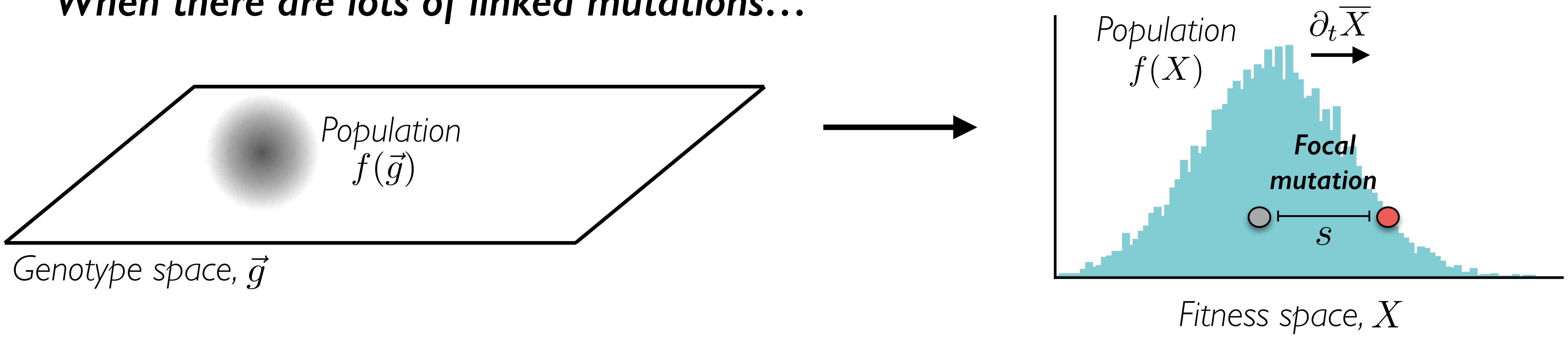

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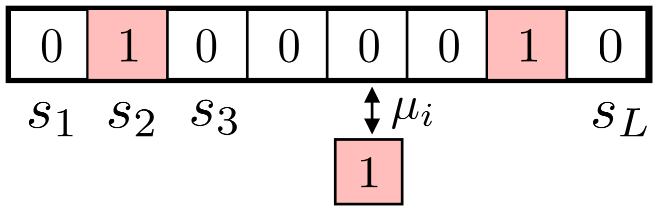

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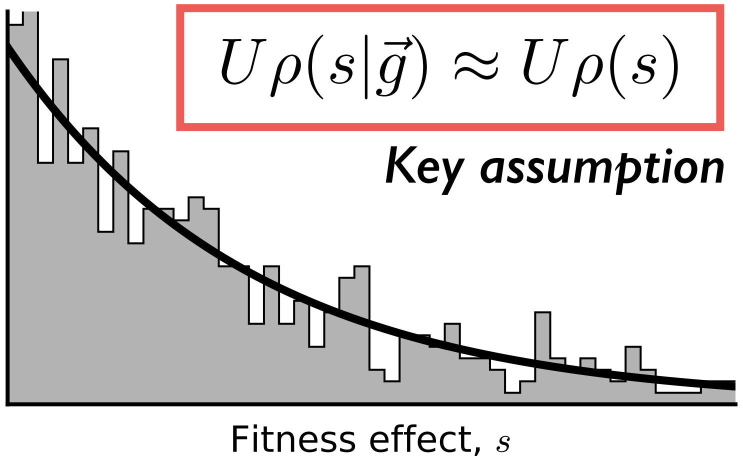

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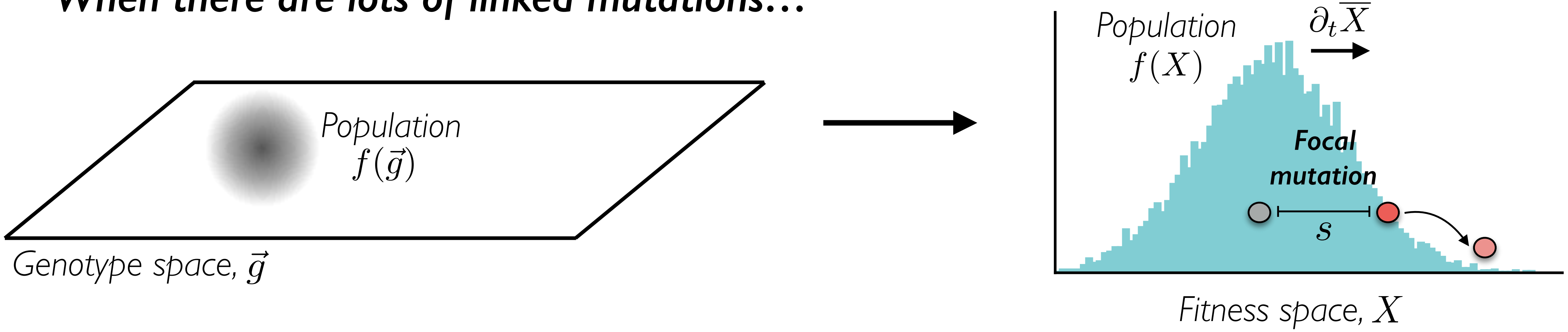

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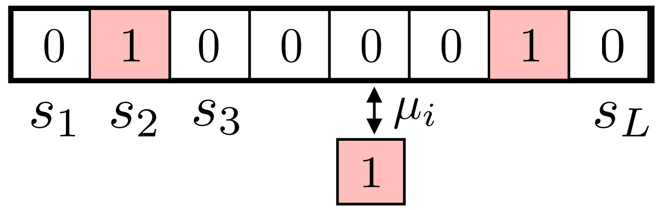

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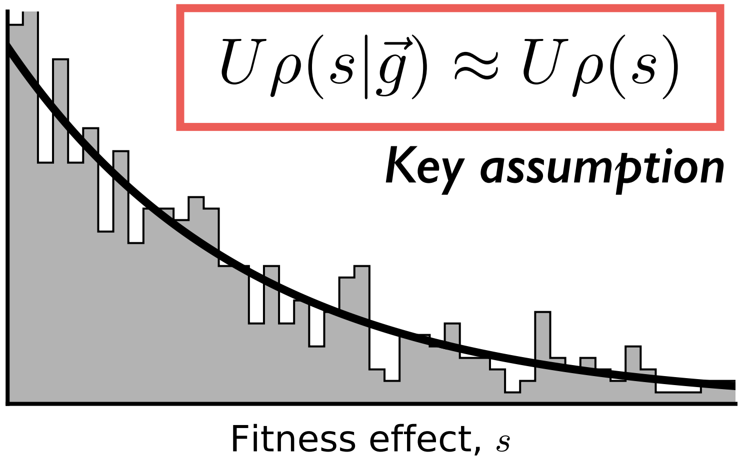
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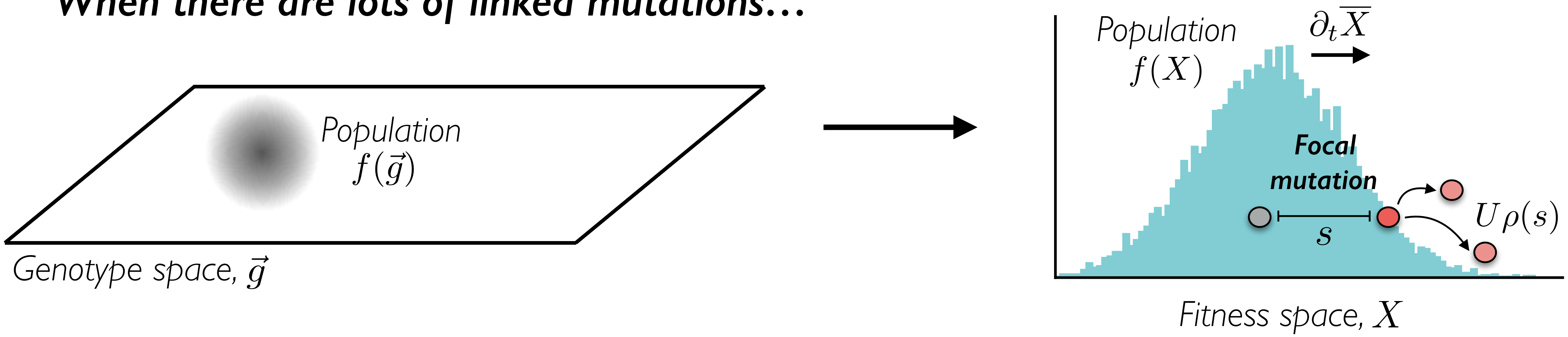

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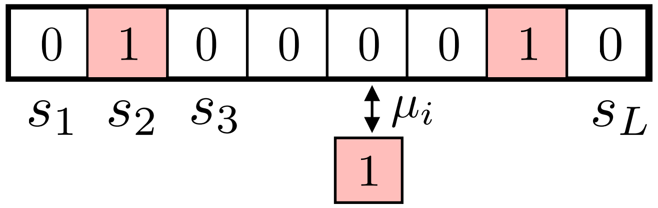

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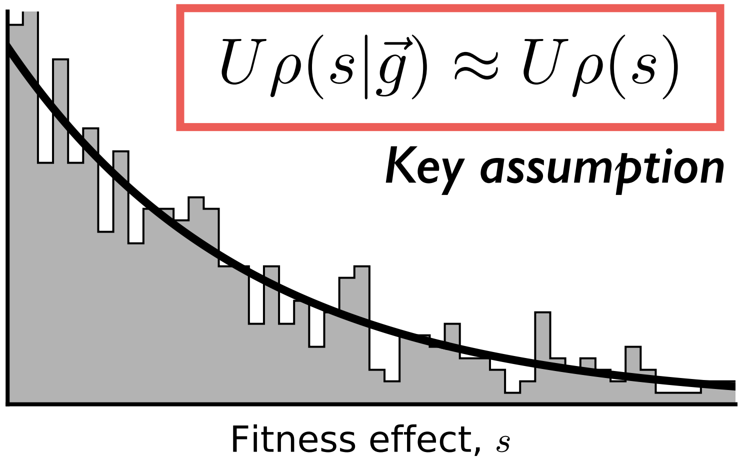

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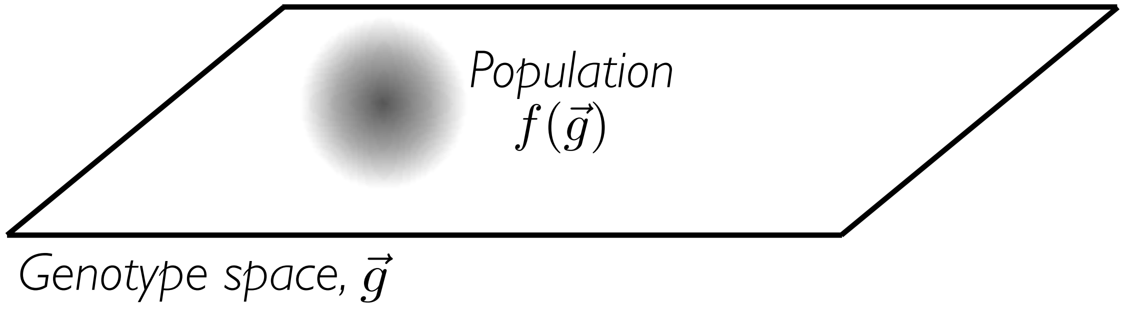

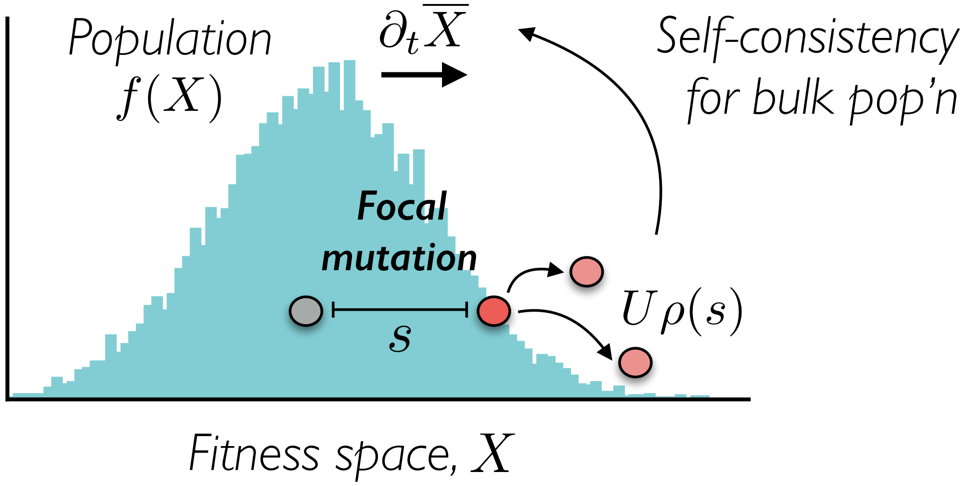

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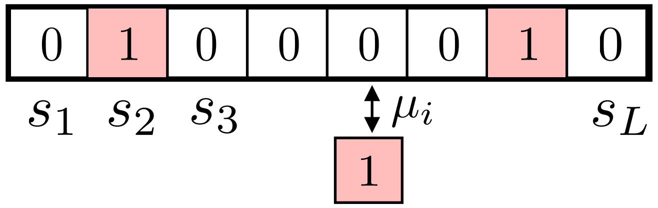

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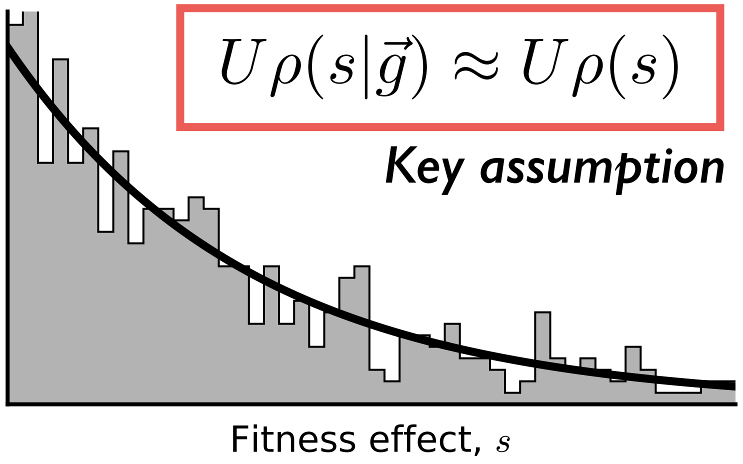

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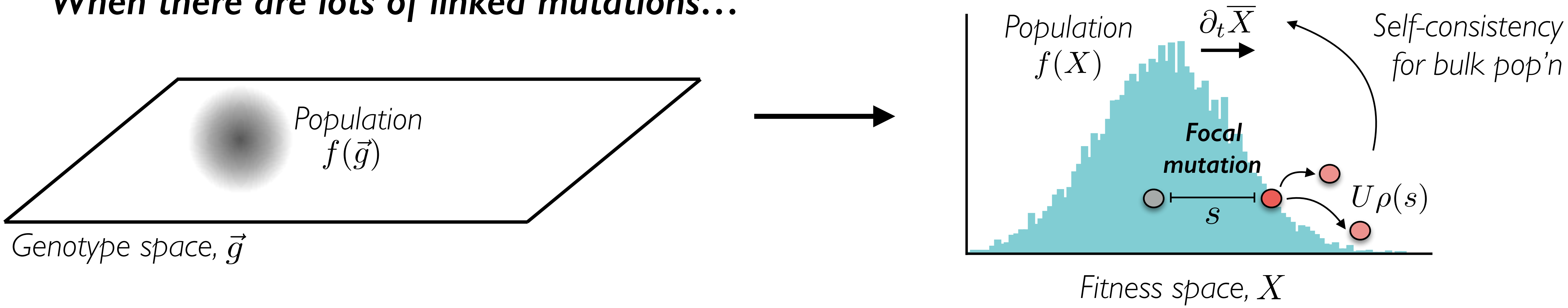

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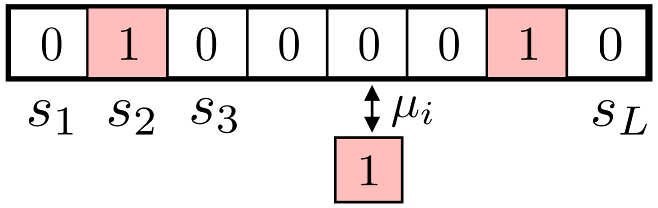

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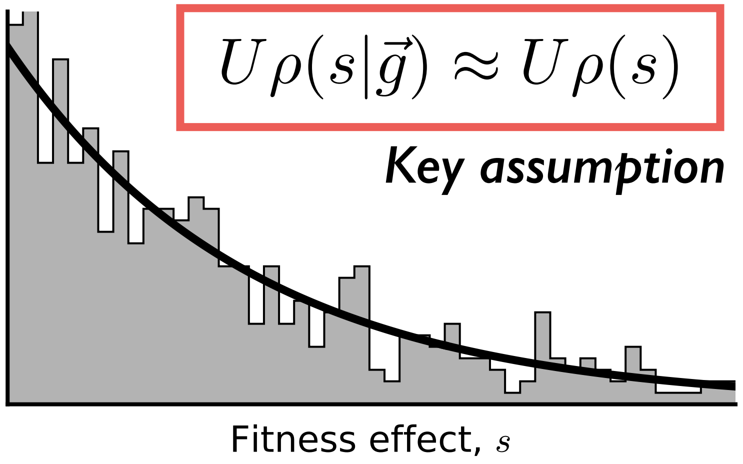

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Predictions for

1. *Common* observables in DNA sequence data (e.g., substitution rates, genetic diversity)*

2. *Dependence on underlying parameters,* $U\rho(s)$

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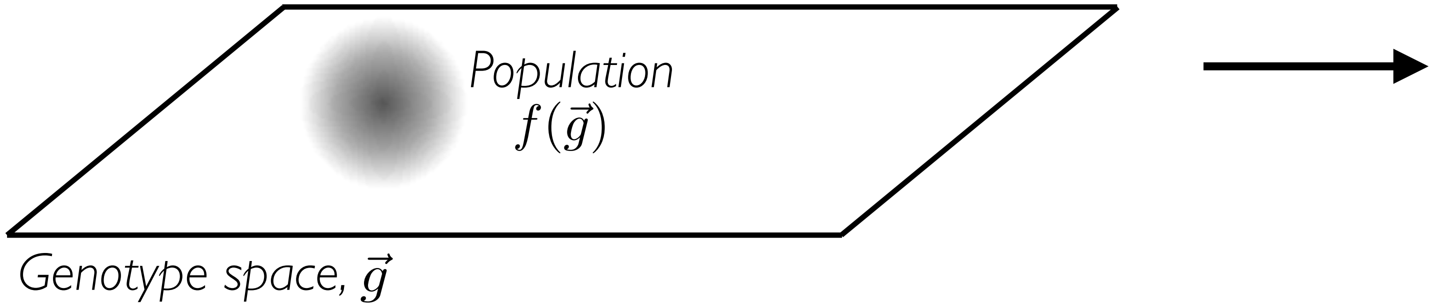

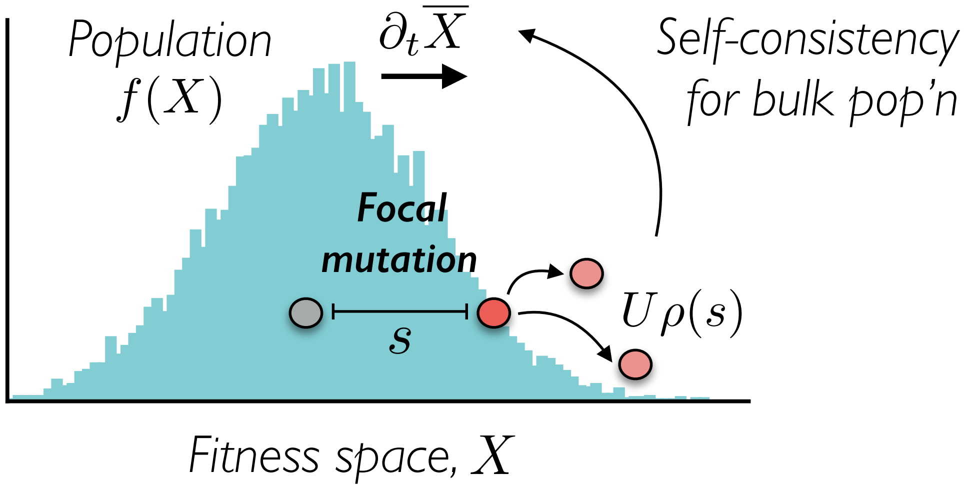

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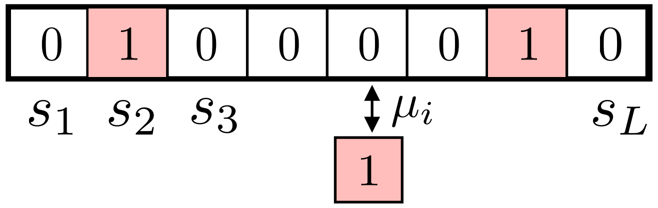

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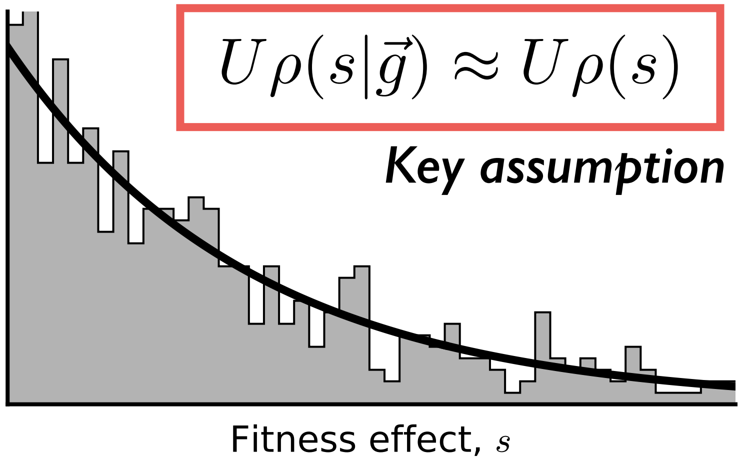

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$$U\rho(s) \approx \underset{(U_b^*,\, s_b^*)}{\text{strongly beneficial}} + \underset{(U_d^*,\, -s_d^*)}{\text{strongly deleterious}} + \underset{(U_n^*,\, s_n^*)}{\text{nearly neutral}}$$

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Key insights from theory

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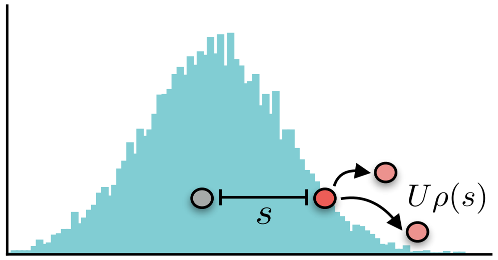
fates of mutations are strongly influenced by ***dynamical processes***, in addition to their ***inherent biological effects***.



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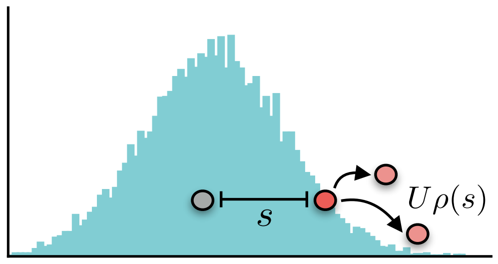

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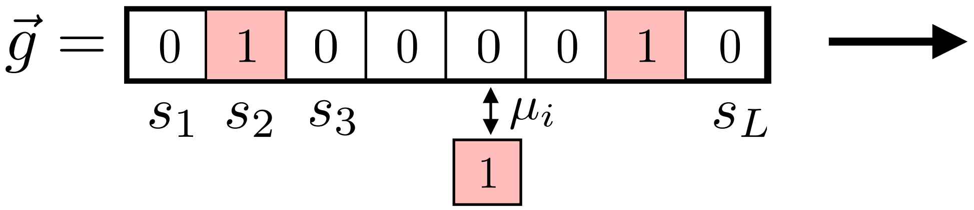

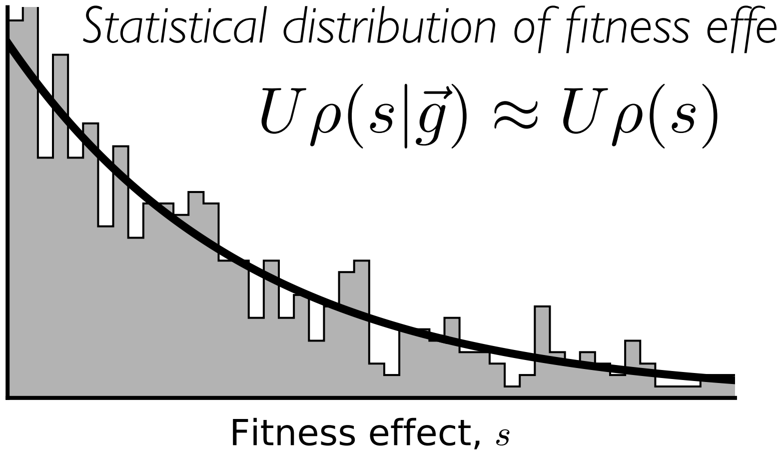

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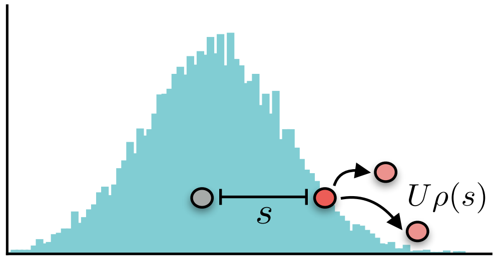

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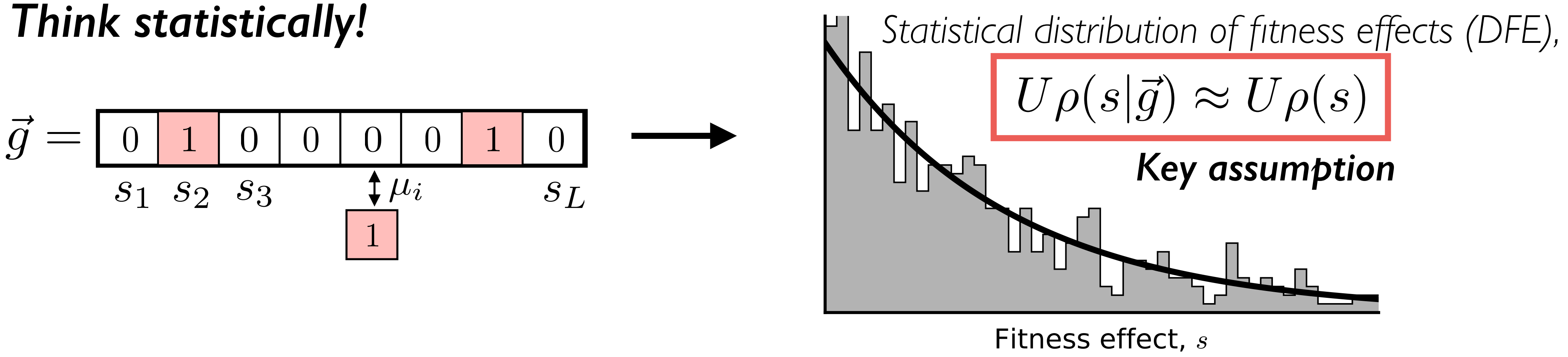

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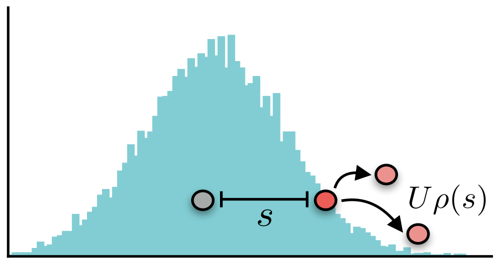

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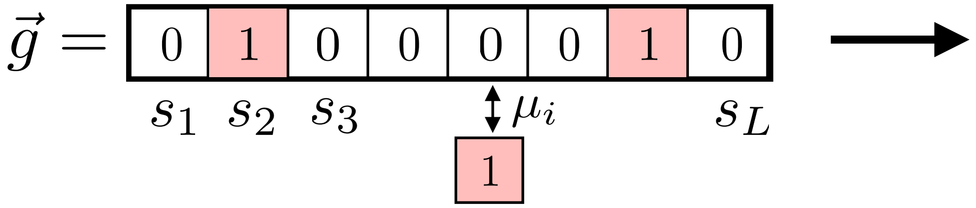

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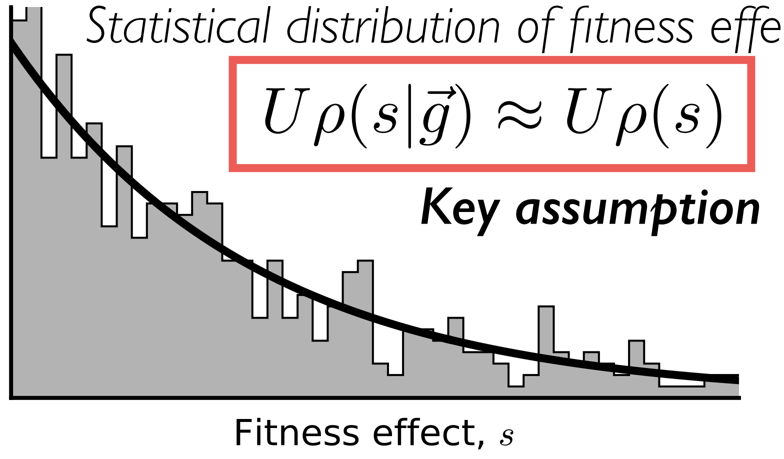
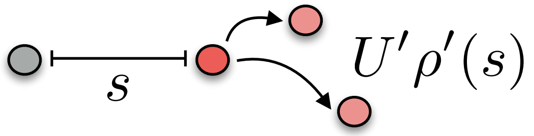


Future direction:

"Macroscopic" epistasis ⟶ *mutations that change rates & fitness effects of other mutations*



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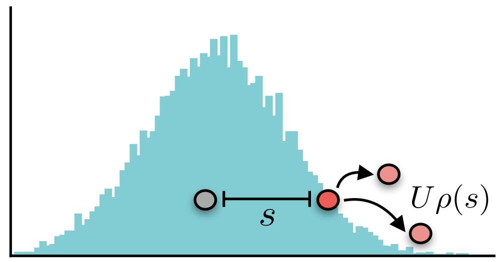

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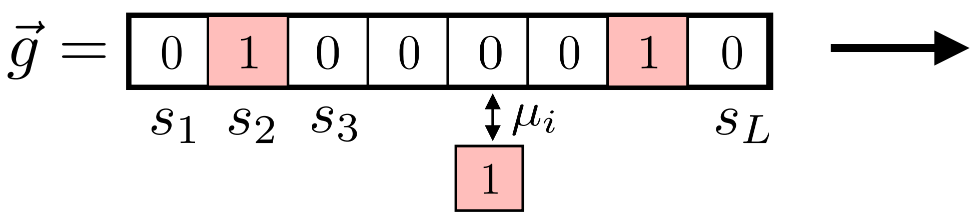
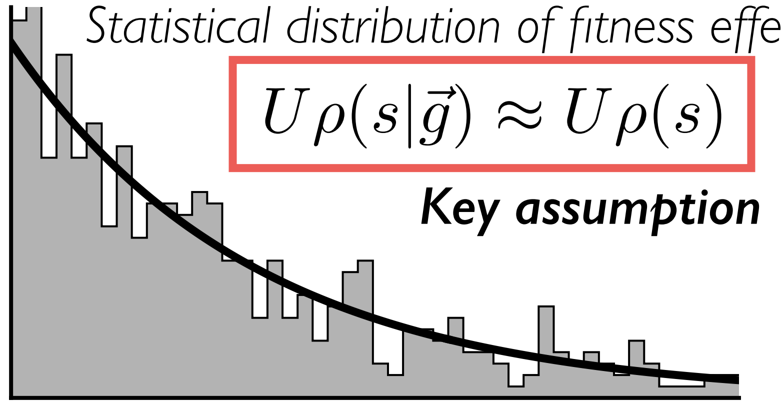




Statistical distribution of fitness effects (DFE),

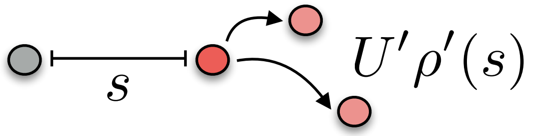
$$\boxed{U\rho(s|\vec{g}) \approx U\rho(s)}$$

Key assumption

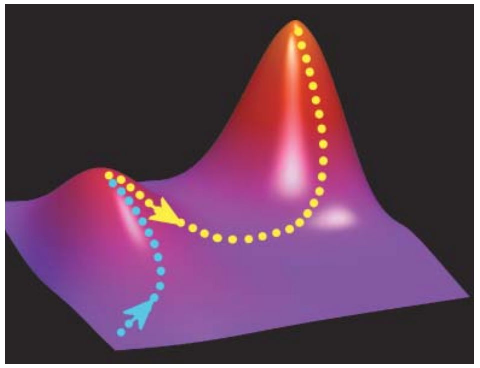
Fitness effect, s

Future direction:

"Macroscopic" epistasis → *mutations that change rates & fitness effects of other mutations*



Questions: *when is invasion* $\neq$ *optimal for population?*
How far can populations "see" in fitness landscape?

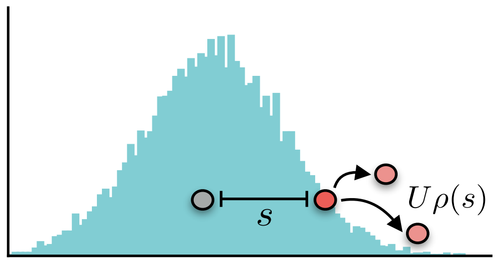


Poelwijk, Kiviet* et al (2007)*

Key insights from theory

1. In rapidly evolving populations…

fates of mutations are strongly influenced by ***dynamical processes***, in addition to their ***inherent biological effects***.



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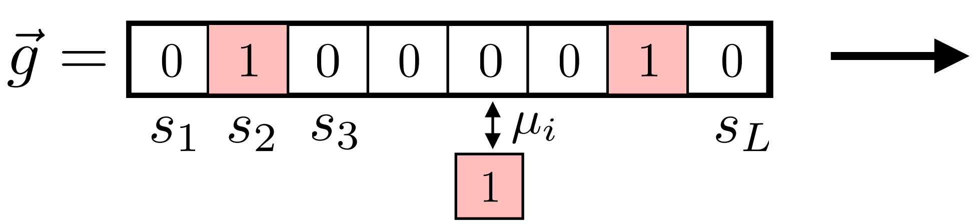

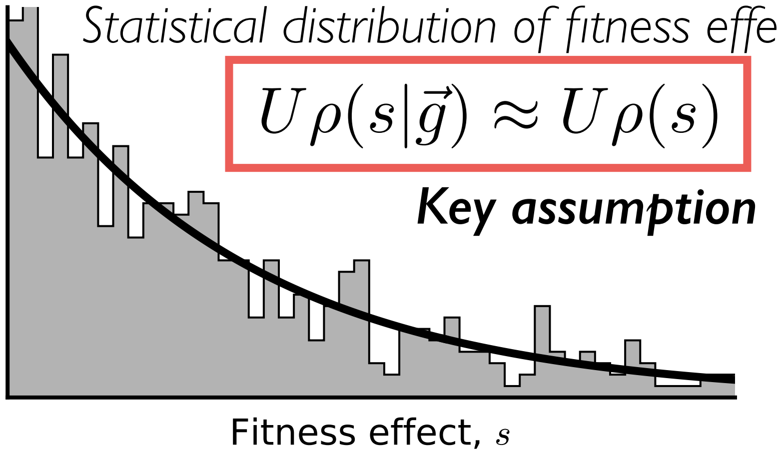

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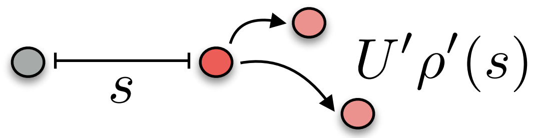
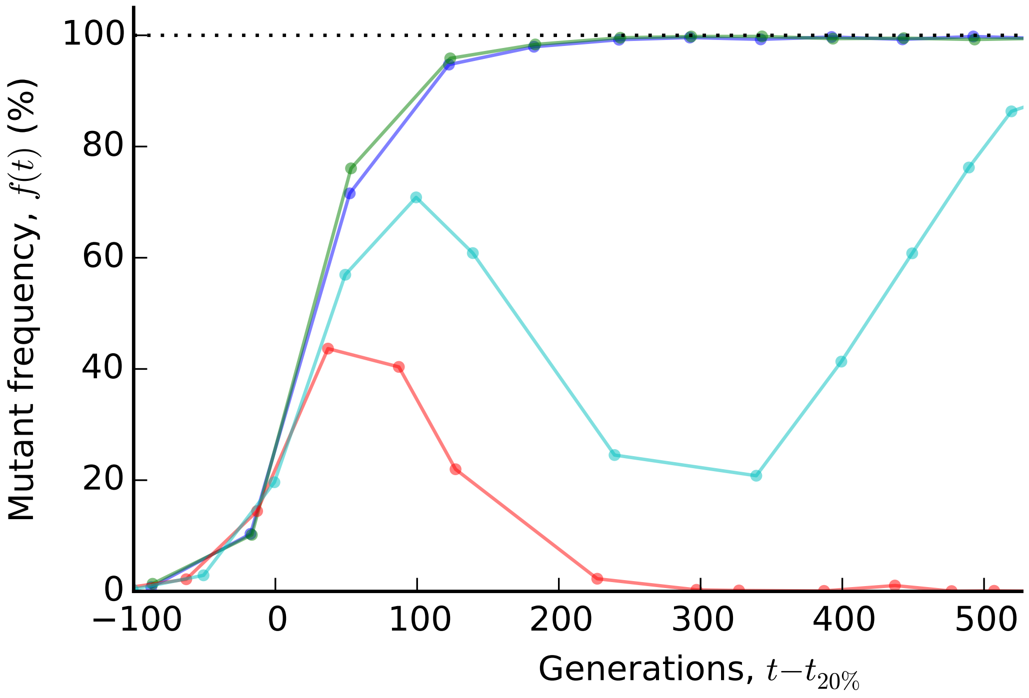


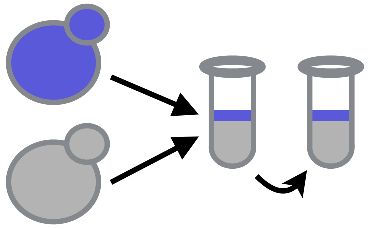
vs traditional "microscopic" expansion

$$X(\vec{g}) \approx \sum_i s_i g_i + \sum_{ij} \epsilon_{ij} g_i g_j + \dots$$

Questions: *when is invasion* $\neq$ *optimal for population?*
How far can populations "see" in fitness landscape?

But how relevant are these models, really?





Short-term adaptation
to ***new*** environment…

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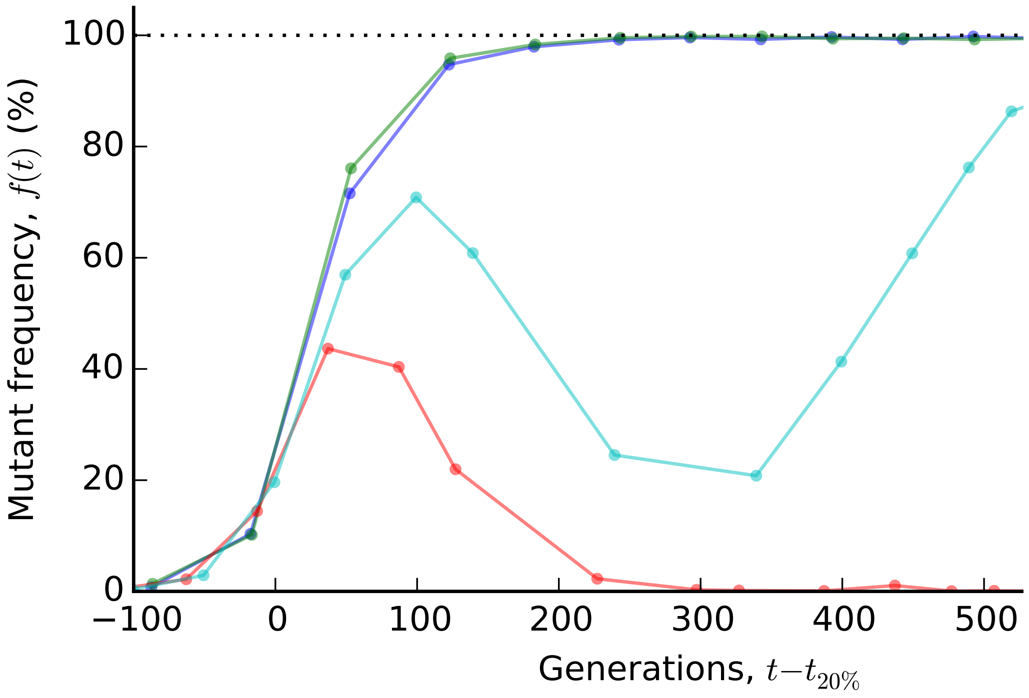

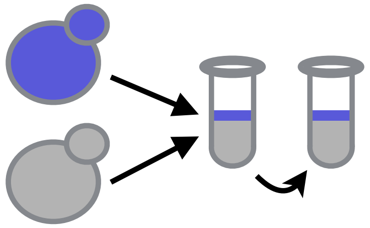

Short-term adaptation
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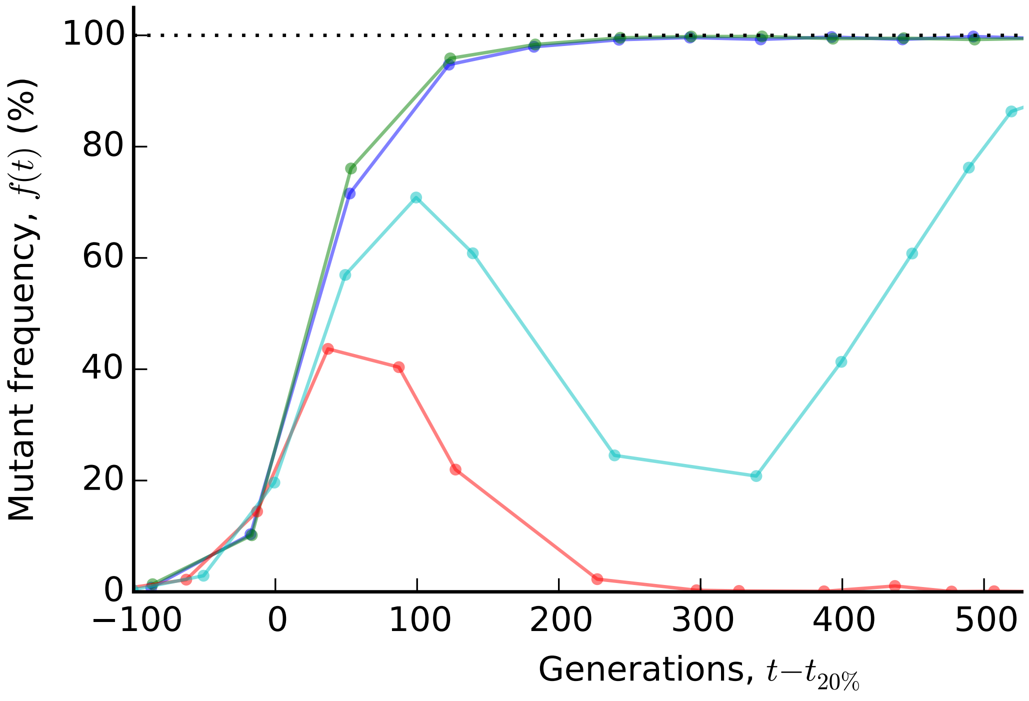

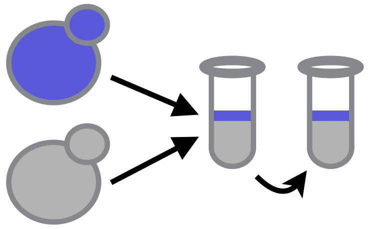

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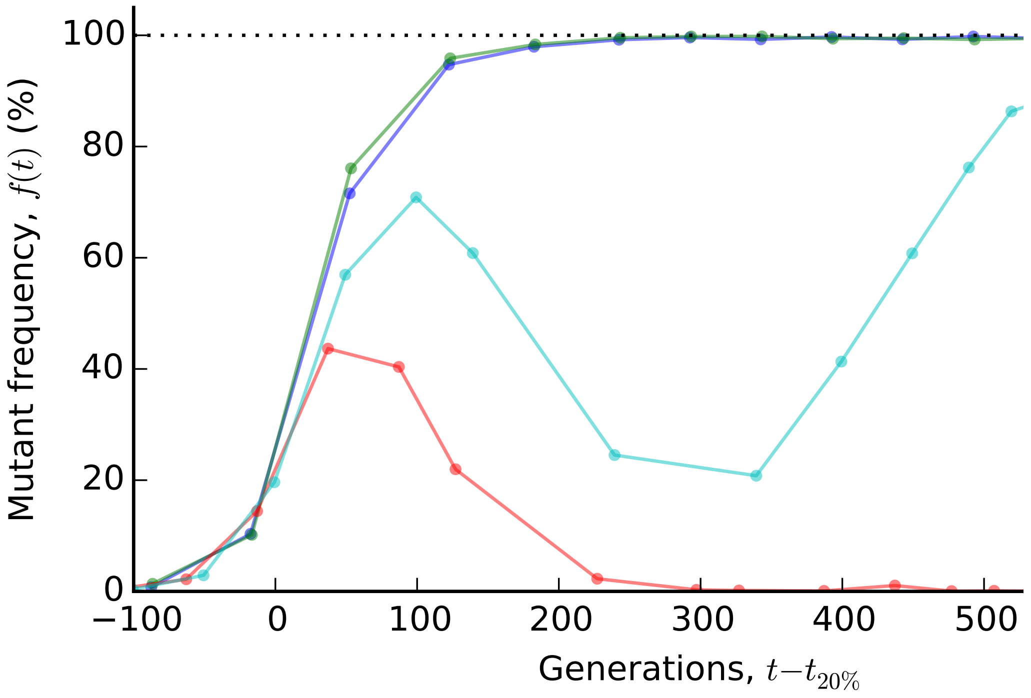
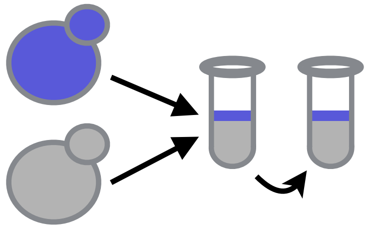




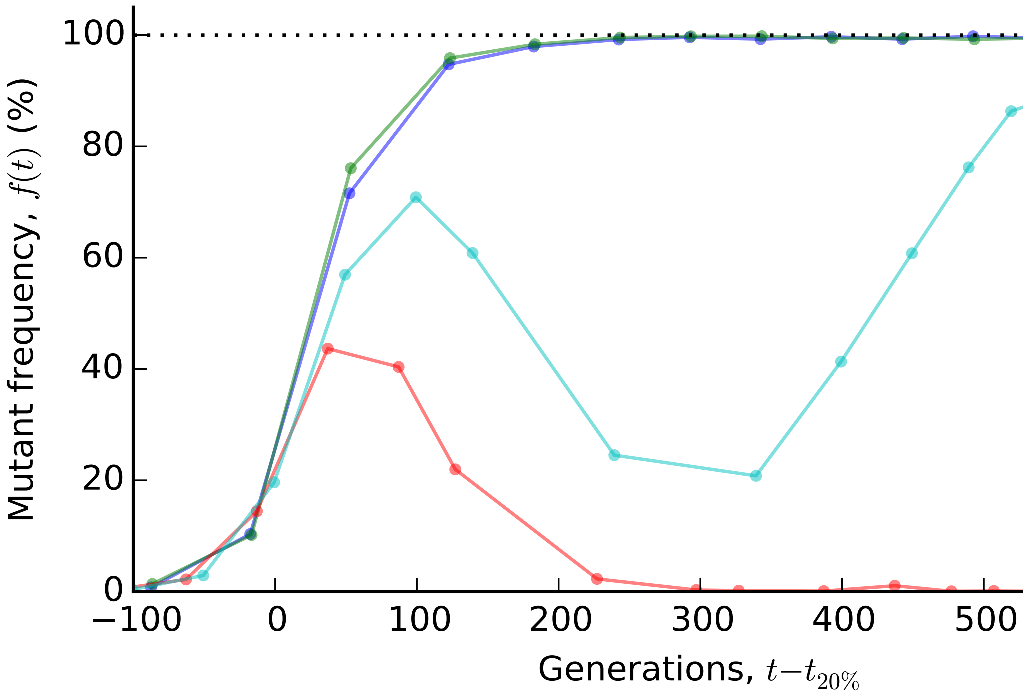
Short-term adaptation
to ***new*** environment…

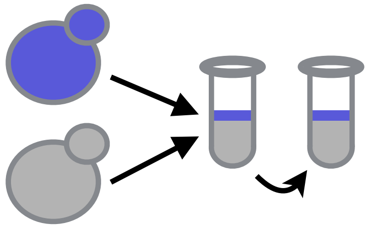
Does ***long-term*** adaptation look different?

Questions: Do dynamics eventually become “simple” again?

or do new complications arise that require revisions to the model?

But how relevant are these models, really?



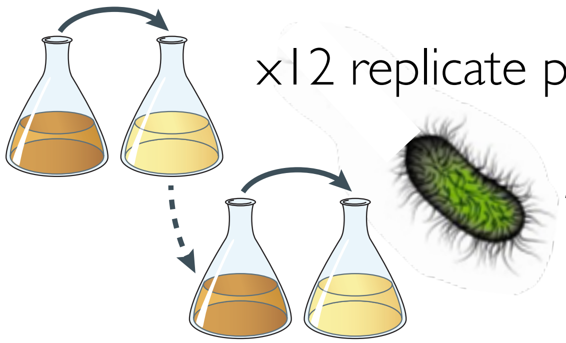


Short-term adaptation to ***new*** environment…

Does ***long-term*** adaptation look different?

A long-term experiment, "the LTEE"

Richard Lenski

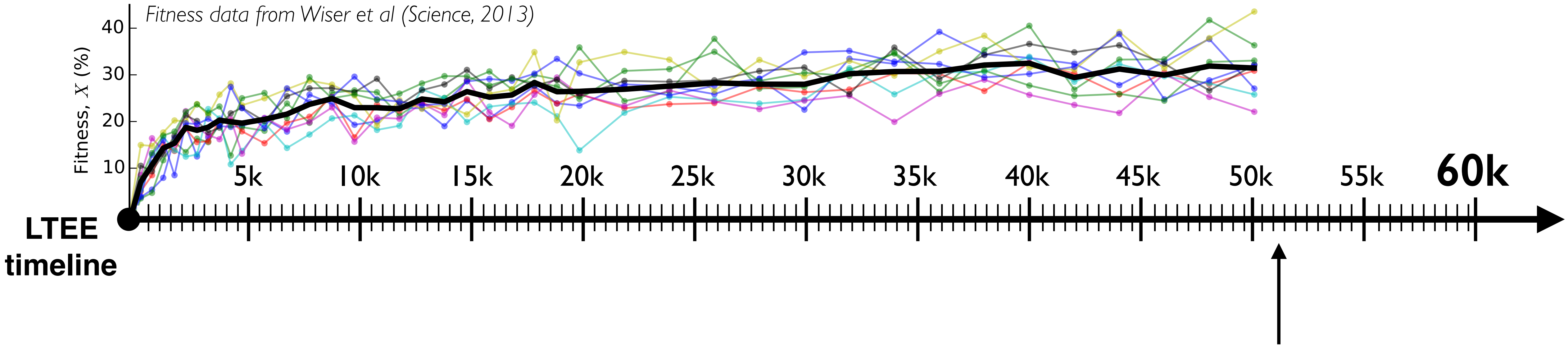


×12 replicate pop'ns

E. coli

× 30 years…
(& counting!)

Long-term adaptation to a constant environment

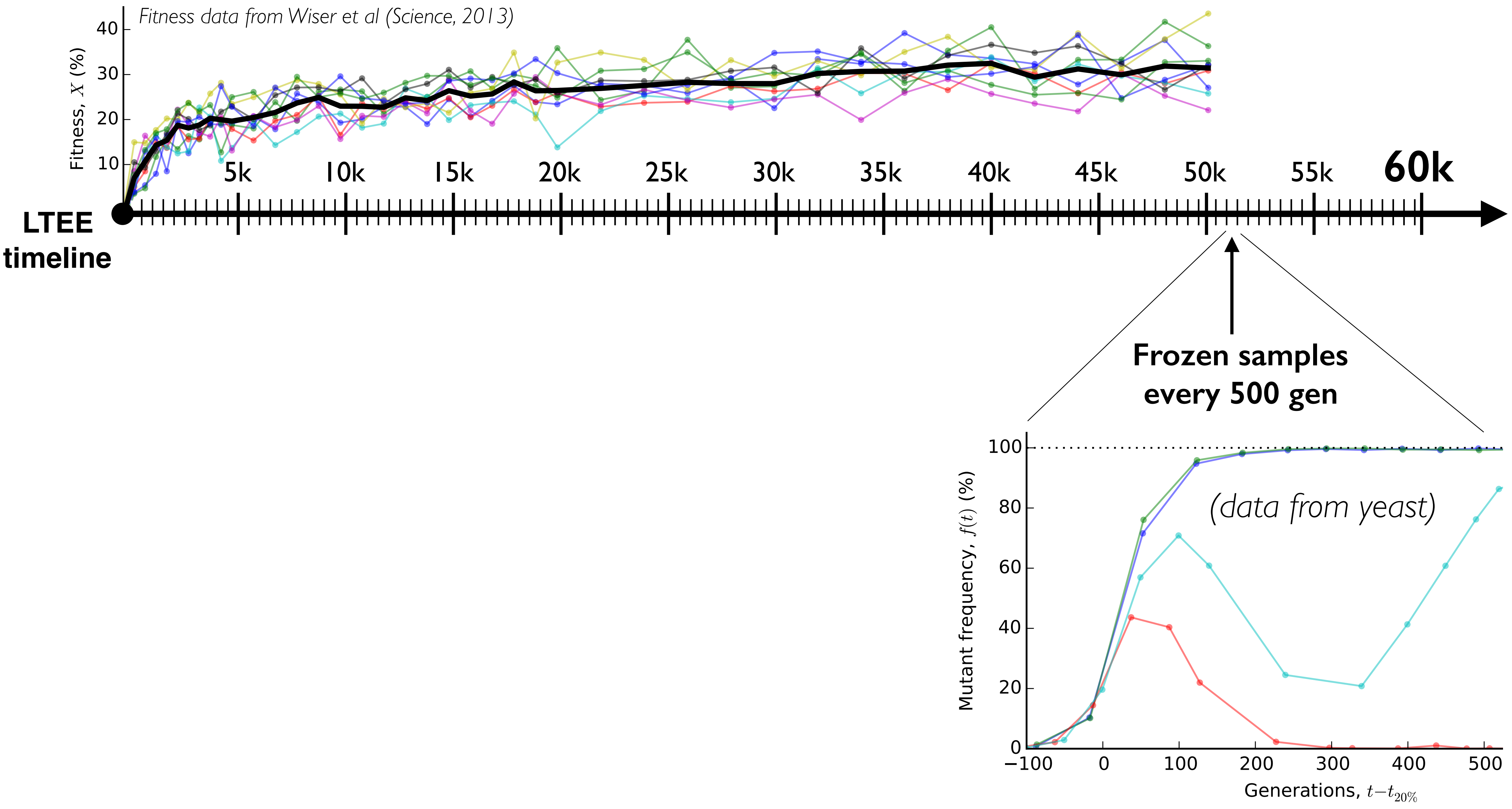


Fitness data from Wiser et al (Science, 2013)

LTEE timeline

Frozen samples every 500 gen

Long-term adaptation to a constant environment



Fitness data from Wiser et al (Science, 2013)

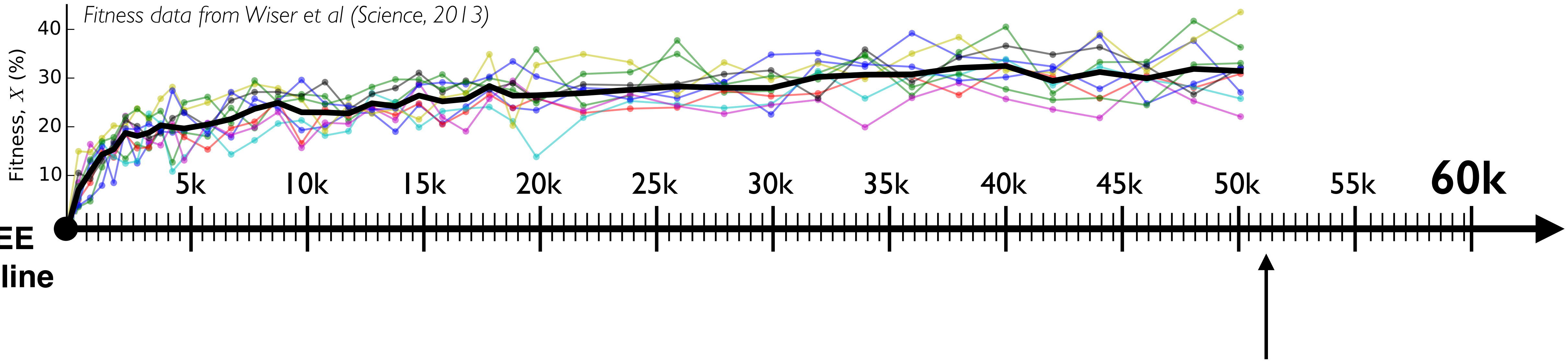
LTEE timeline

Frozen samples every 500 gen

(data from yeast)

Problem: Samples too far apart?

Long-term adaptation to a constant environment



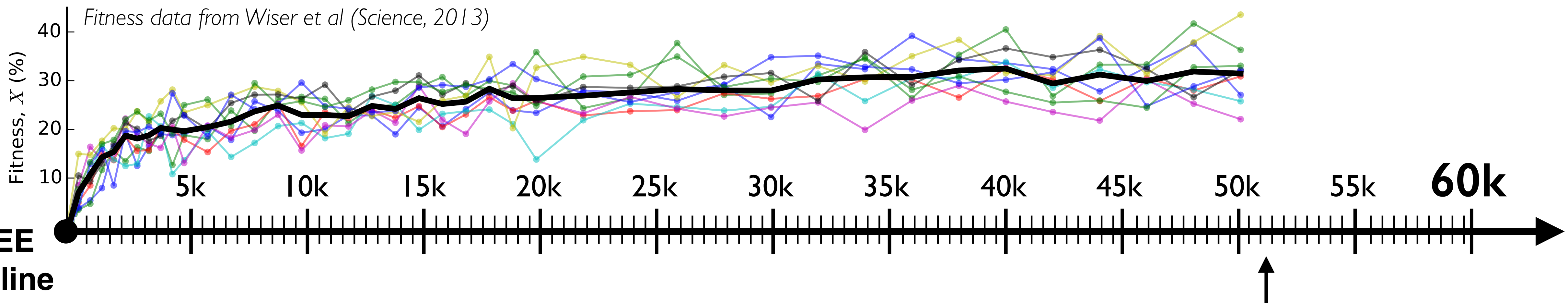
LTEE timeline

Frozen samples every 500 gen

Solution: Fit to ***model*** suggests that we can see dynamics!

[***"knobs":*** $U\rho(s) \approx (U_b^*, s_b^*) + (U_n^*, 0)$]

Long-term adaptation to a constant environment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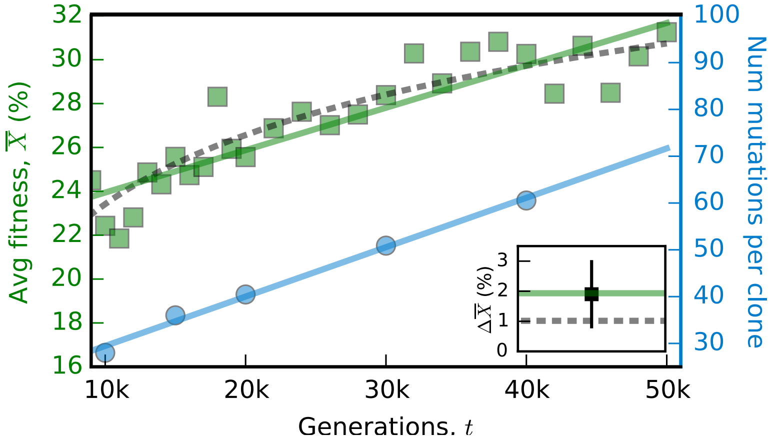
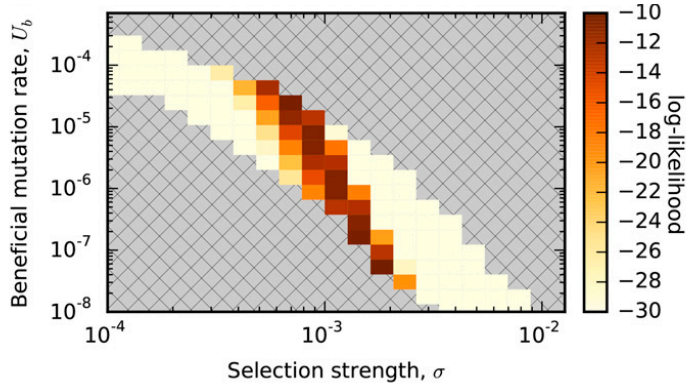
---

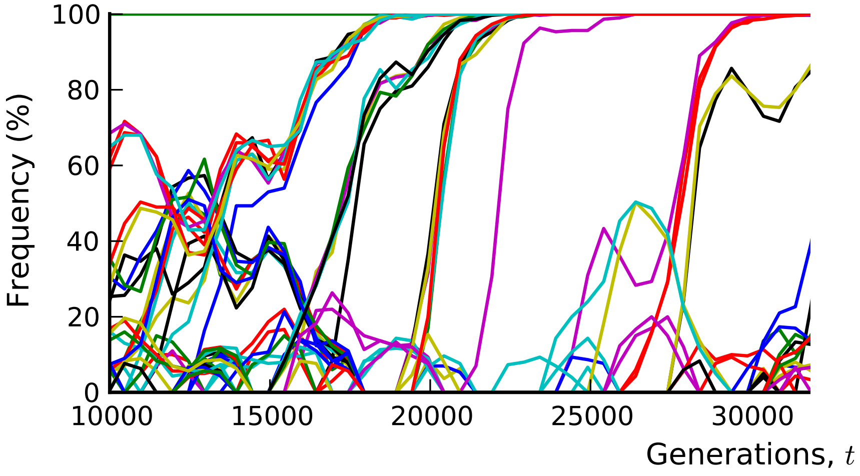
1. Previous data



2. Fit* to model

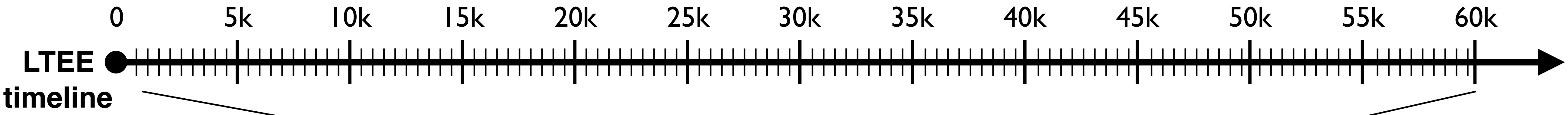


3. Simulated sequence data



Good and Desai (Genetics, 2015)

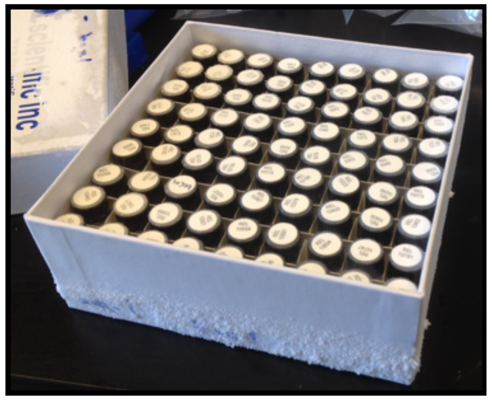
Reconstructing a “molecular fossil record”



w/ Michael McDonald

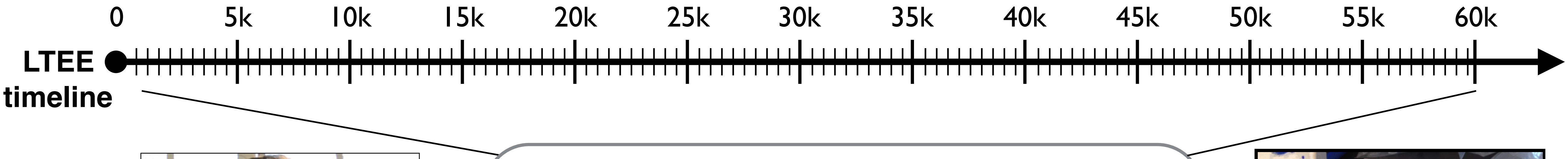
Sequencing strategy

Frozen mixed-population samples ~ 500 gen
x 12 populations
= ~1500 timepoints @ 10-100x coverage



“Ancient” DNA from Ara-1

Reconstructing a "molecular fossil record"



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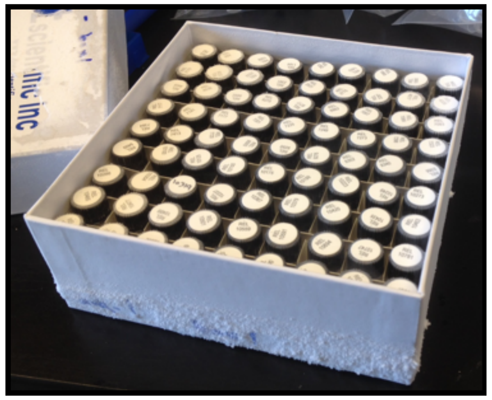

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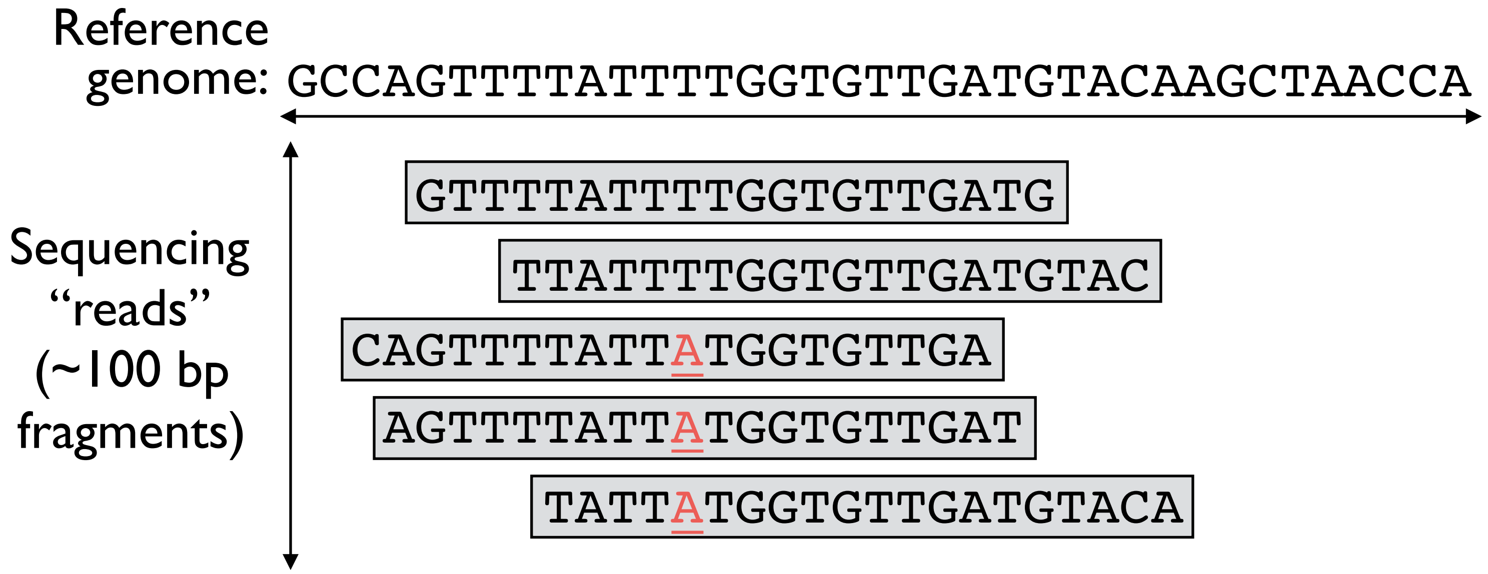

Reference genome: GCCAGTTTTATTTTGGTGTTGATGTACAAGCTAACCA

Sequencing "reads" (~100 bp fragments)

GTTTTATTTTGGTGTTGATG
TTATTTTGGTGTTGATGTAC
CAGTTTTATTATGGTGTTGA
AGTTTTATTATGGTGTTGAT
TATTATGGTGTTGATGTACA

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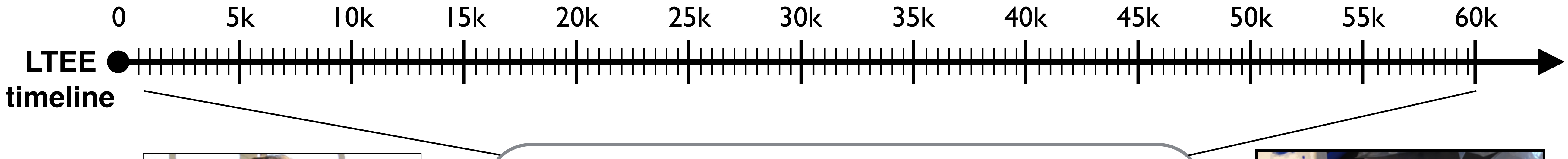

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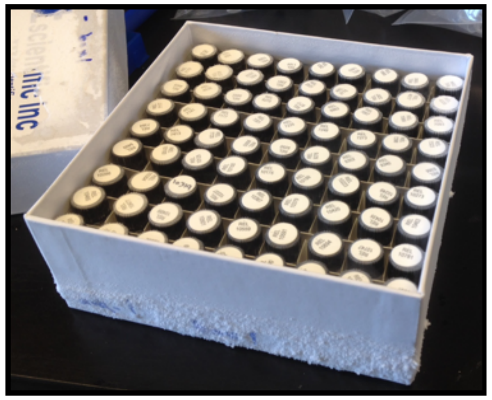

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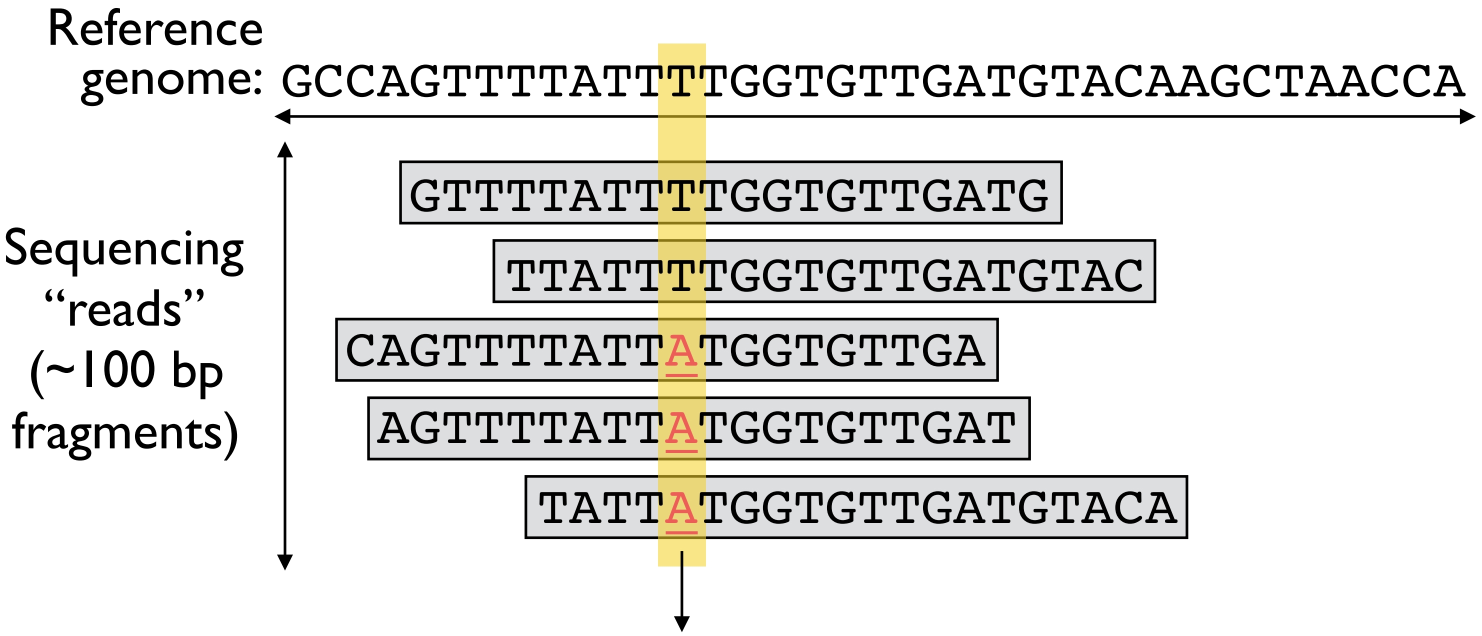

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`GTTTTATTTTGGTGTTGATG`
`TTATTTTGGTGTTGATGTAC`
`CAGTTTTATTATGGTGTTGA`
`AGTTTTATTATGGTGTTGAT`
`TATTATGGTGTTGATGTACA`

"T→**A**" mutation @ 60% frequency
in this population in this timepjoint

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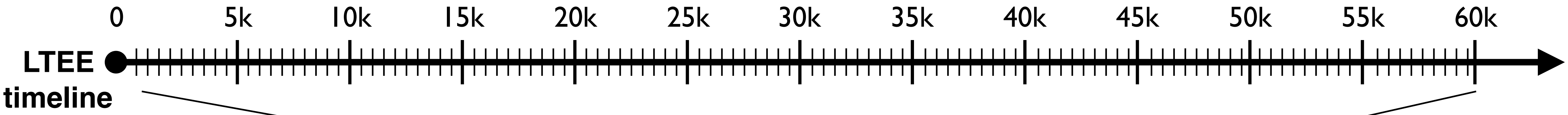

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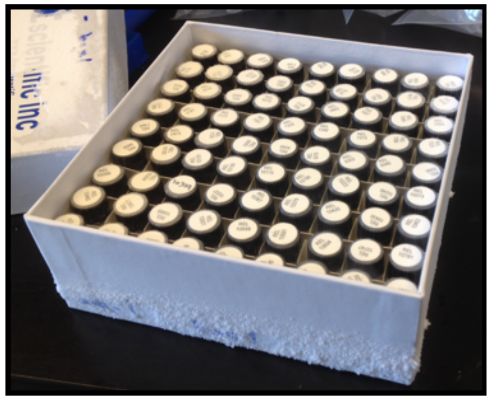

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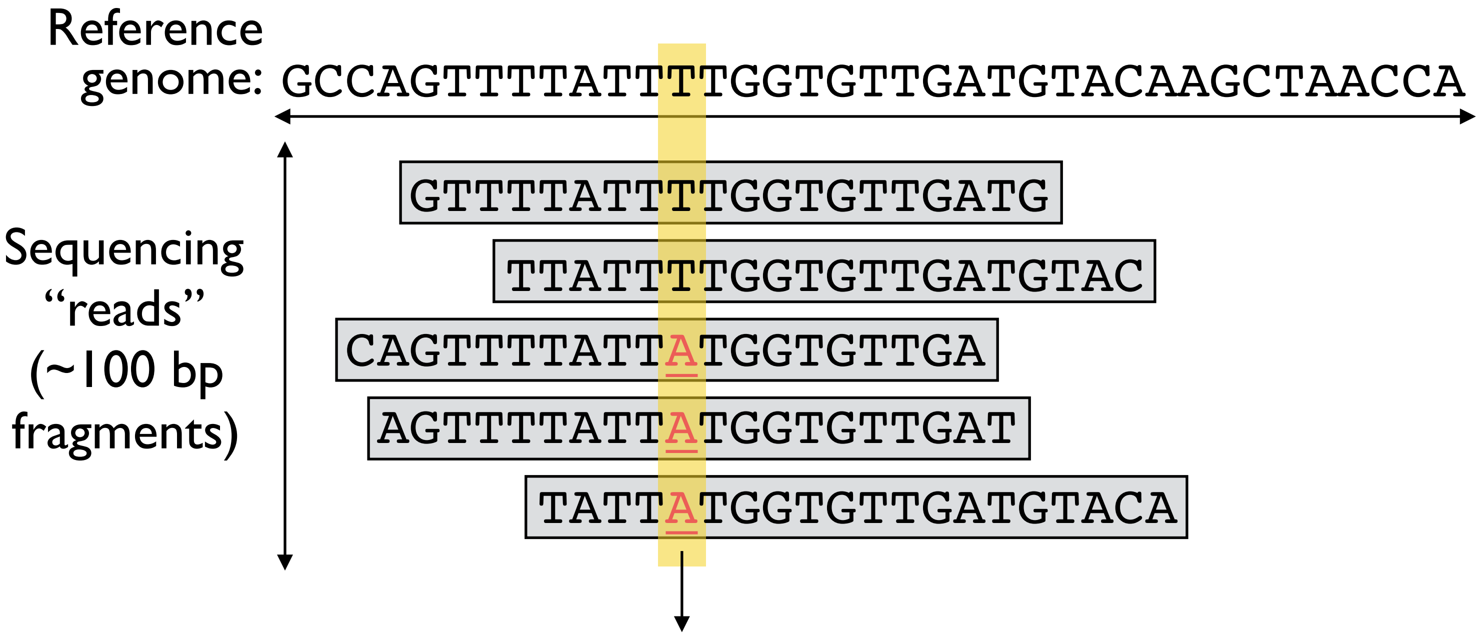

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GTTTTATTTTGGTGTTGATG
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```

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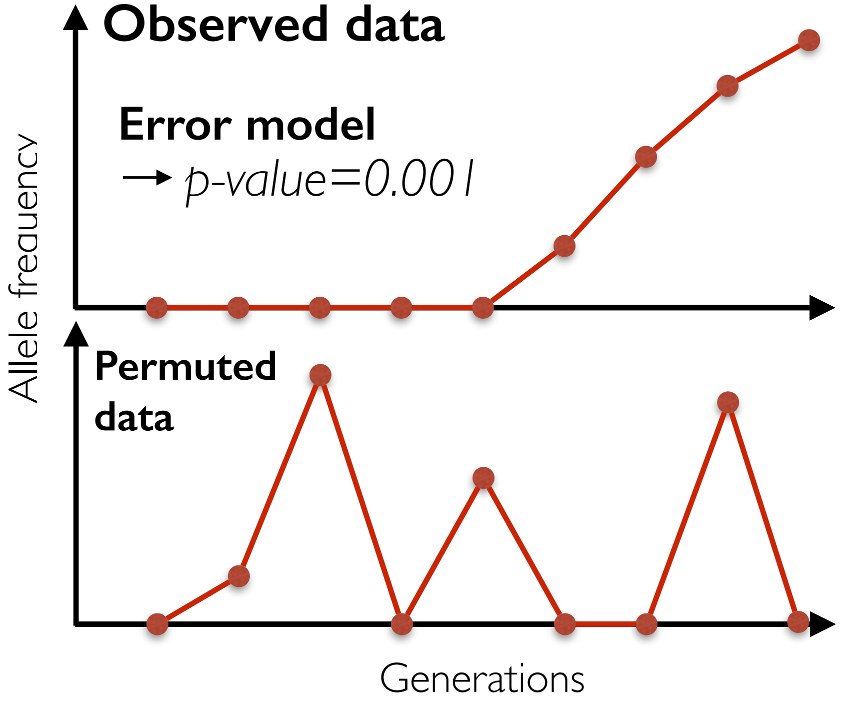
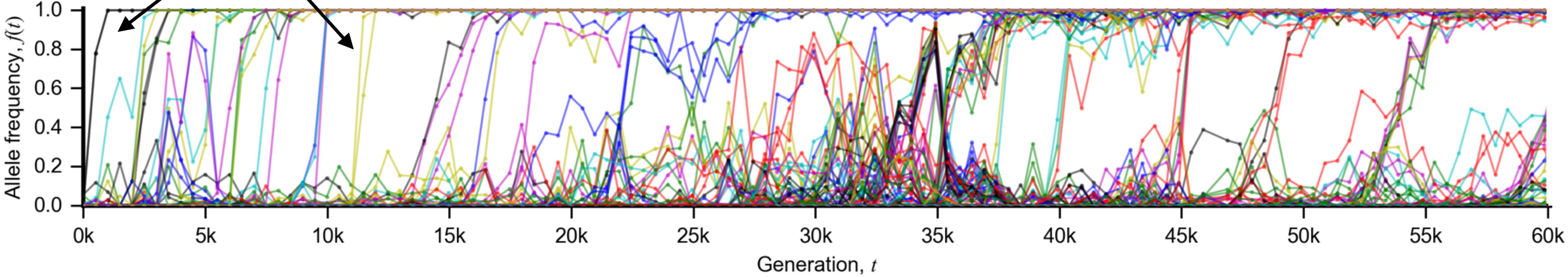


Dynamics of molecular evolution over 60,000 generations

frequency trajectories
of different mutations

One population ("Ara+2") through time



Good, McDonald* et al (Nature, 2017)*

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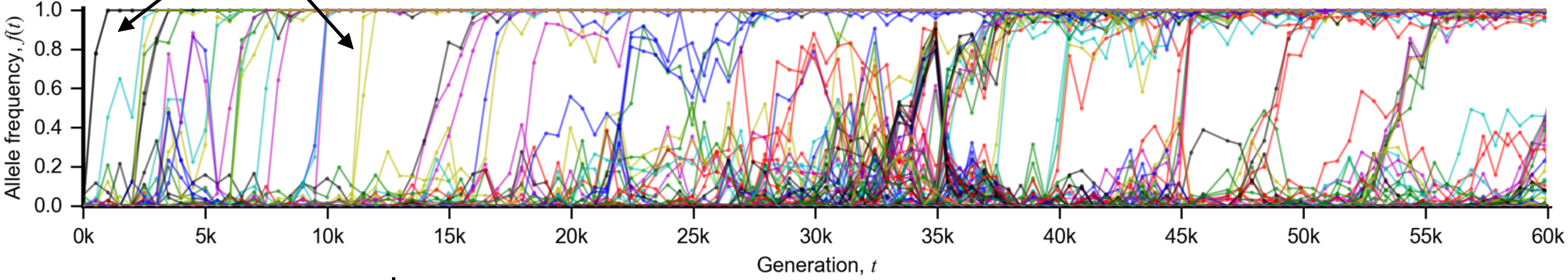
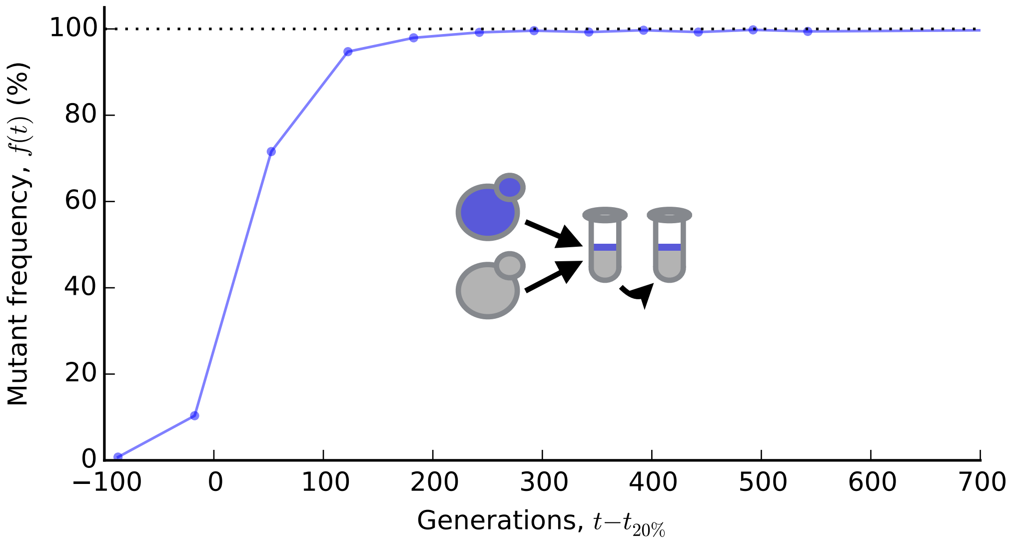
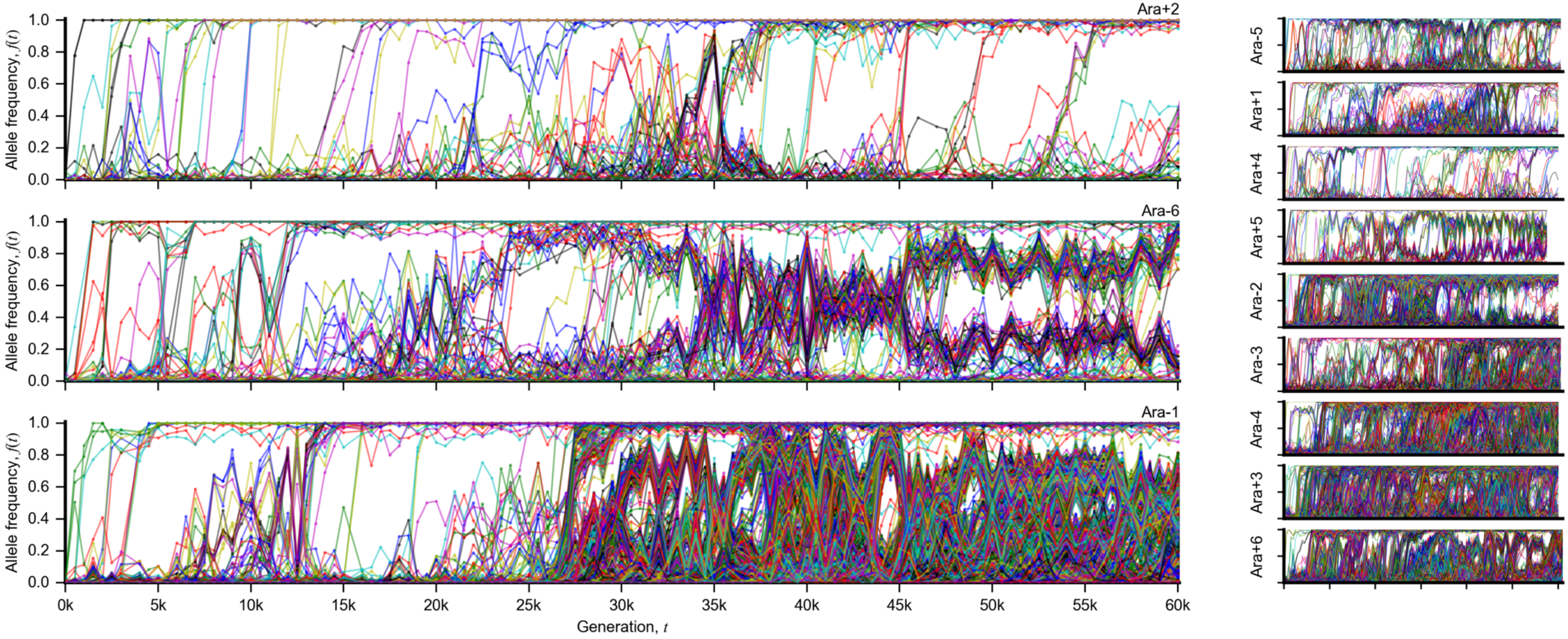




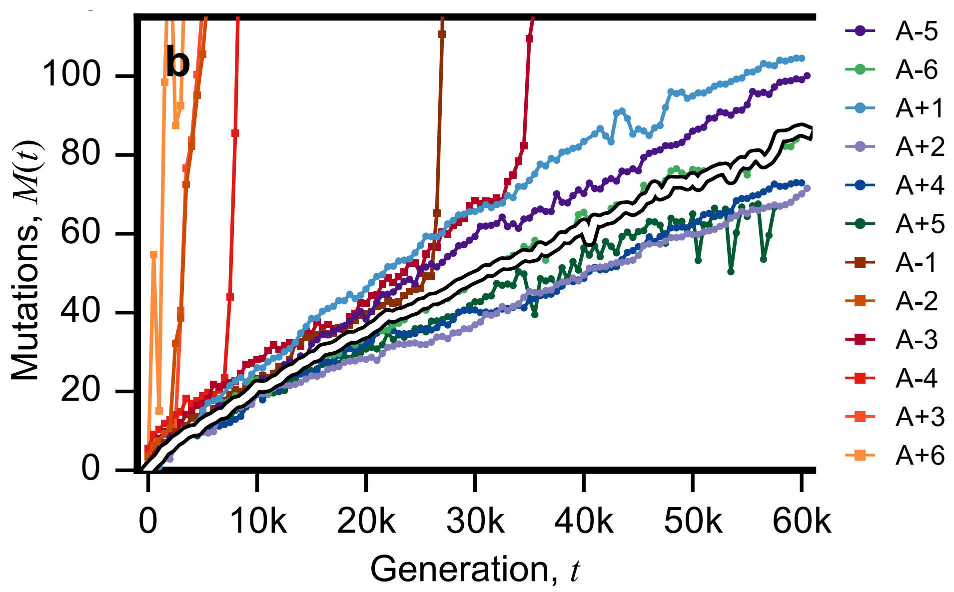
Good, McDonald* et al (Nature, 2017)*

Dynamics of molecular evolution over 60,000 generations in 12 replicate populations



Good, McDonald* et al (Nature, 2017)*

Dynamics of molecular evolution over 60,000 generations

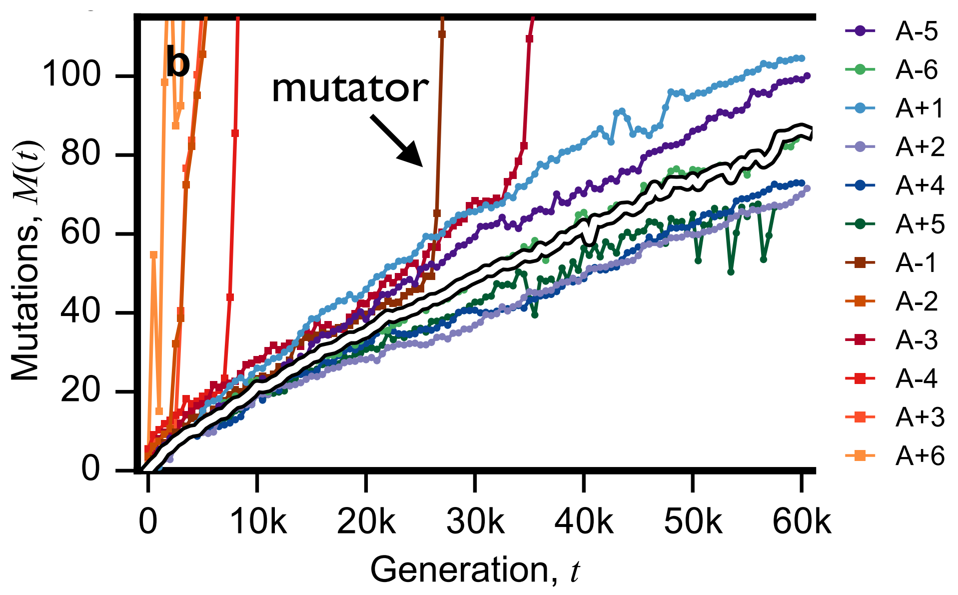


Avg # mutations / cell

$$M(t) \equiv \sum f_i(t)$$

Good, McDonald* et al (Nature, 2017)*

Dynamics of molecular evolution over 60,000 generations



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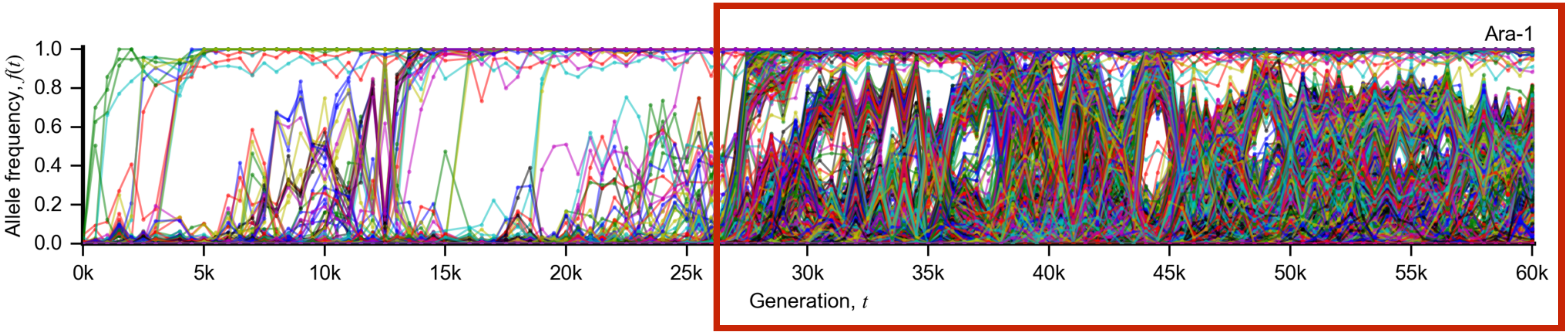

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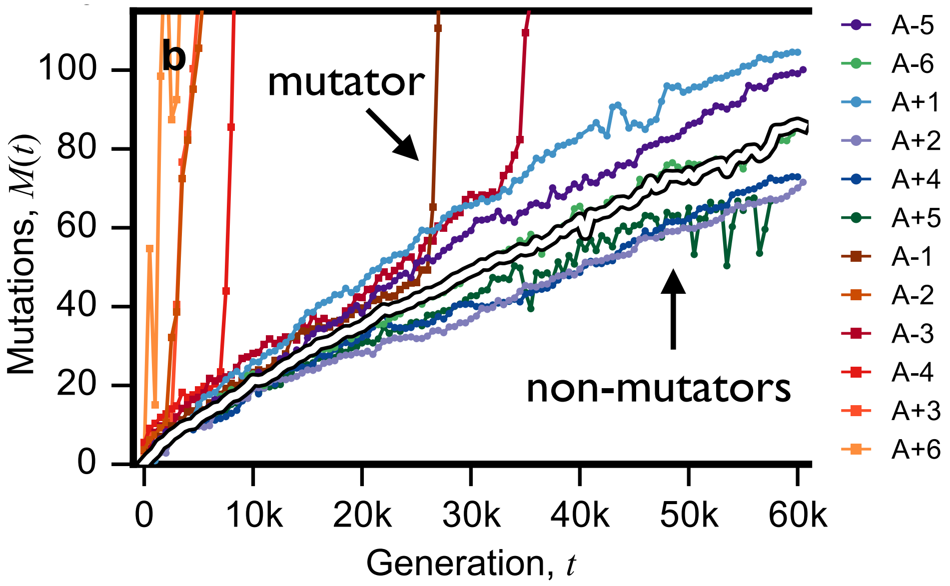

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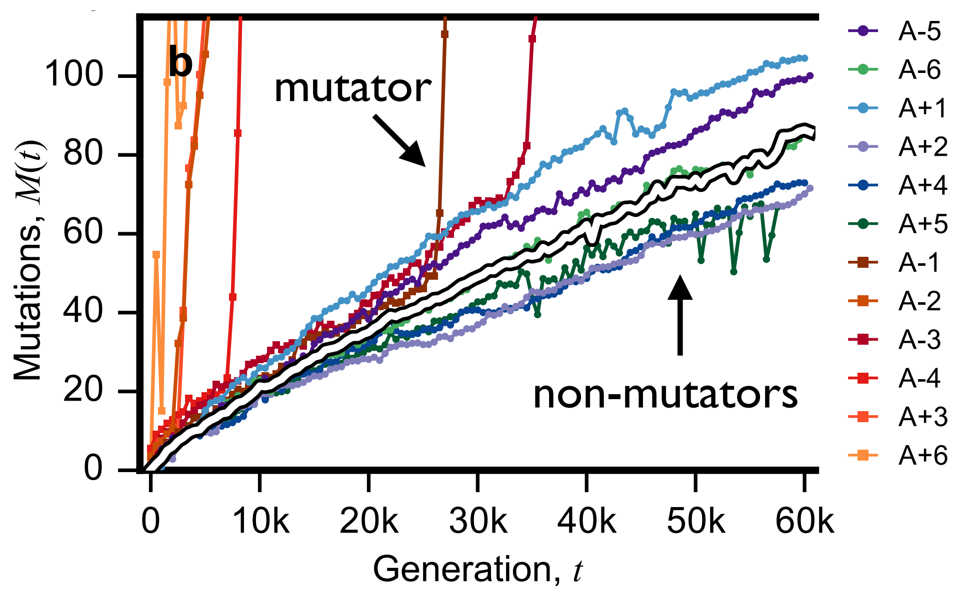

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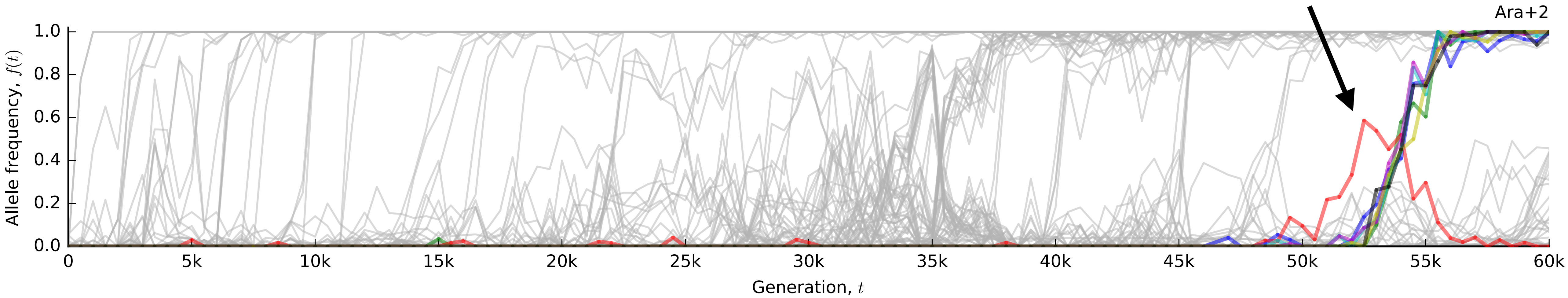

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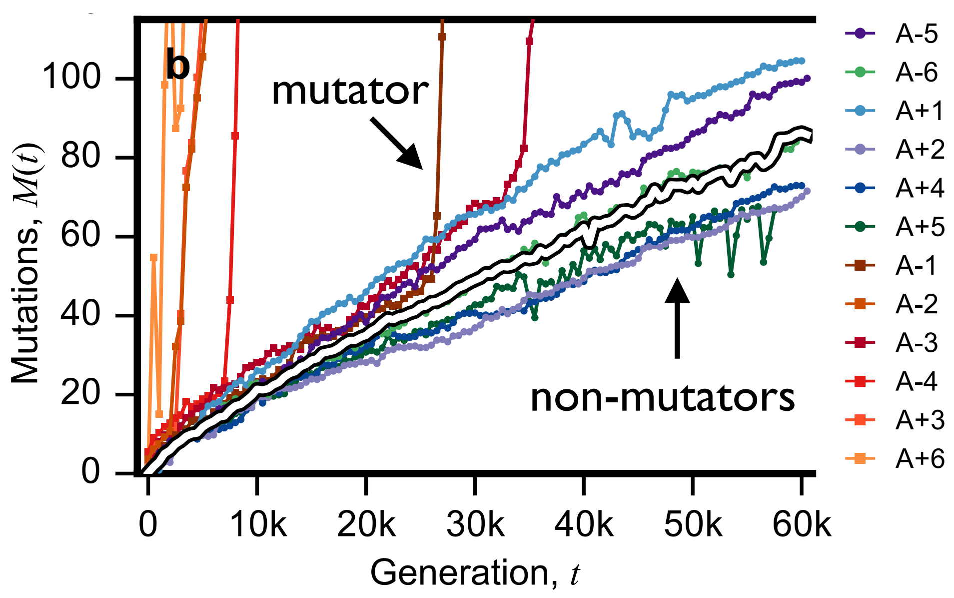
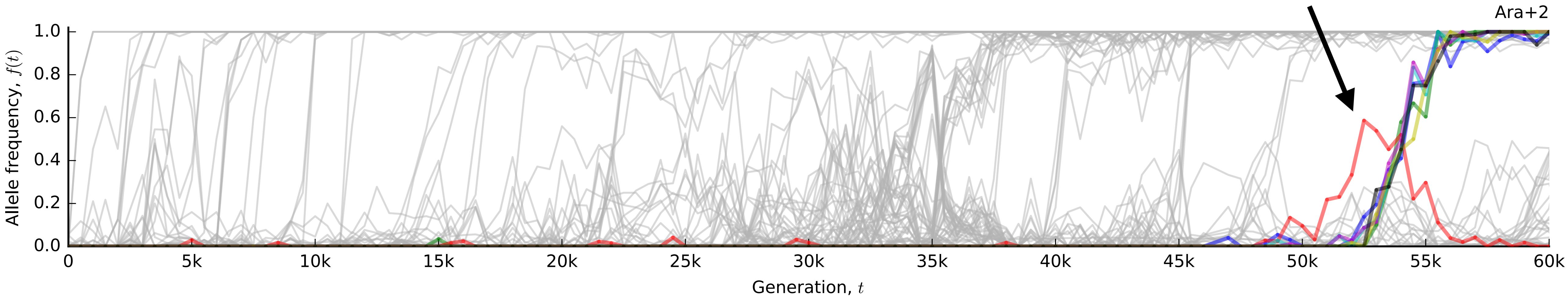


Avg # mutations / cell

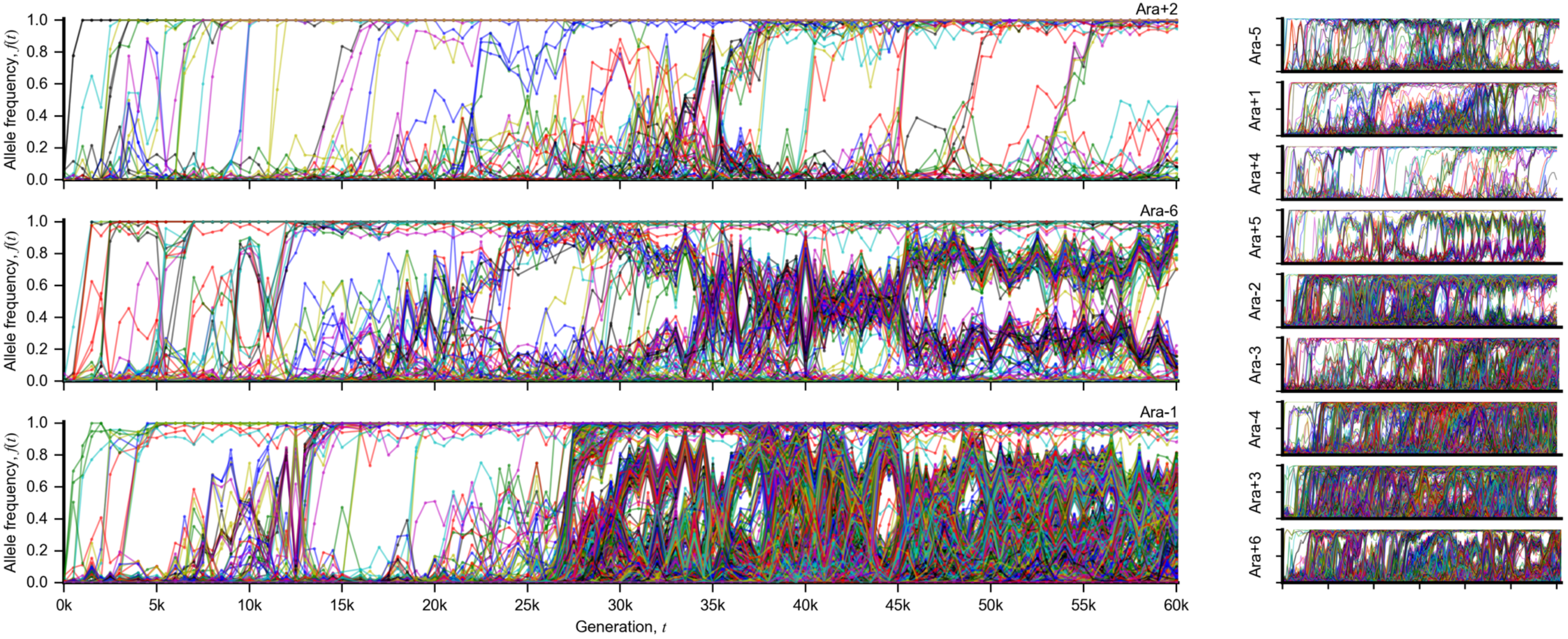
$$M(t) \equiv \sum f_i(t)$$

Adaptation ***still*** proceeds at rapid pace; linkage important!



Good, McDonald* et al (Nature, 2017)*

…but something is weird

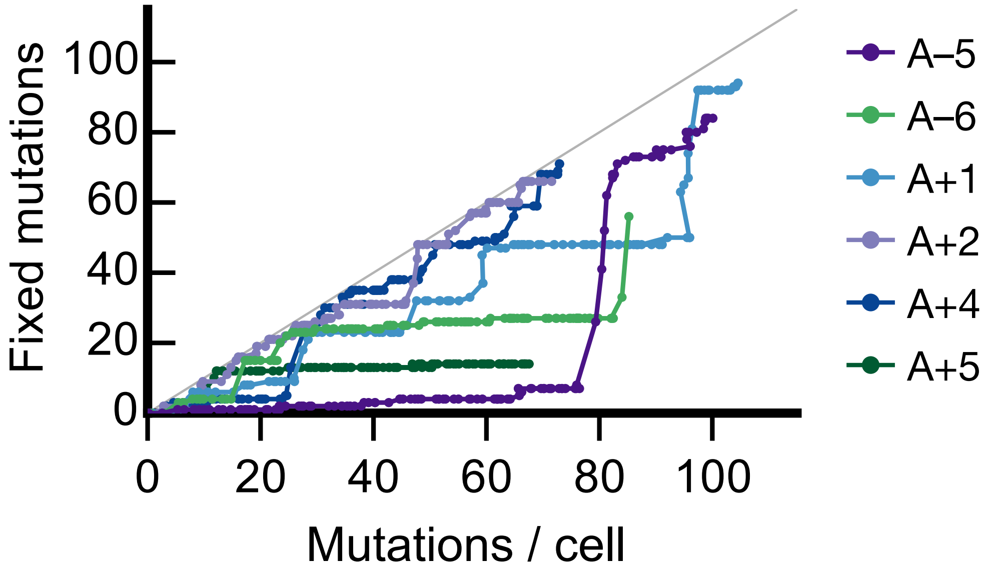


Good, McDonald* et al (Nature, 2017)*

Rapid evolution, but deficit of fixed mutations

Model predicts:

“fixed” mutations ~ avg # mutations / cell



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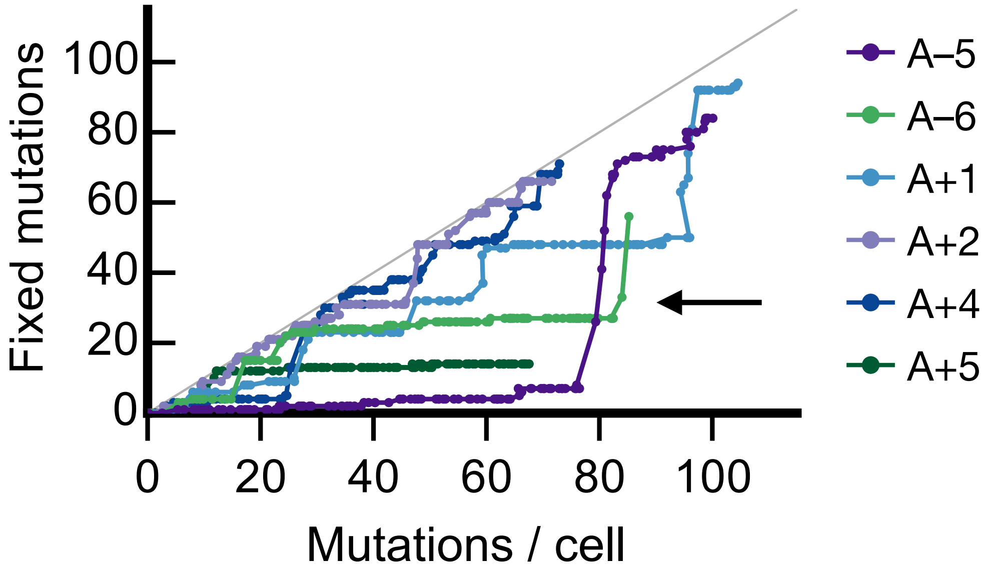
Too few fixed muts!



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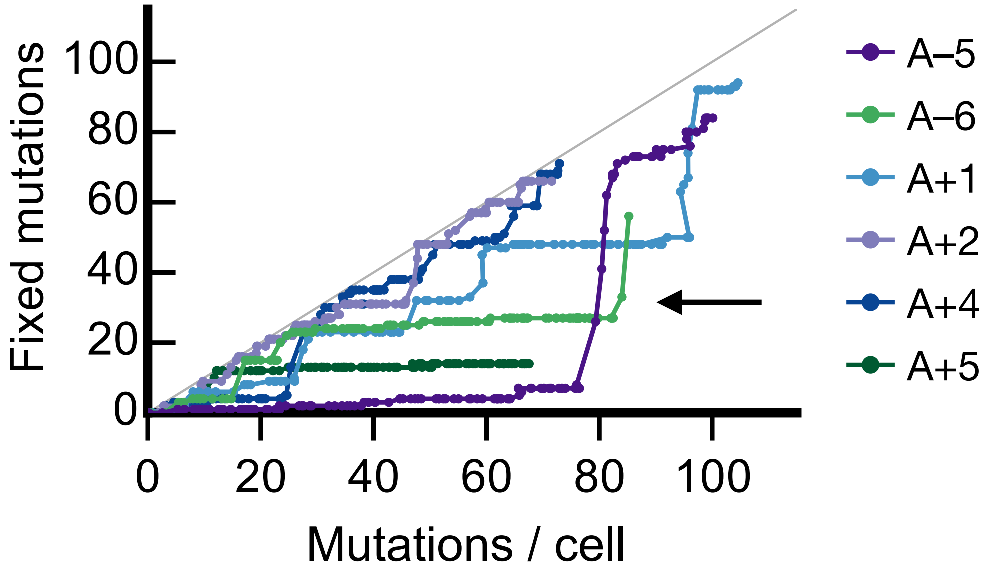
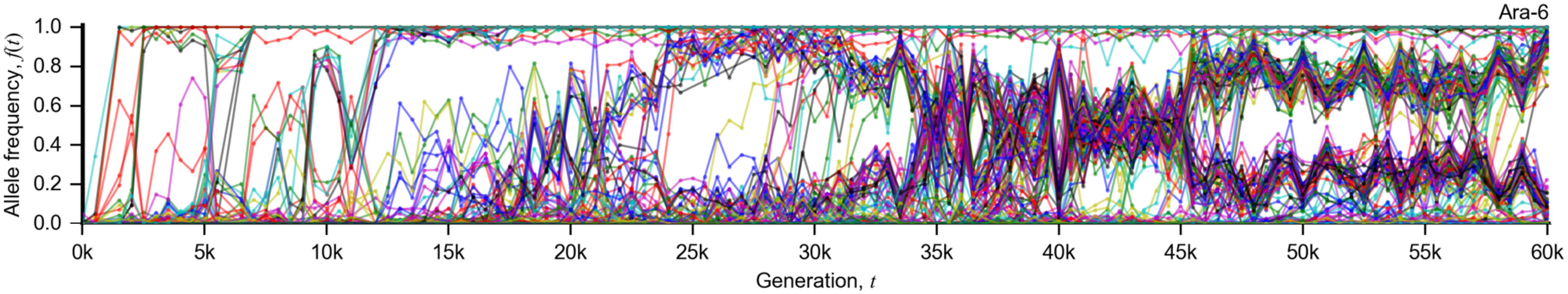
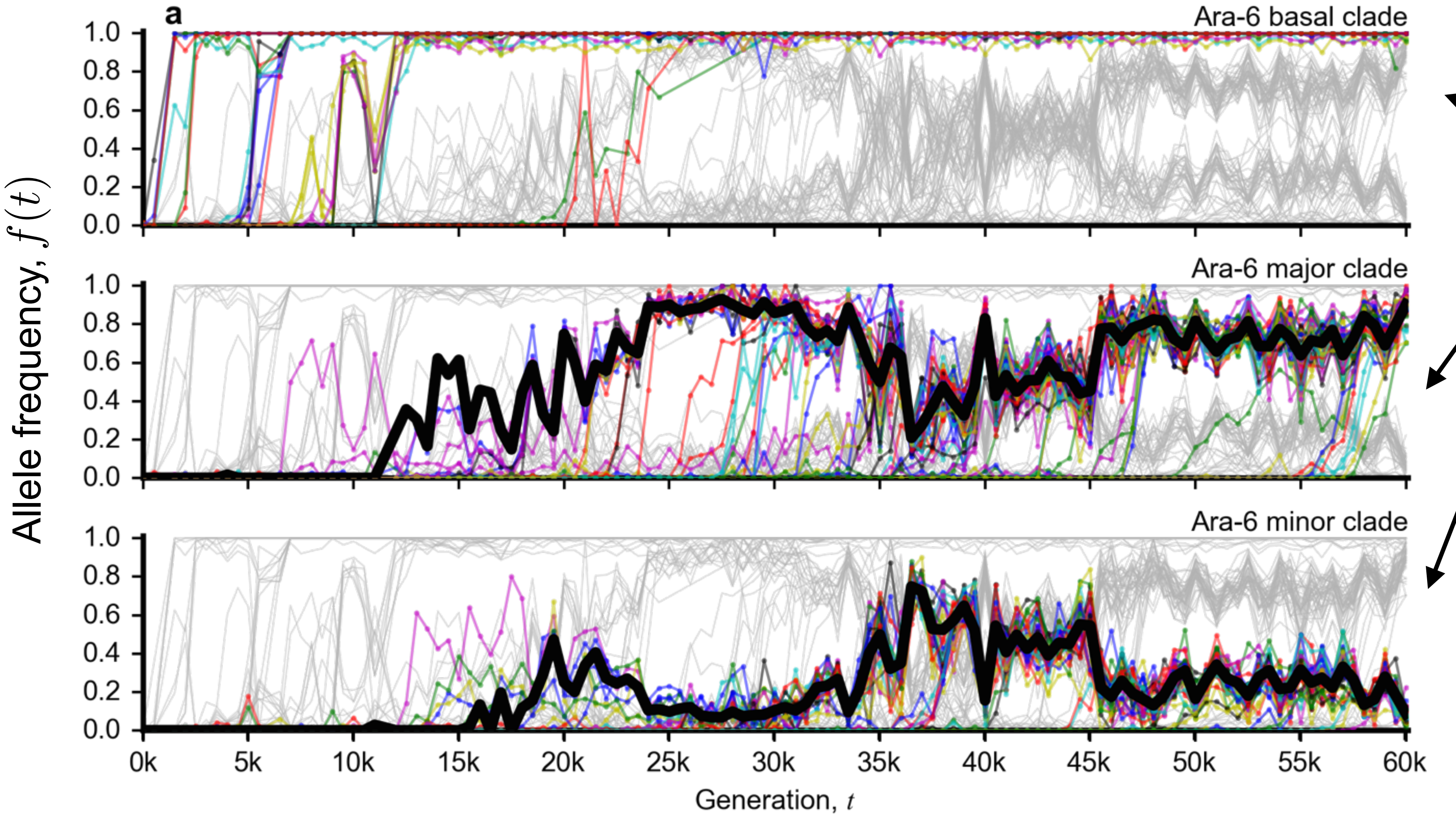




Mutations "pile up" in 2 clades that coexist for $\gtrsim 10,000$ ***gens***

Good, McDonald* et al (Nature, 2017)*

Inferring clade dynamics with hidden Markov models

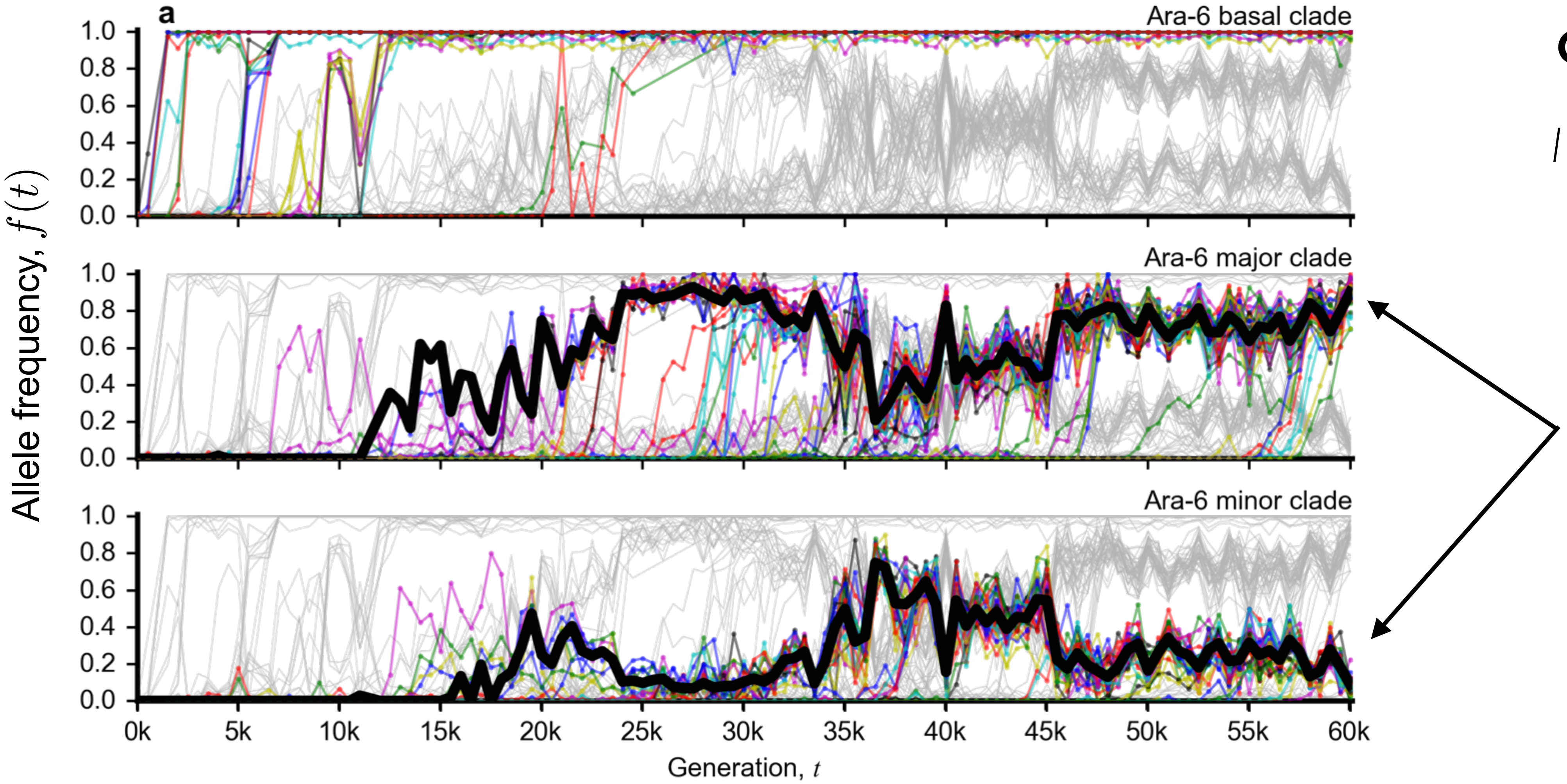


CladeHMM

1. Classifies mutations into clades

Good, McDonald* et al (Nature, 2017)*

Inferring clade dynamics with hidden Markov models



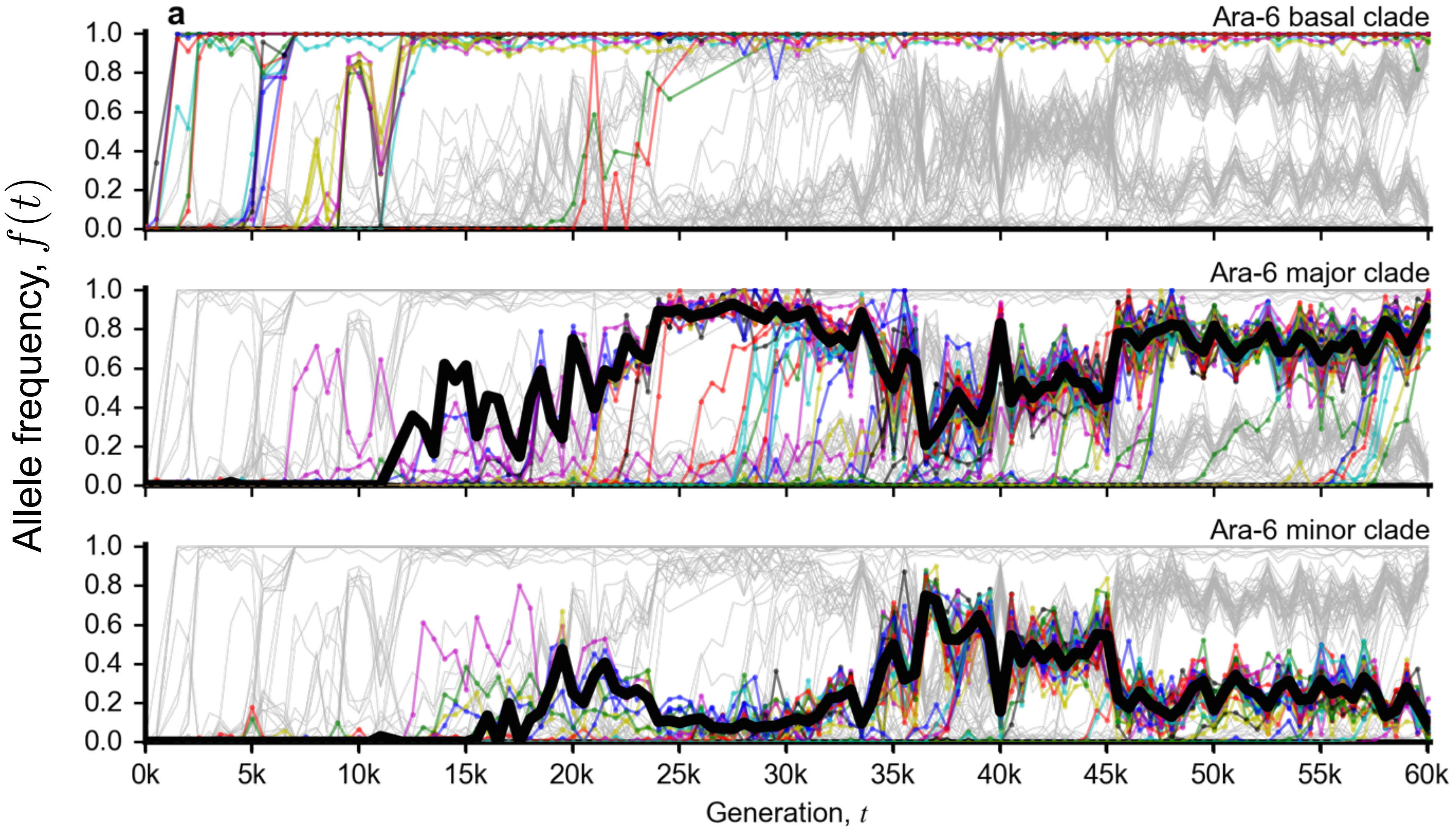
CladeHMM

1. Classifies mutations into clades

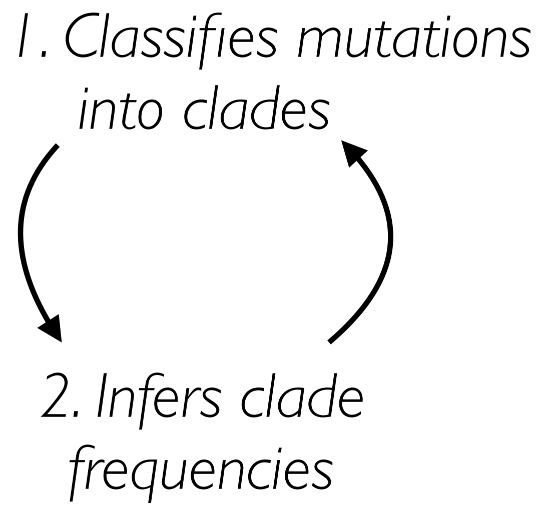
2. Infers clade frequencies

Good, McDonald* et al (Nature, 2017)*

Inferring clade dynamics with hidden Markov models



CladeHMM



1. Classifies mutations into clades

2. Infers clade frequencies

Good, McDonald* et al (Nature, 2017)*

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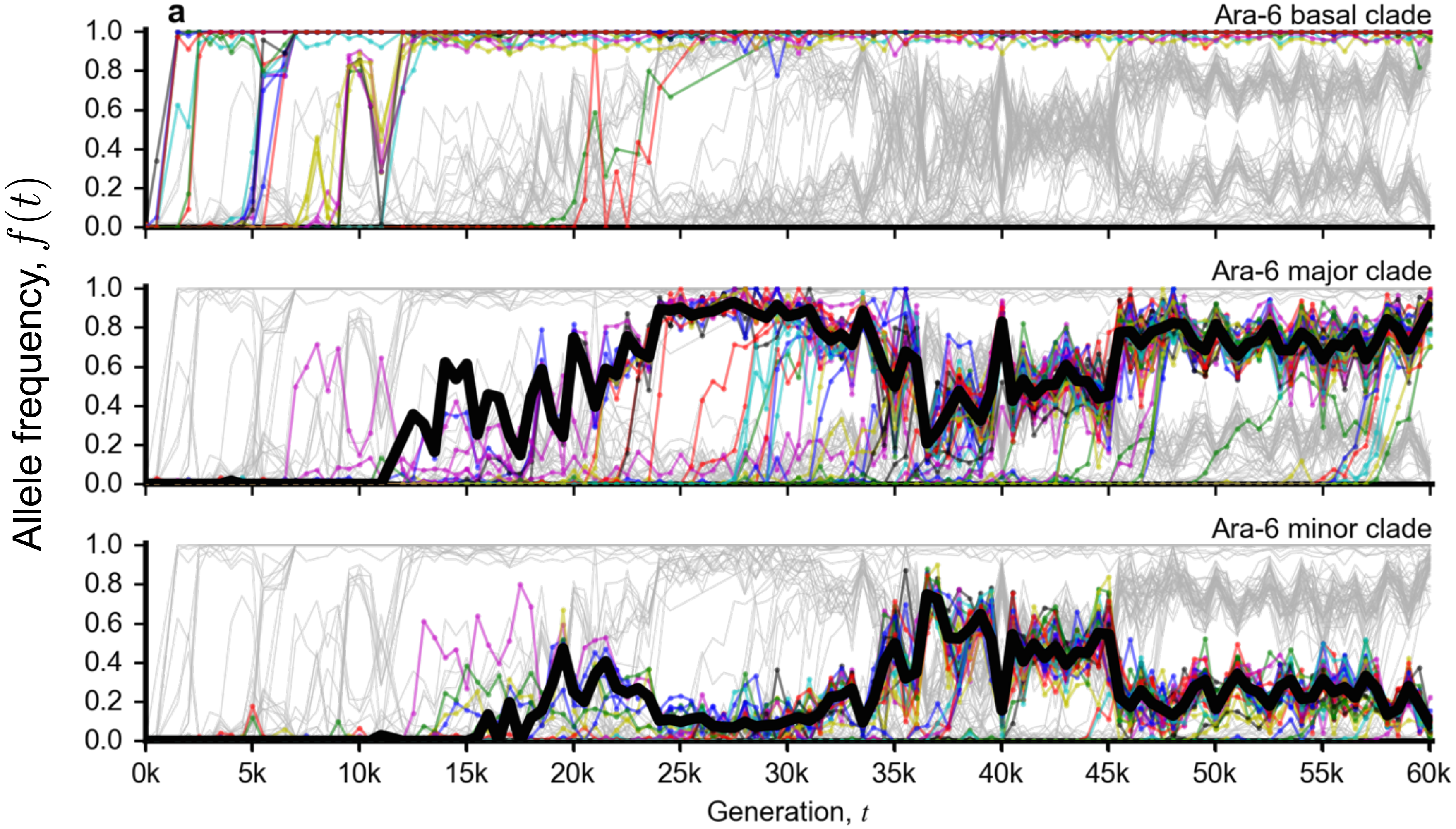
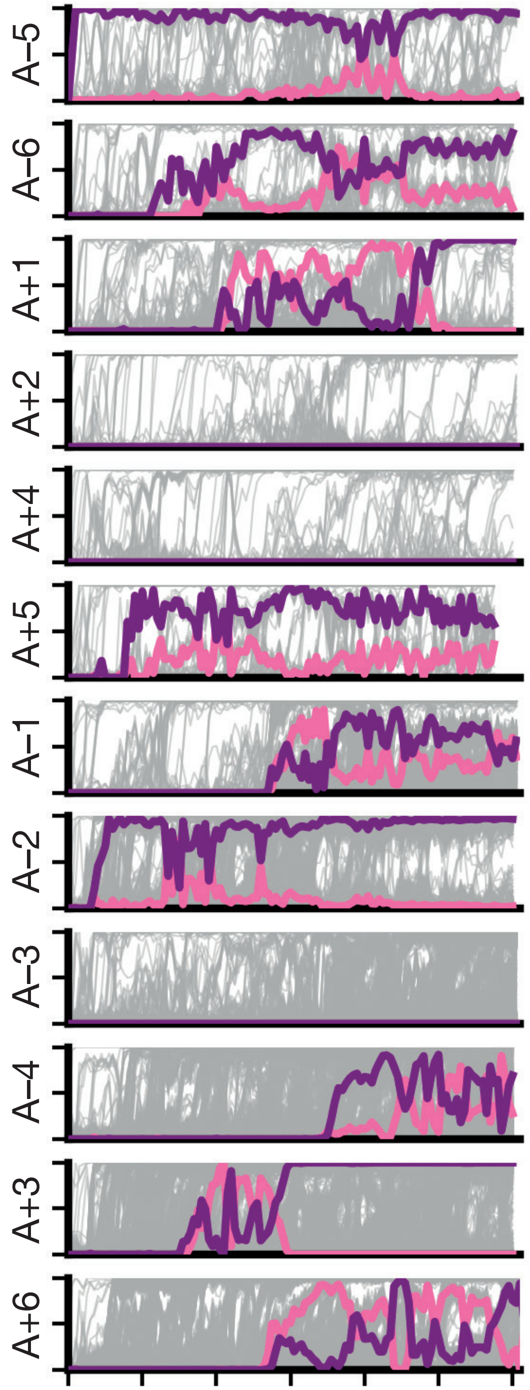


All 12 pop'ns



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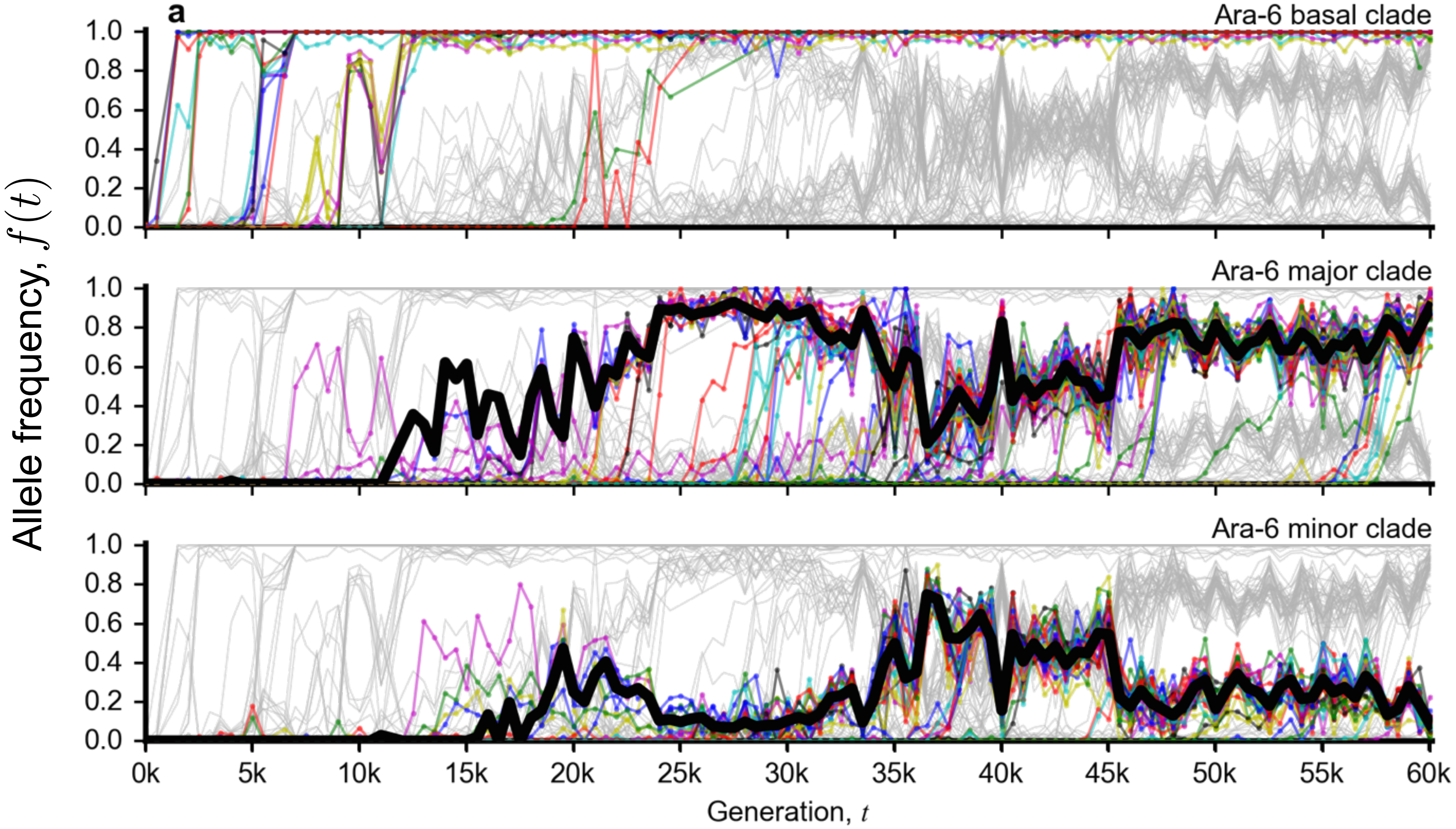

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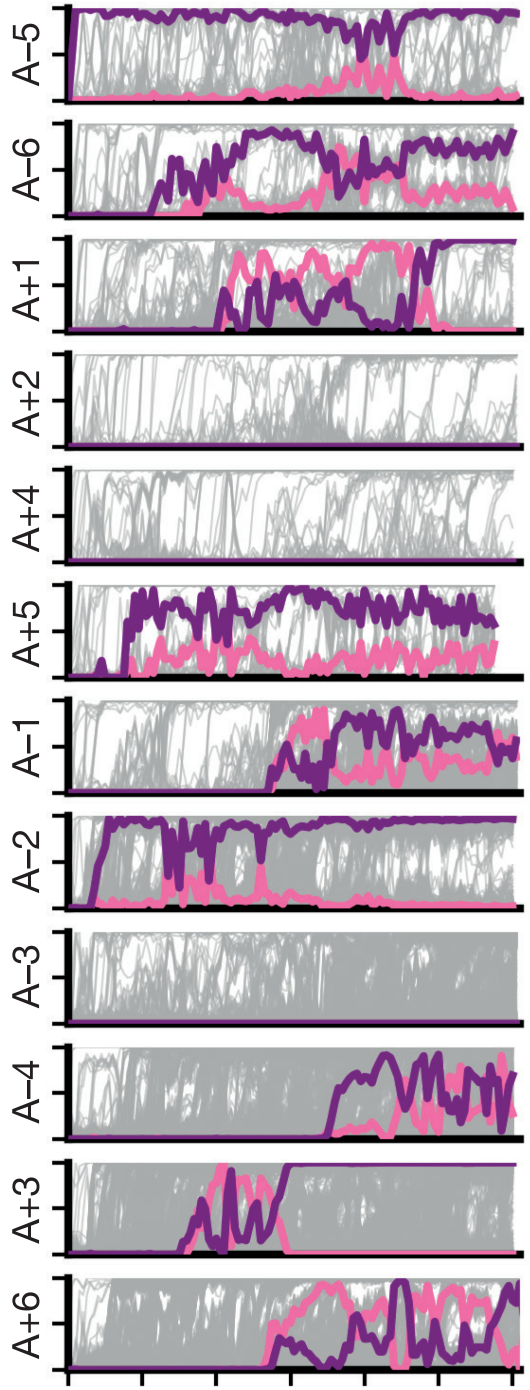

1. Long-lived clades are ***common*** in the LTEE.

Good, McDonald* et al (Nature, 2017)*

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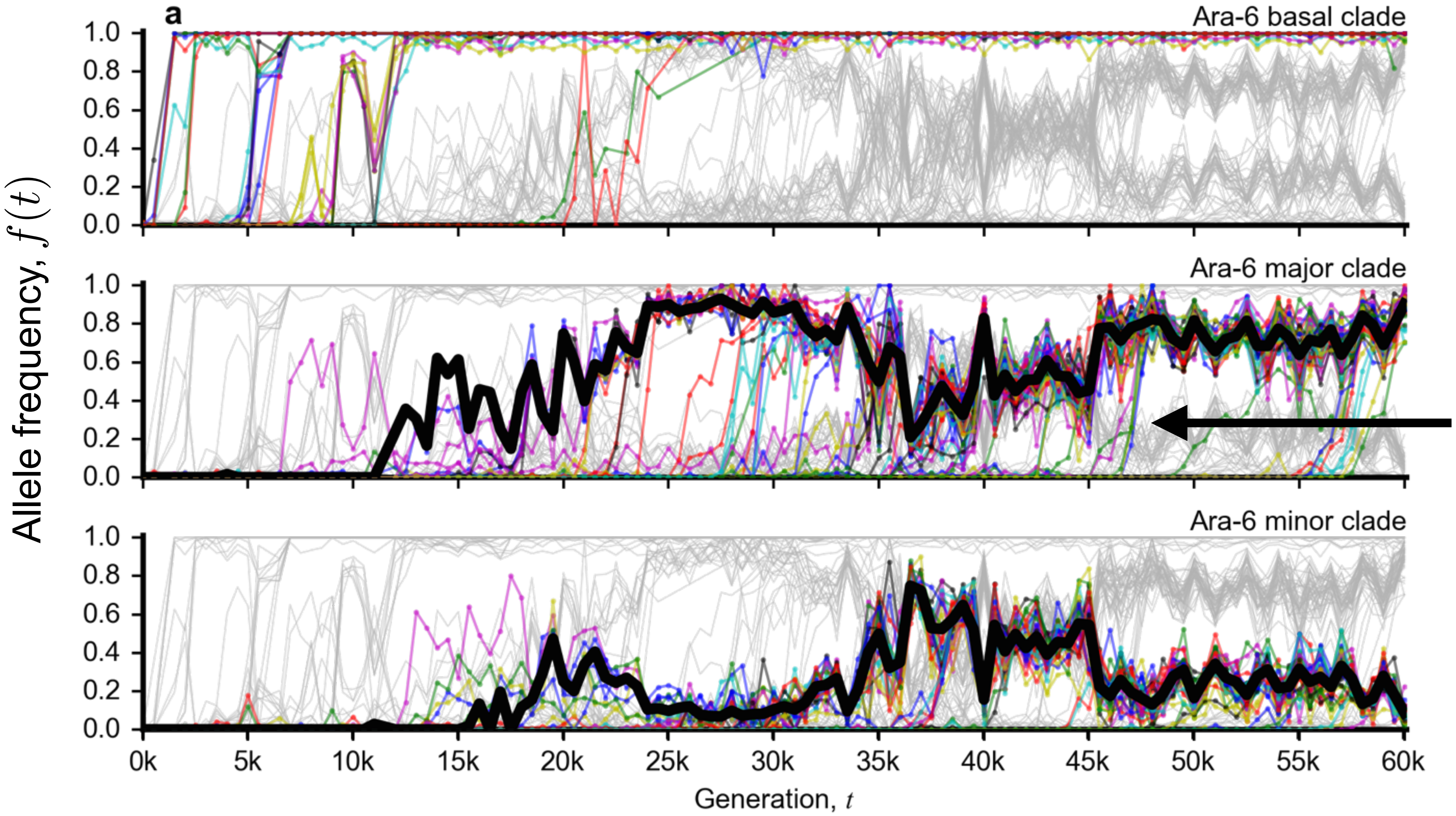

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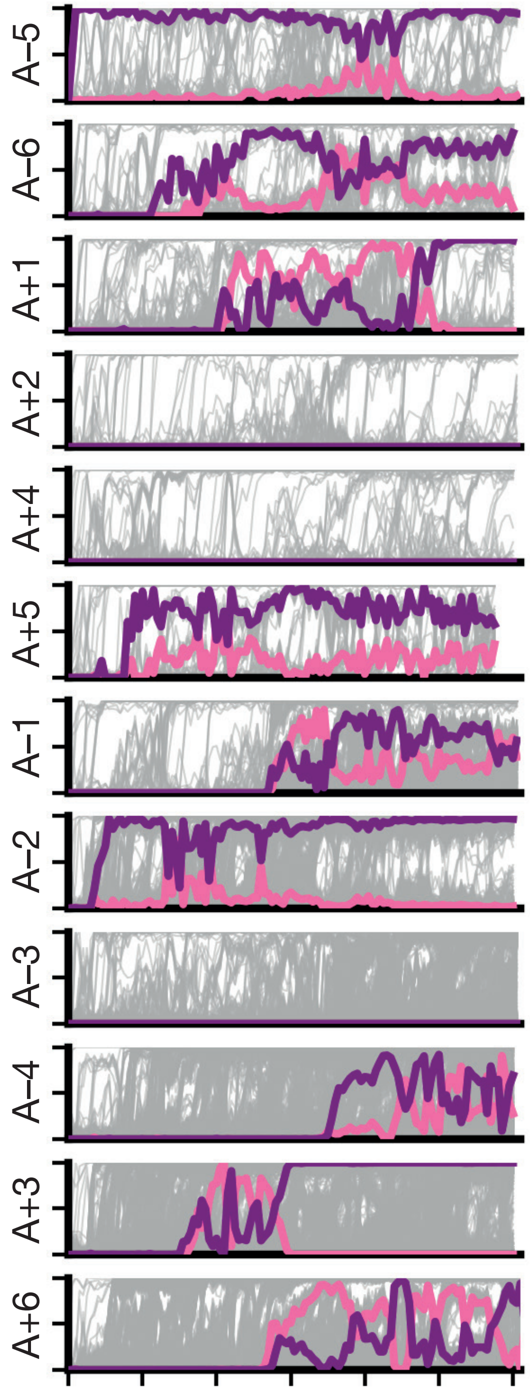
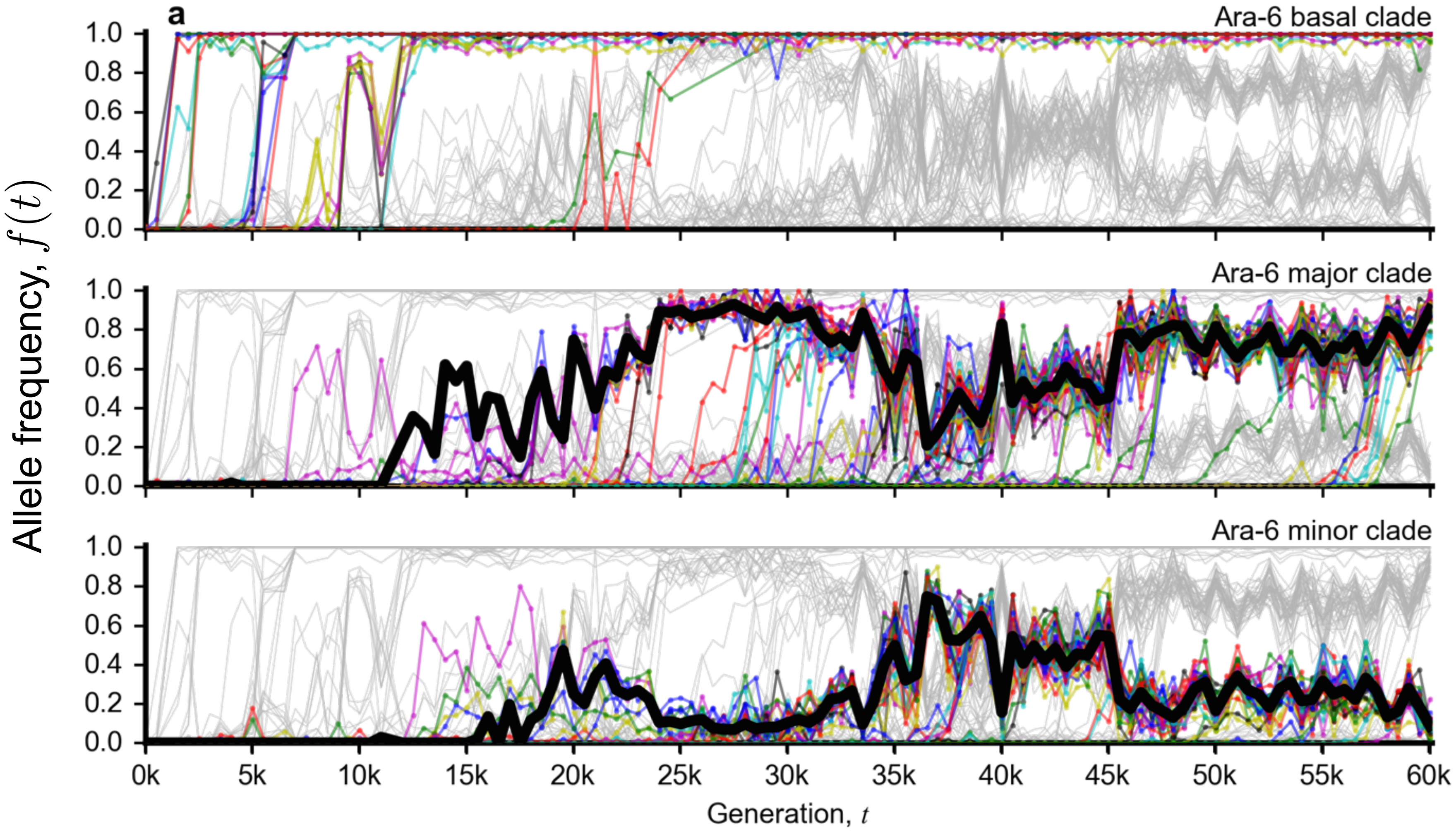


2. Mutations continue to fix ***within*** clades.

$$\tau_{\text{within}} \ll \tau_{\text{clade}}$$

Good, McDonald* et al (Nature, 2017)*

Inferring clade dynamics with hidden Markov models



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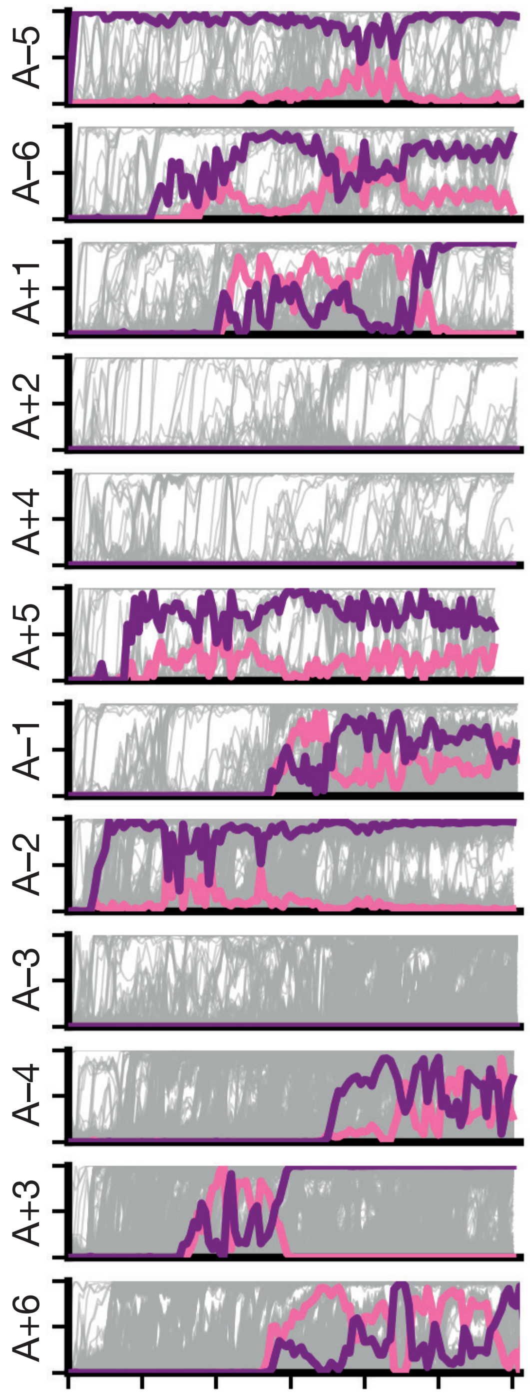
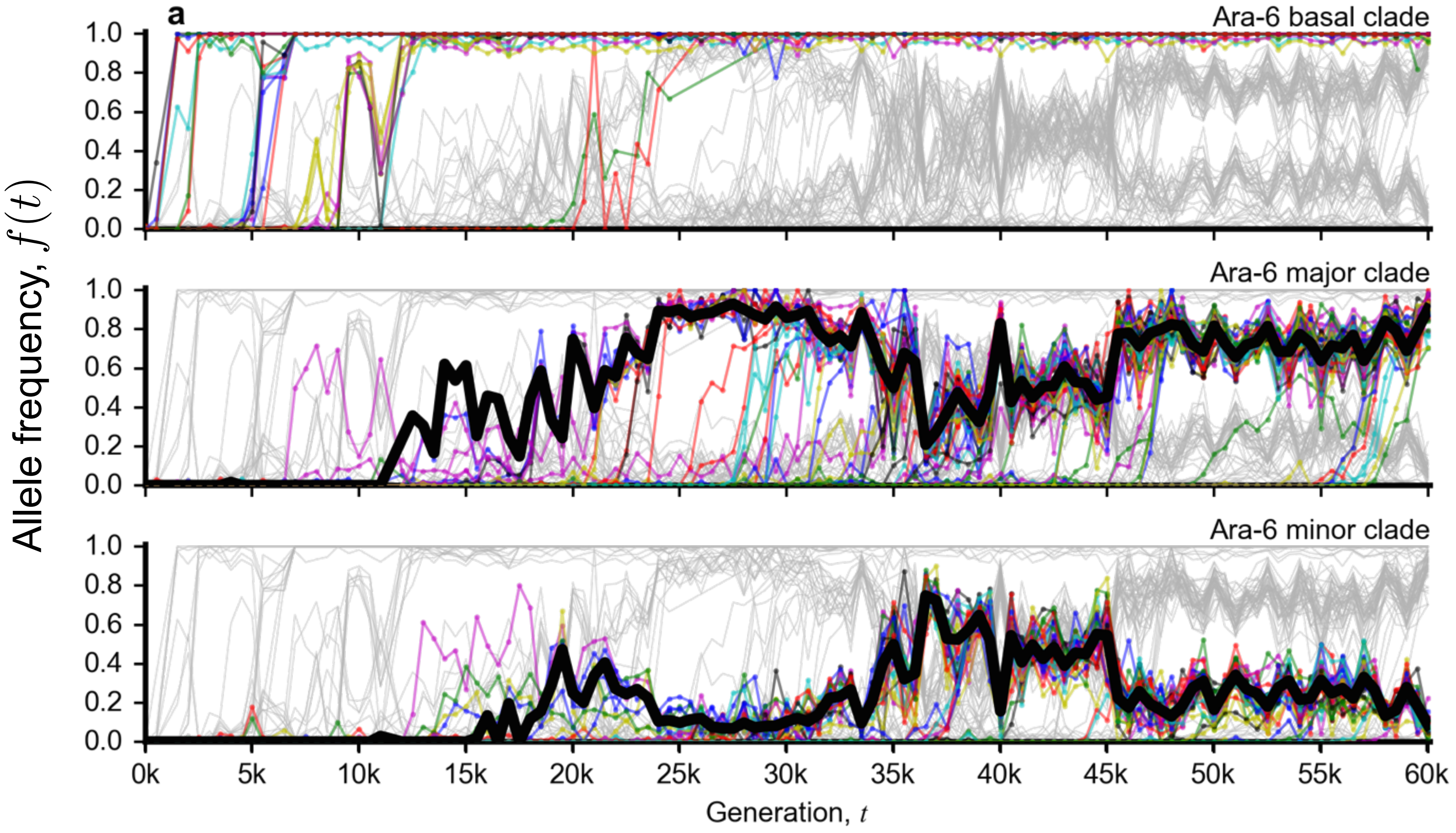


3. Separation of timescales ***inconsistent*** with null model of adaptation with linkage

Good, McDonald* et al (Nature, 2017)*

Inferring clade dynamics with hidden Markov models



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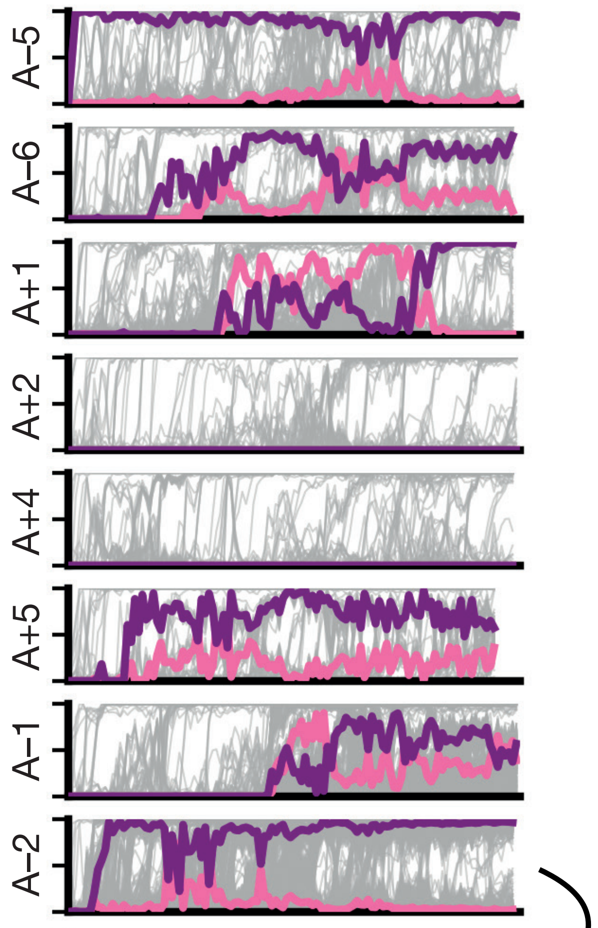
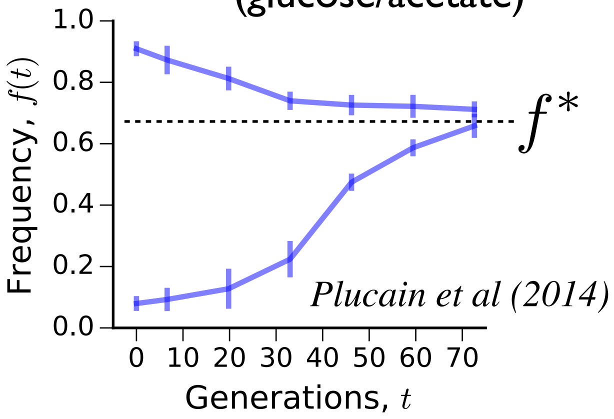


Stable coexistence
(glucose/acetate)



Plucain et al (2014)

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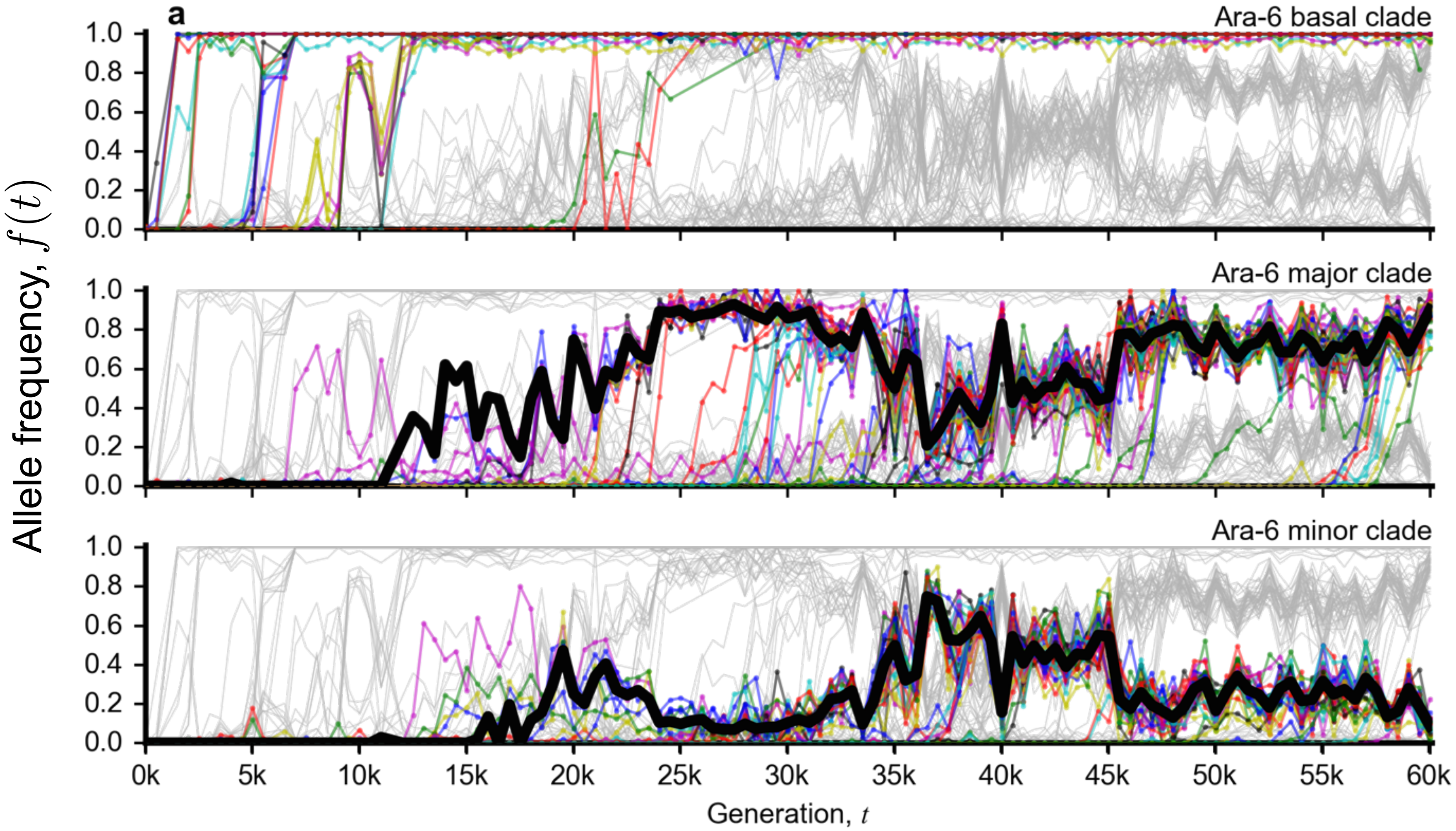
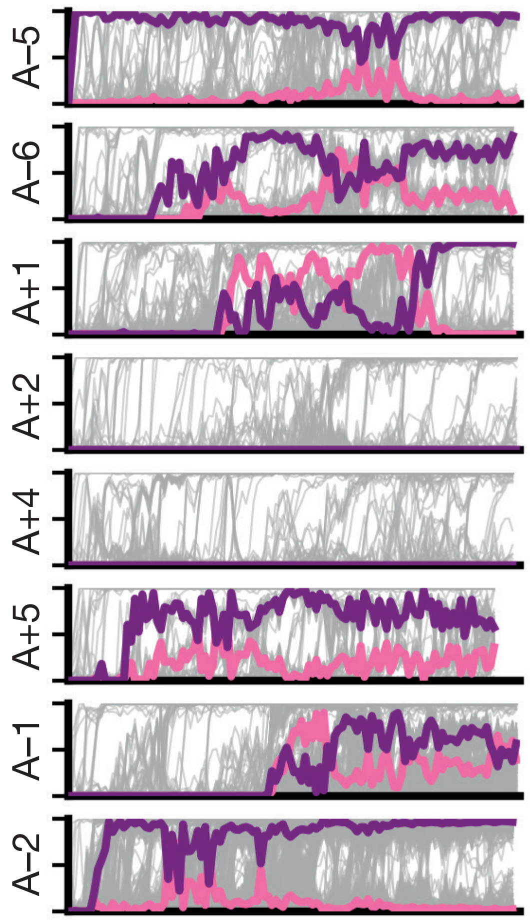


4. But ***quasi-stable*** on evolutionary timescales

All 12 pop'ns



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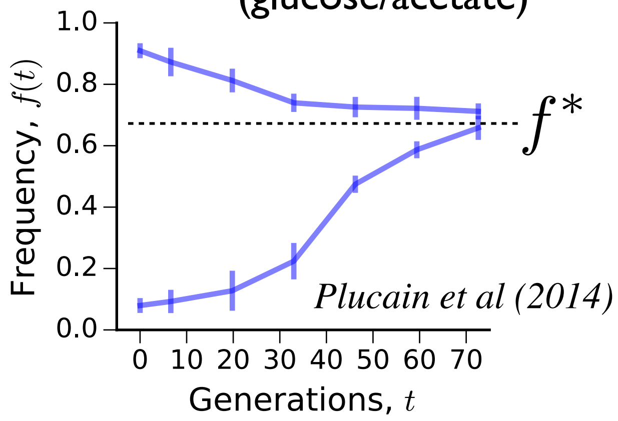

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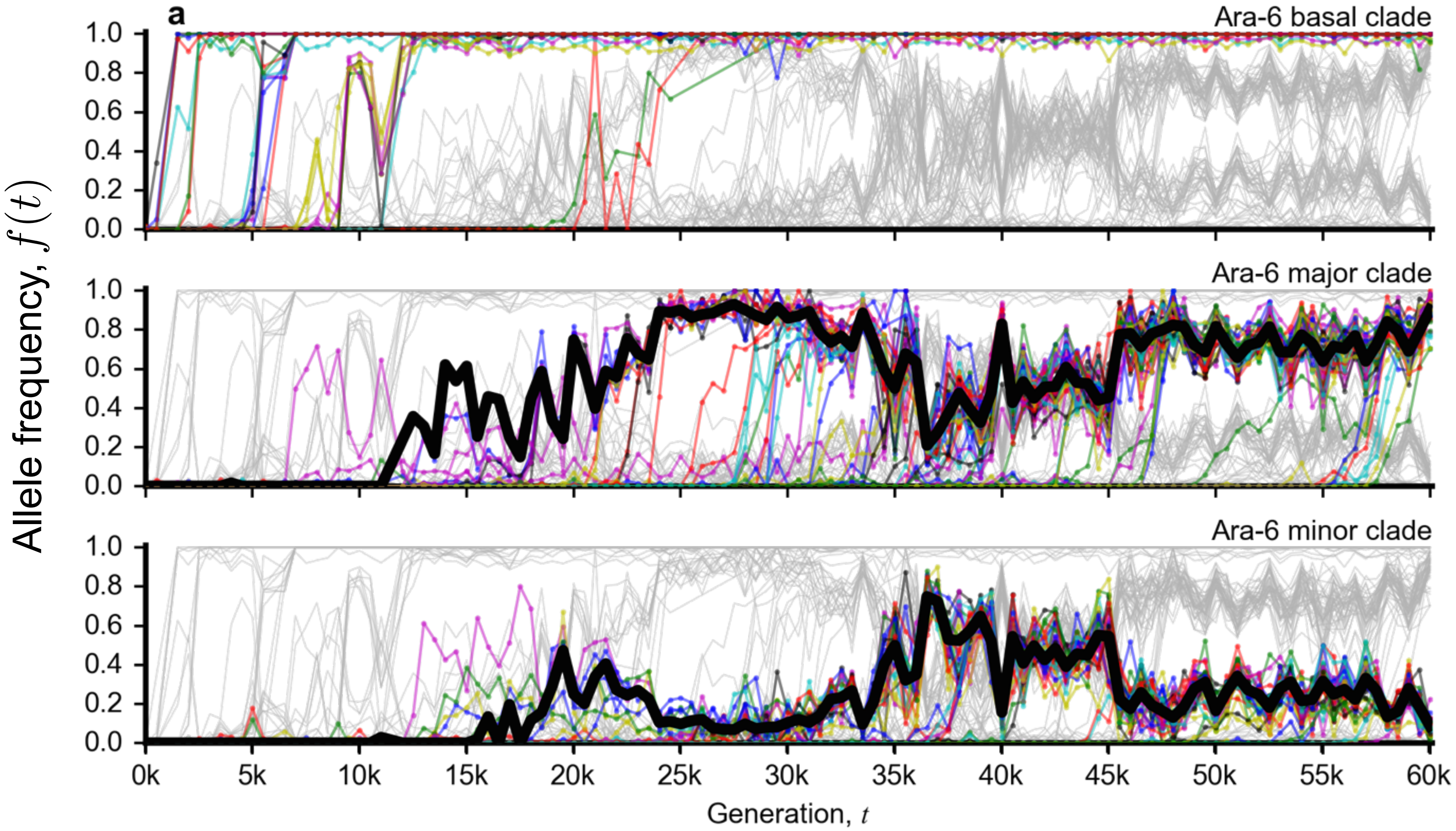

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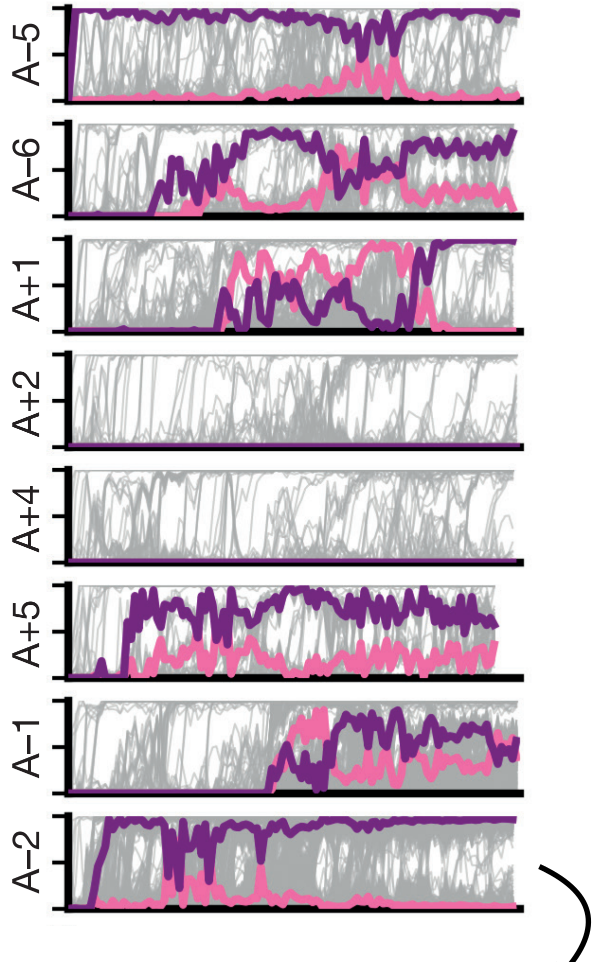

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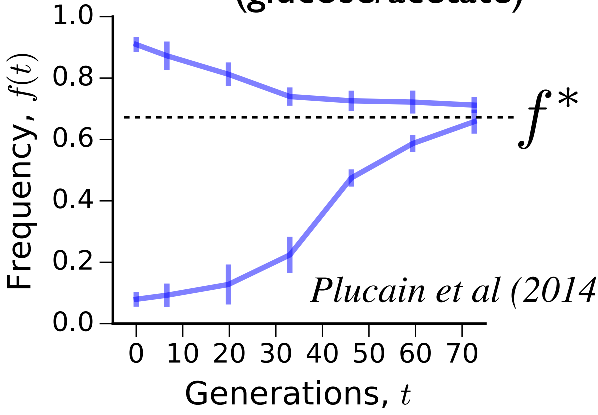

Plucain et al (2014)

5. High variability in clade freqs across replicates (both at endpoint and over time)

Good, McDonald* et al (Nature, 2017)*

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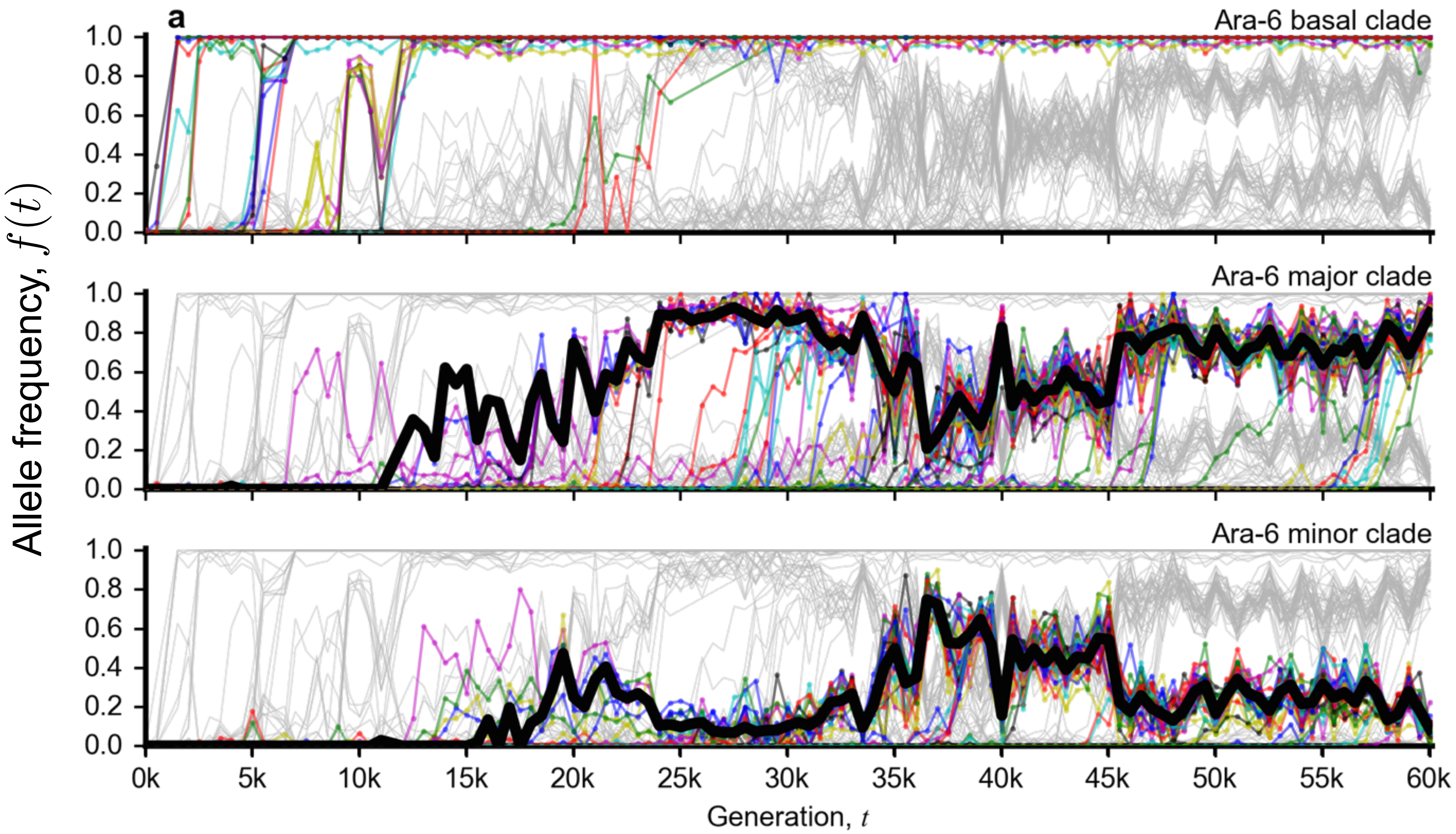

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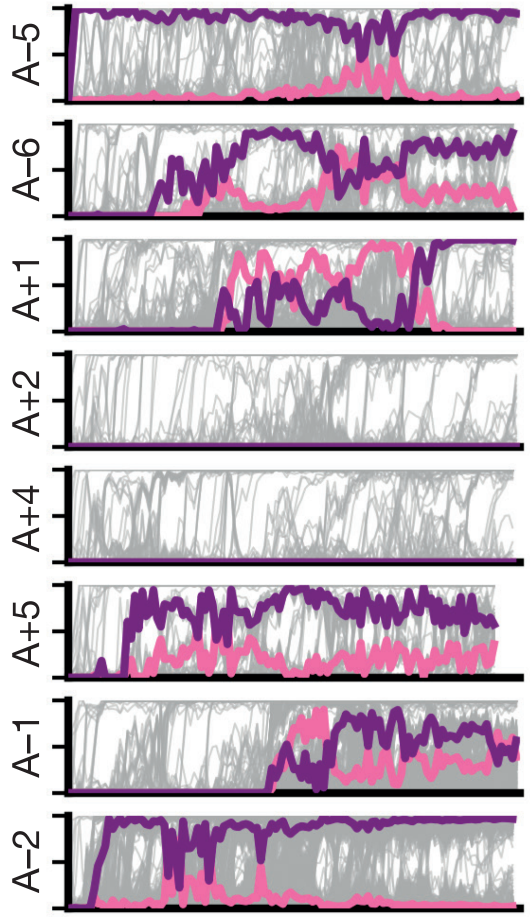

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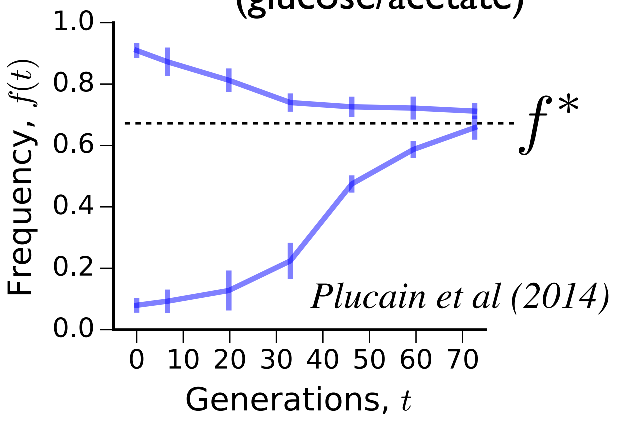
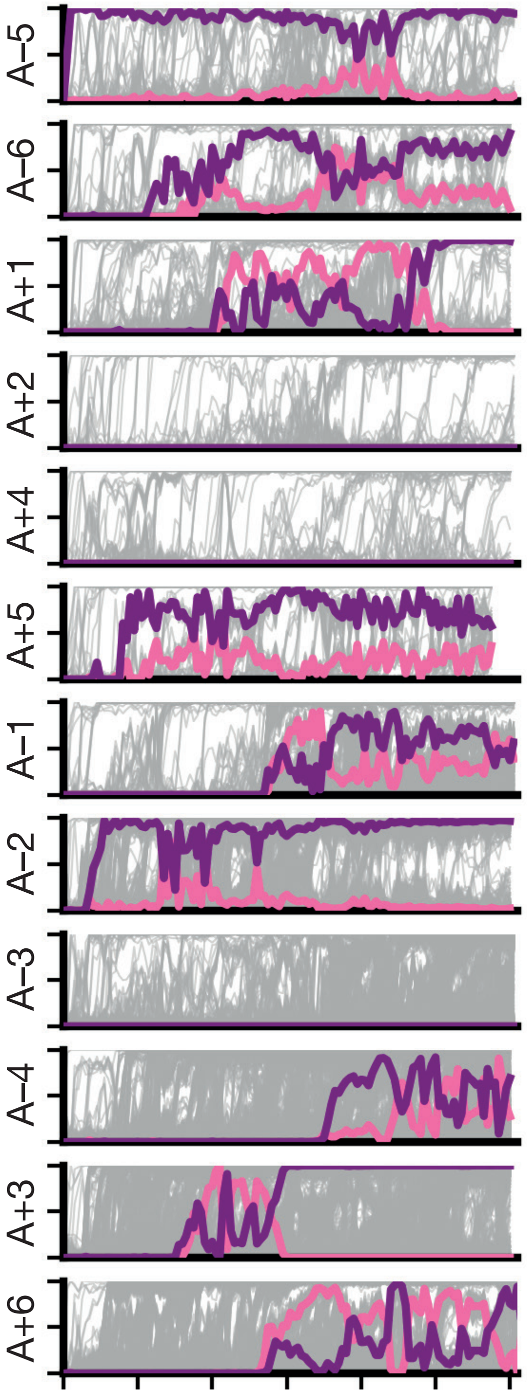


Plucain et al (2014)

Stochastic evolutionary forces play important role in shaping structure of community

Good, McDonald* et al (Nature, 2017)*

Coupled ecological and evolutionary processes



+
other laboratory systems…

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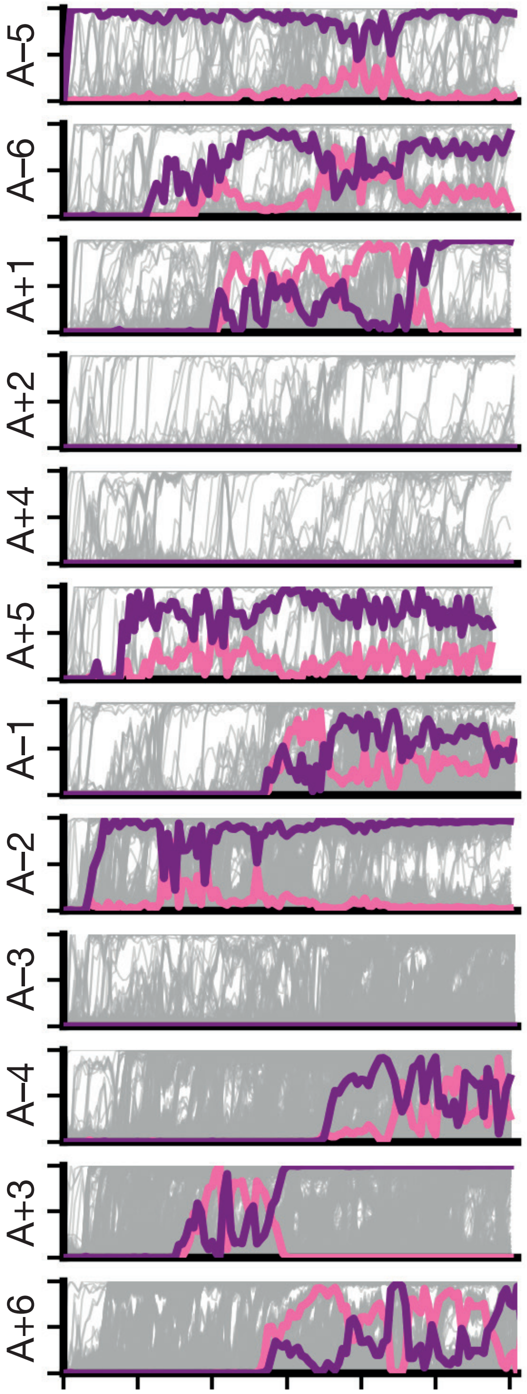

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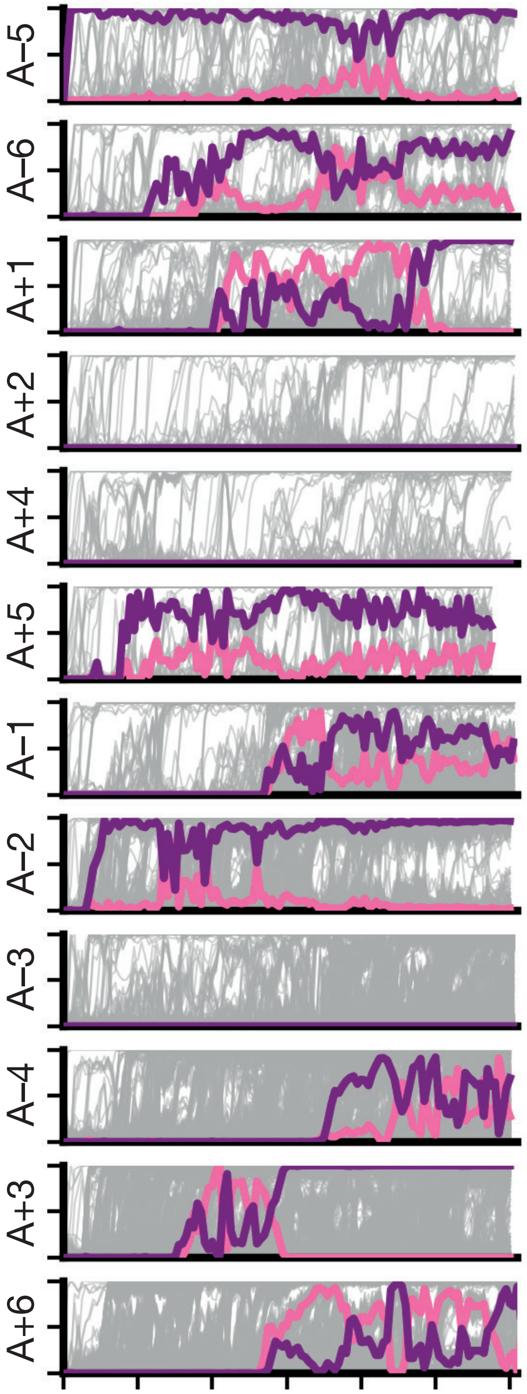

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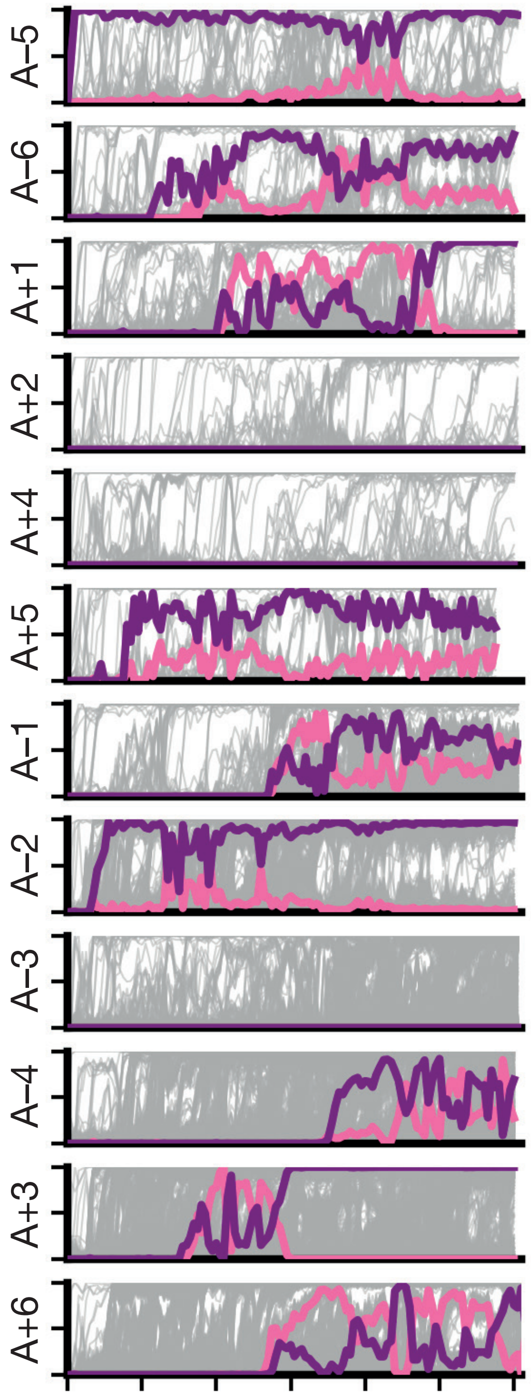

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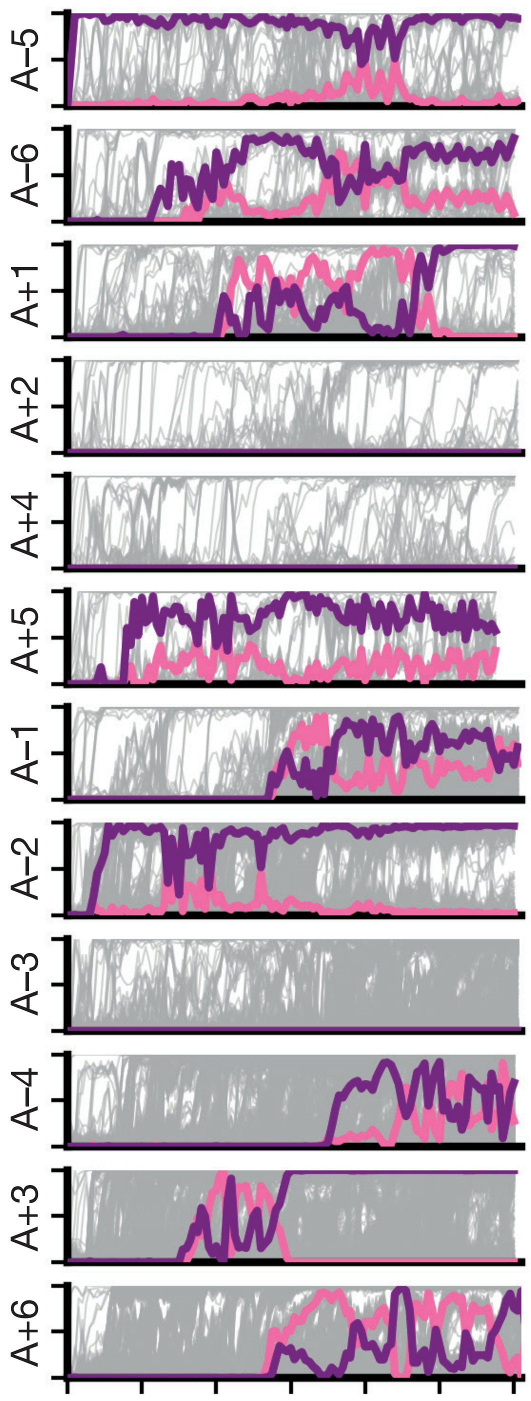

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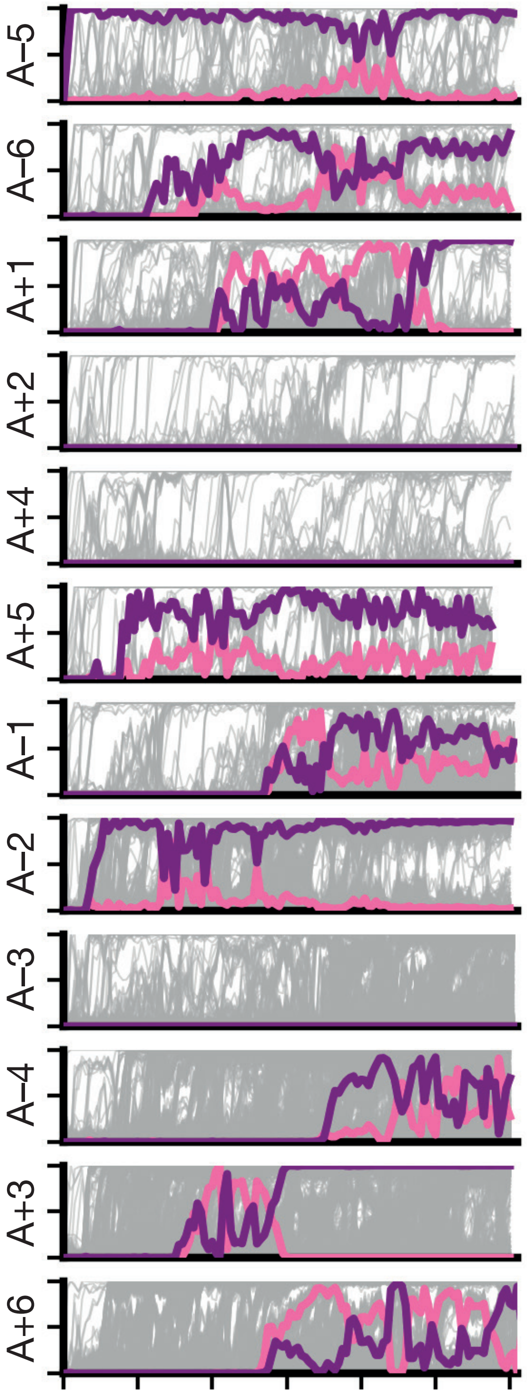

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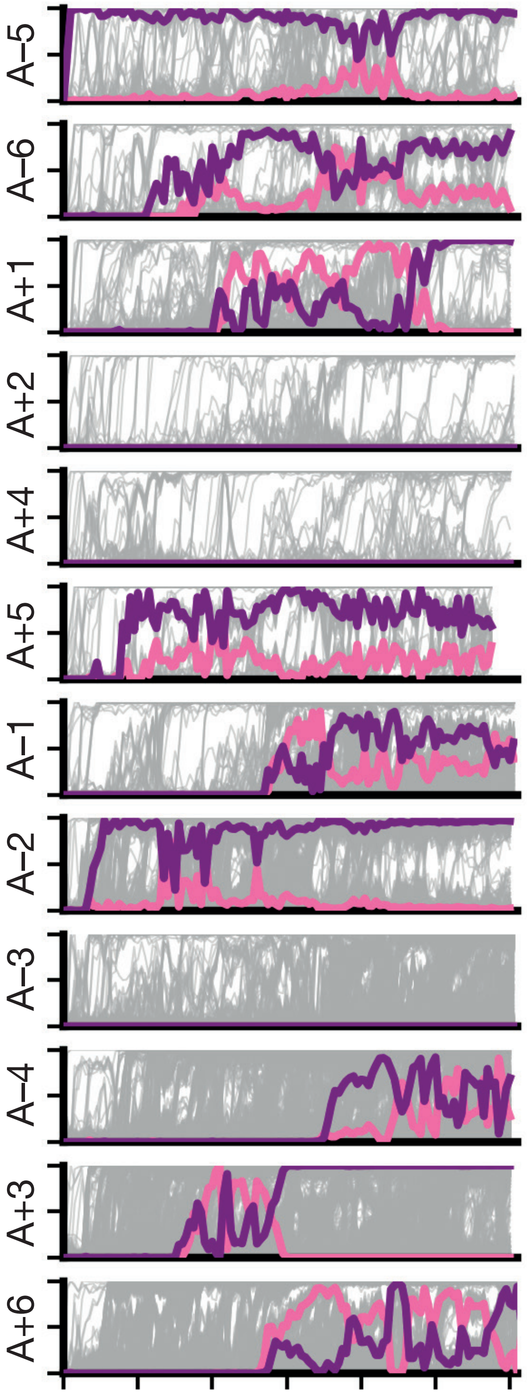

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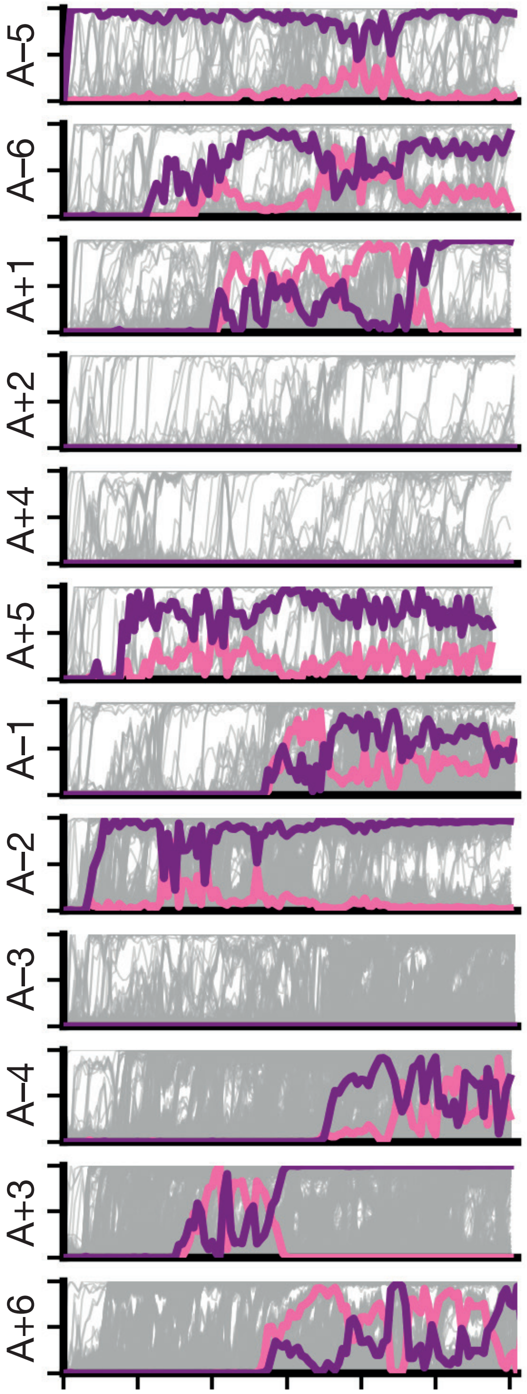

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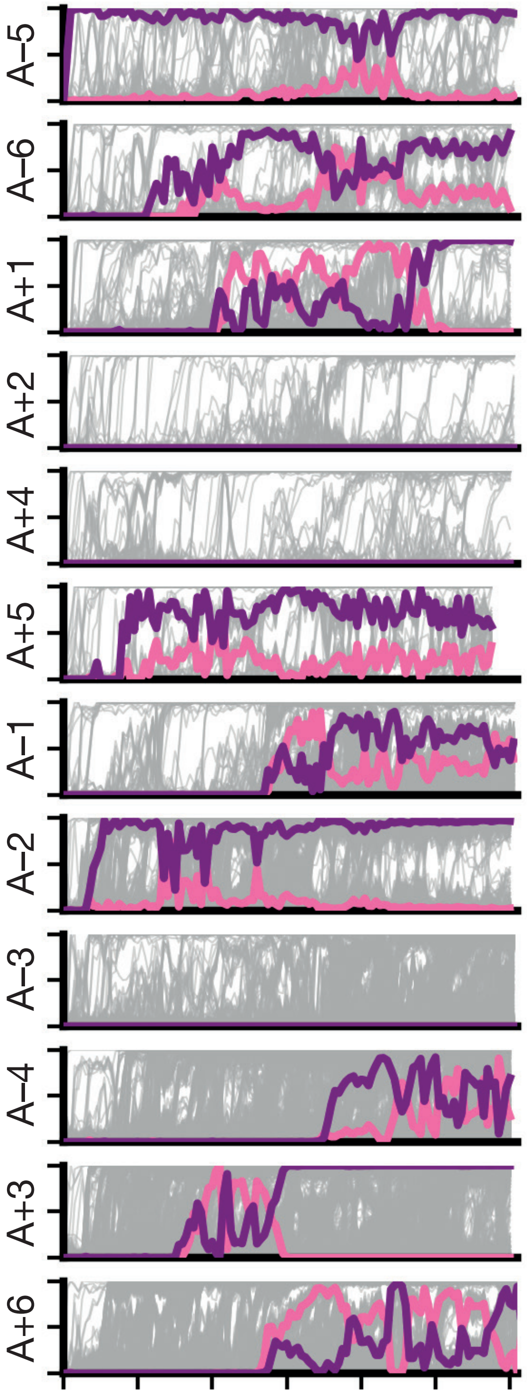

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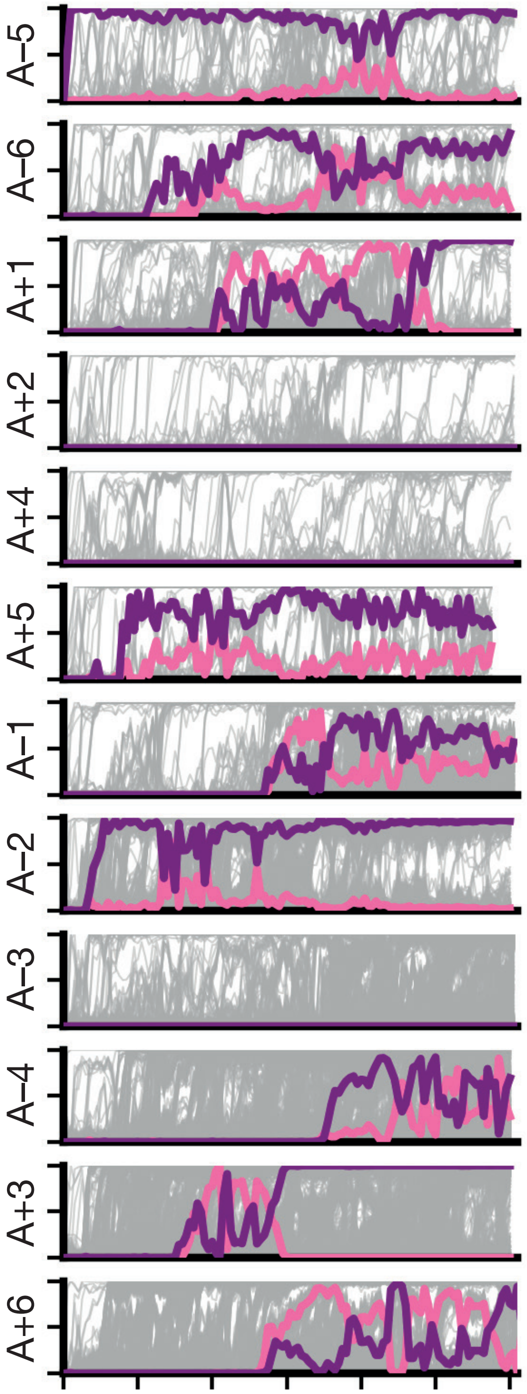

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Need quantitative theory

How to model feedback between ecology and evolution?

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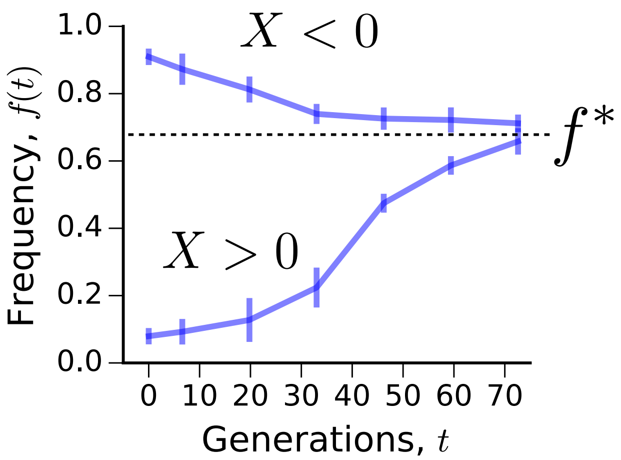

Frequency-dependent selection *(another type of interaction)*

$$X(\vec{g}) \to X[\vec{g}, \{f(\vec{g}')\}]$$

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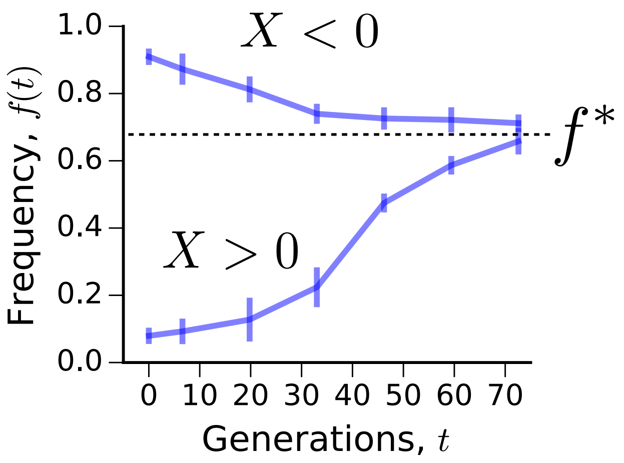

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hard to model!
(many params)

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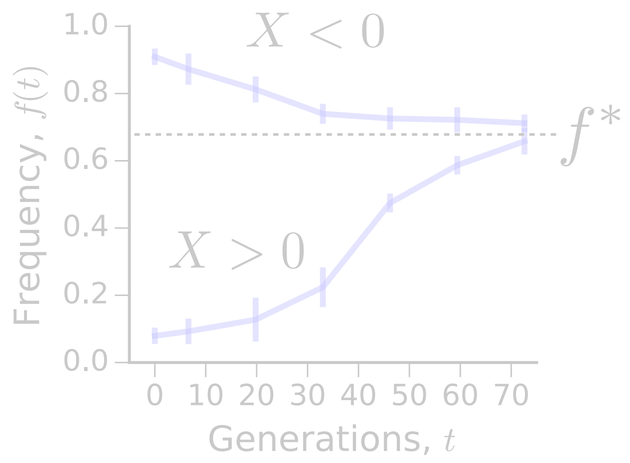

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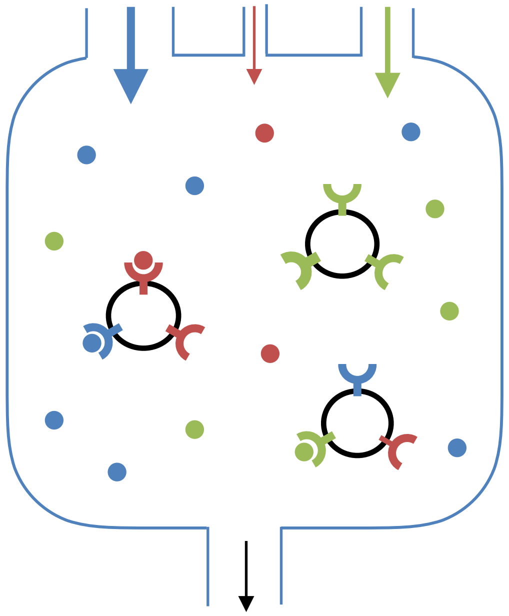
II. An empirically-motivated toy model

a Competition for $\mathcal{R} > 1$ resources



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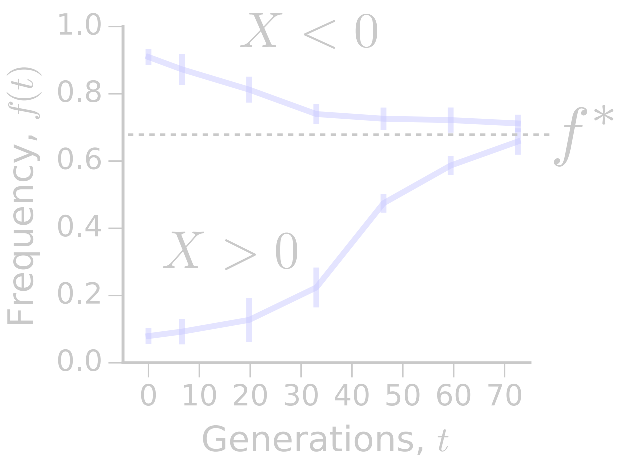

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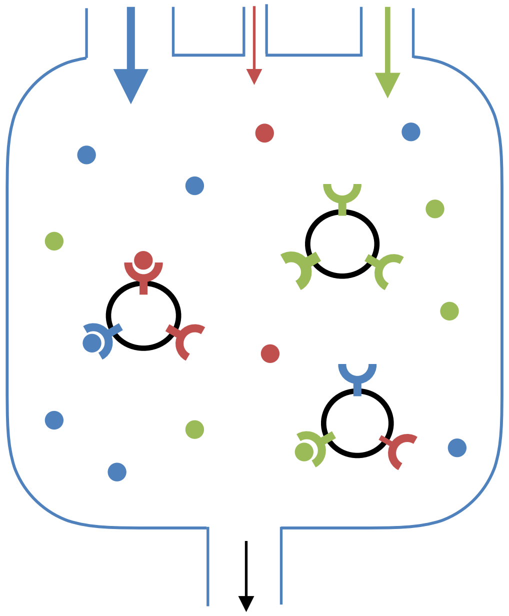

"Environmental supply vector"

β_i = % biomass supplied by resource i

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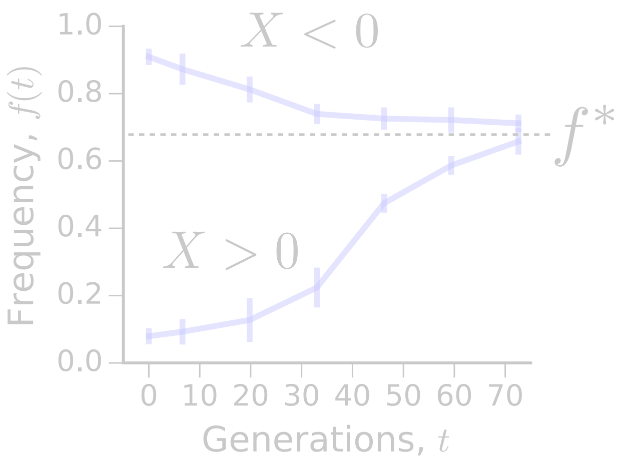

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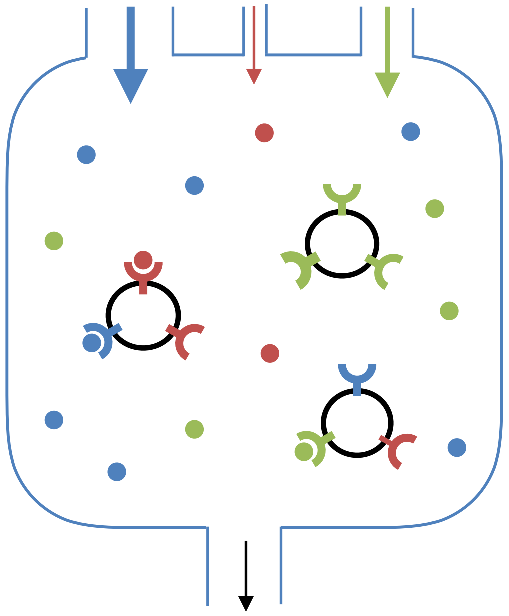

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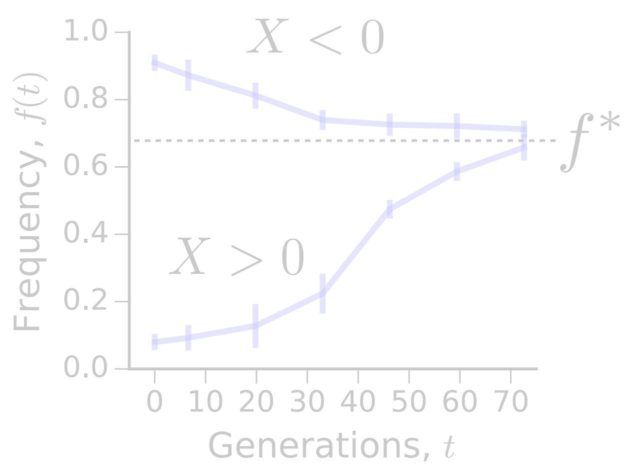

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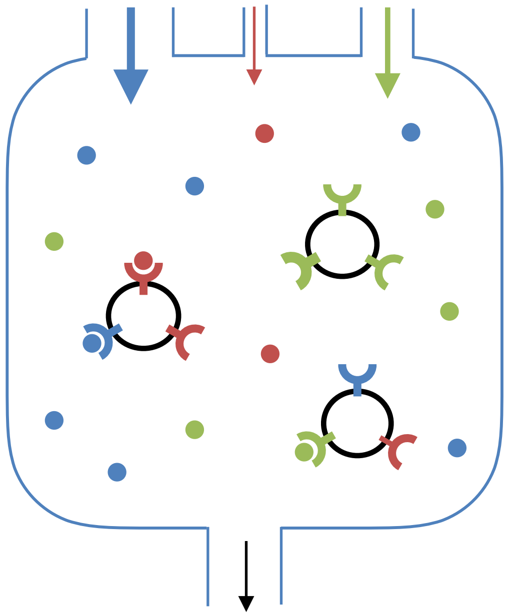

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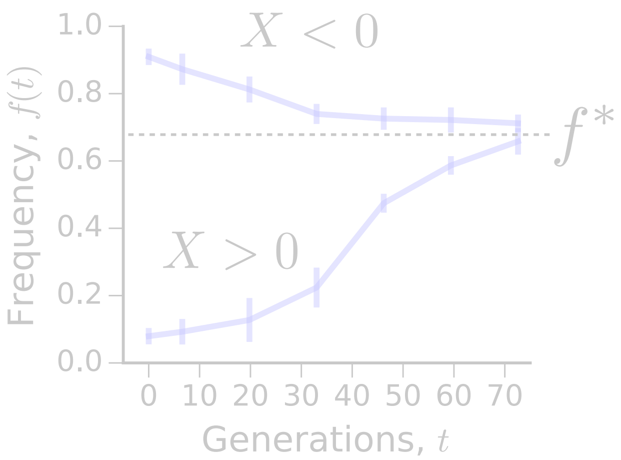

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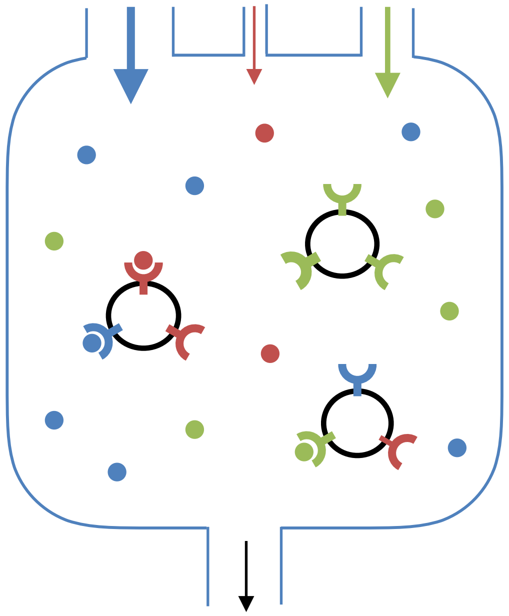

Frequencies of strains

$$\frac{\partial f_\mu}{\partial t} \approx \sum_i \alpha_{\mu,i} \left[X_\mu - \overline{X}_i\right] f_\mu + \text{genetic drift}$$

"Resource-specific mean fitness"

$$\overline{X}_i \equiv \log\left(\sum_\mu \frac{\alpha_{\mu,i}}{\beta_i} e^{X_\mu} f_\mu\right)$$

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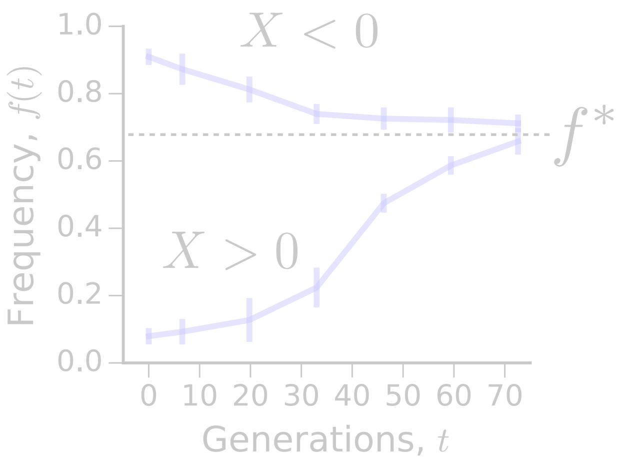

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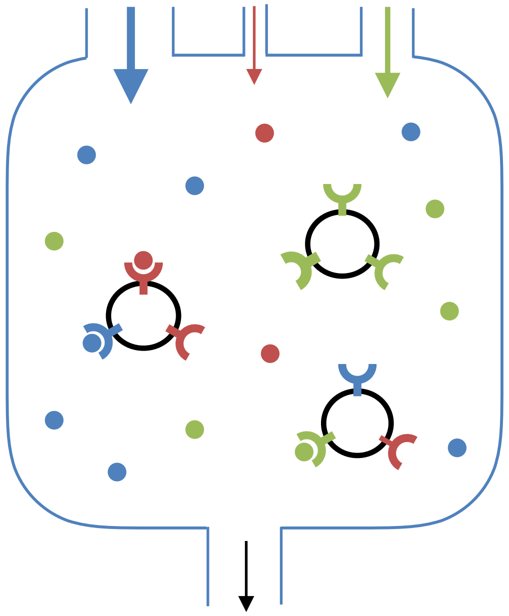

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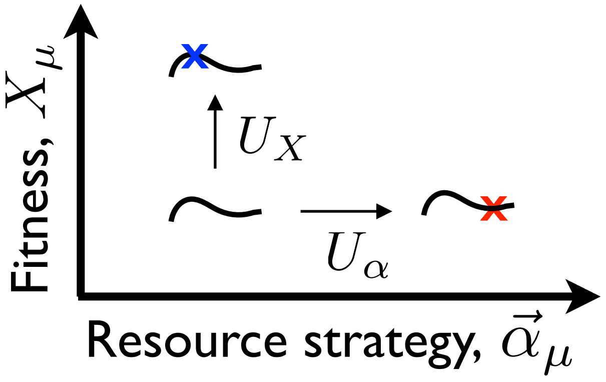
b Heritable mutations



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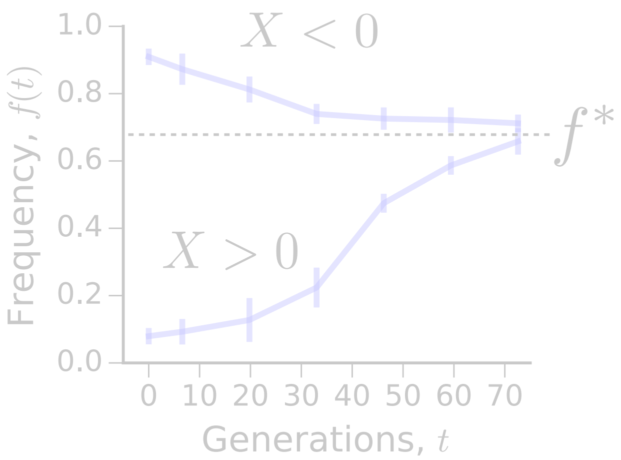

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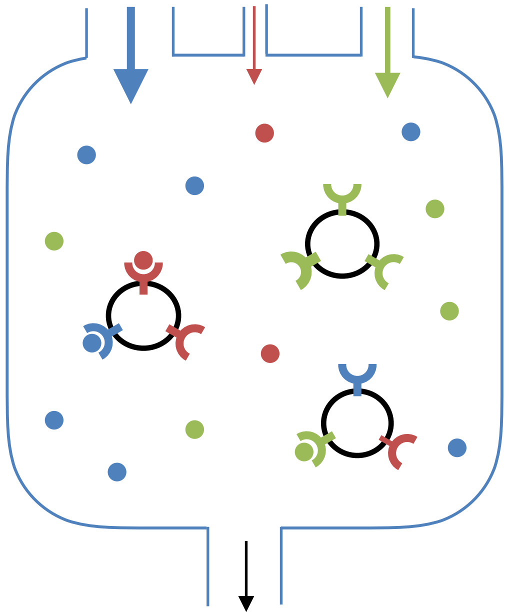
II. An empirically-motivated toy model

a Competition for $\mathcal{R} > 1$ resources



Frequencies of strains

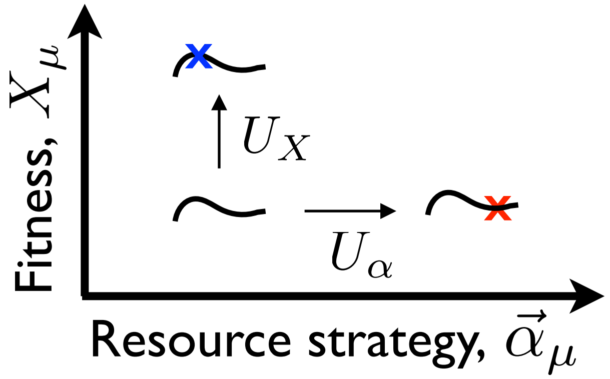
$$\frac{\partial f_\mu}{\partial t} \approx \sum_i \alpha_{\mu,i} \left[X_\mu - \overline{X}_i \right] f_\mu + \text{genetic drift}$$

"Resource-specific mean fitness"

$$\overline{X}_i \equiv \log \left(\sum_\mu \frac{\alpha_{\mu,i}}{\beta_i} e^{X_\mu} f_\mu \right)$$

Experiments: lots of "non-metabolic" adaptation going on at same time!

b Heritable mutations



"Environmental supply vector"

β_i = % biomass supplied by resource i

"Resource strategy"

$\alpha_{\mu,i}$ = % energy strain μ spends to import resource i

"General fitness"

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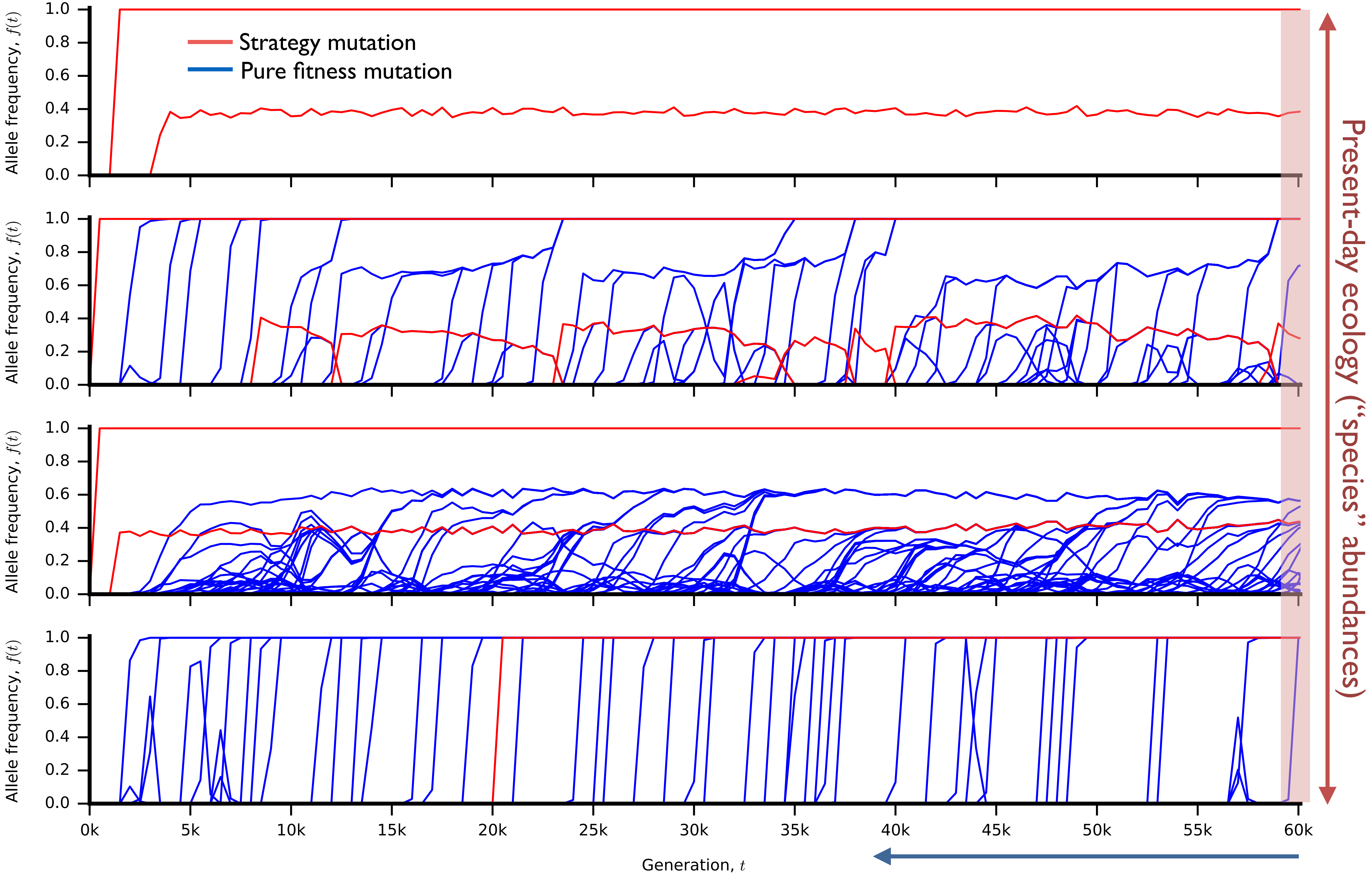
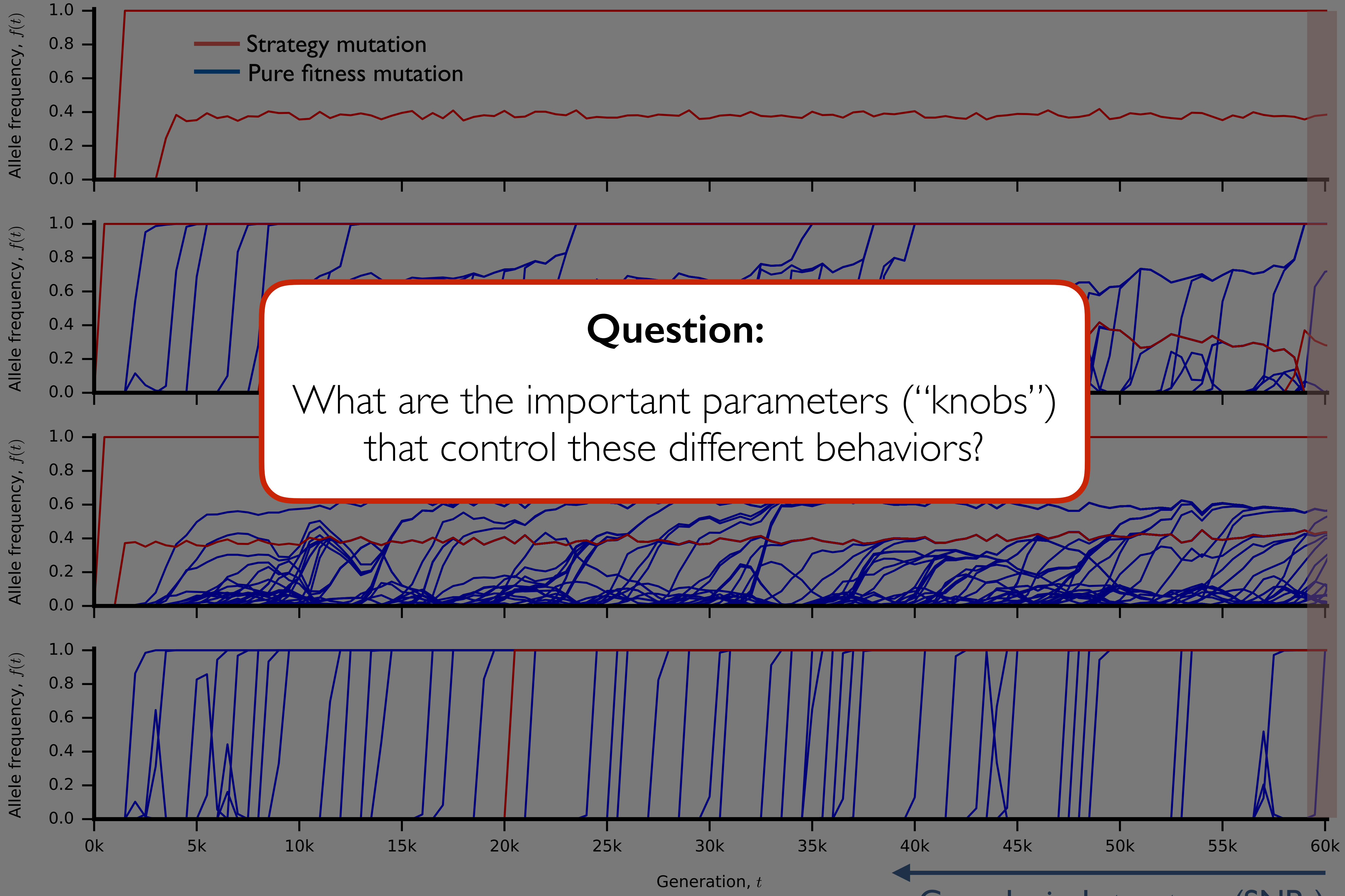
Simulations w/ same ecological opportunities, different supply of "fitness" mutations



Present-day ecology ("species" abundances)

Genealogical structure (SNPs)

Simulations w/ same ecological opportunities, different supply of "fitness" mutations



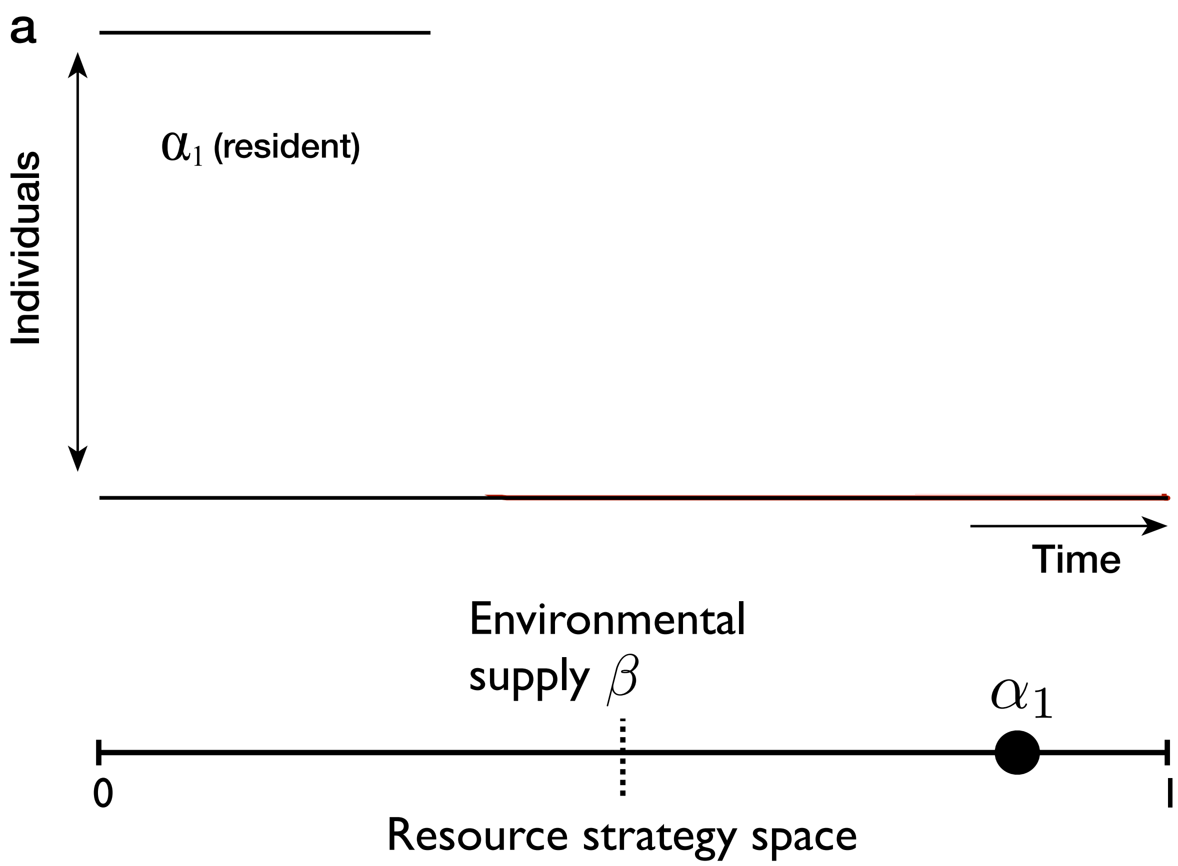
Question:

What are the important parameters ("knobs") that control these different behaviors?

Present-day ecology ("species" abundances)

Genealogical structure (SNPs)

“Neutral” case: selection for *ecosystem* to match environment



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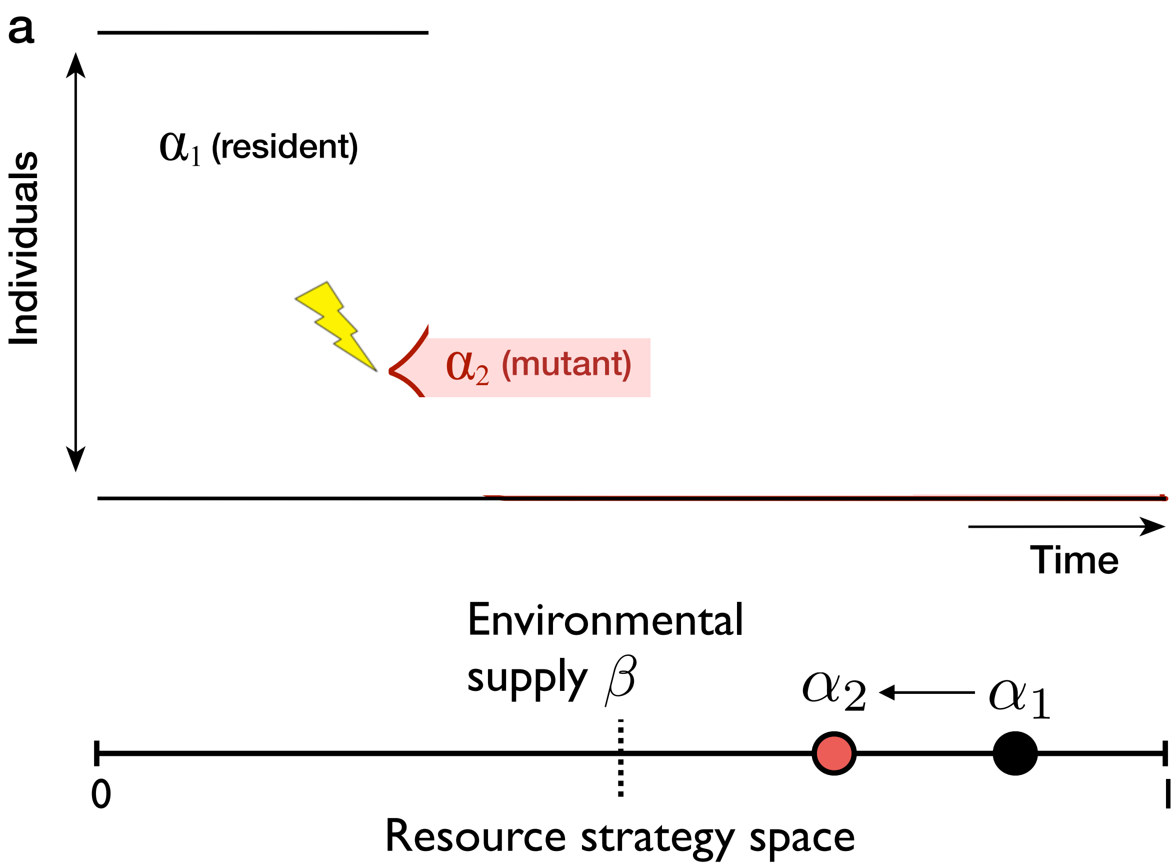

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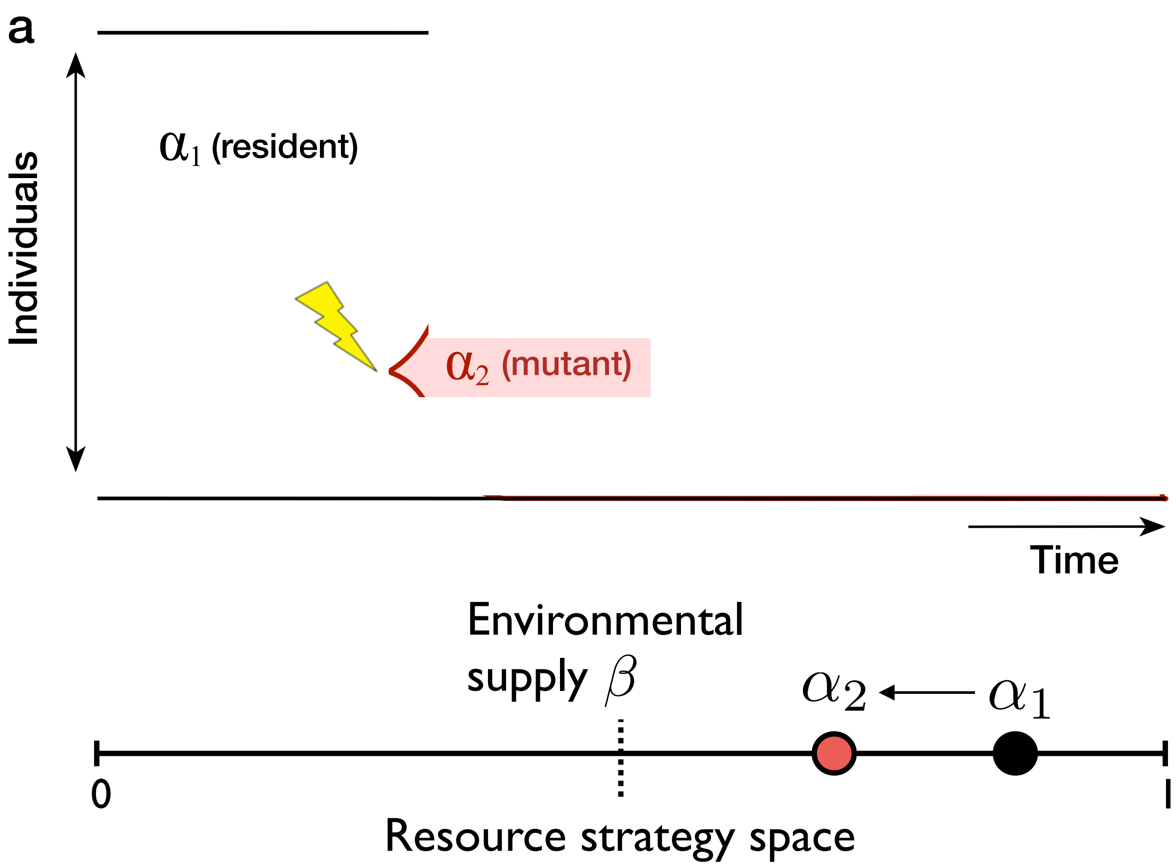

“Ecological” selection pressure:

$$s_{\text{eff}}(\alpha_1 \to \alpha_2) \propto \Delta\alpha(\beta - \alpha_1)$$

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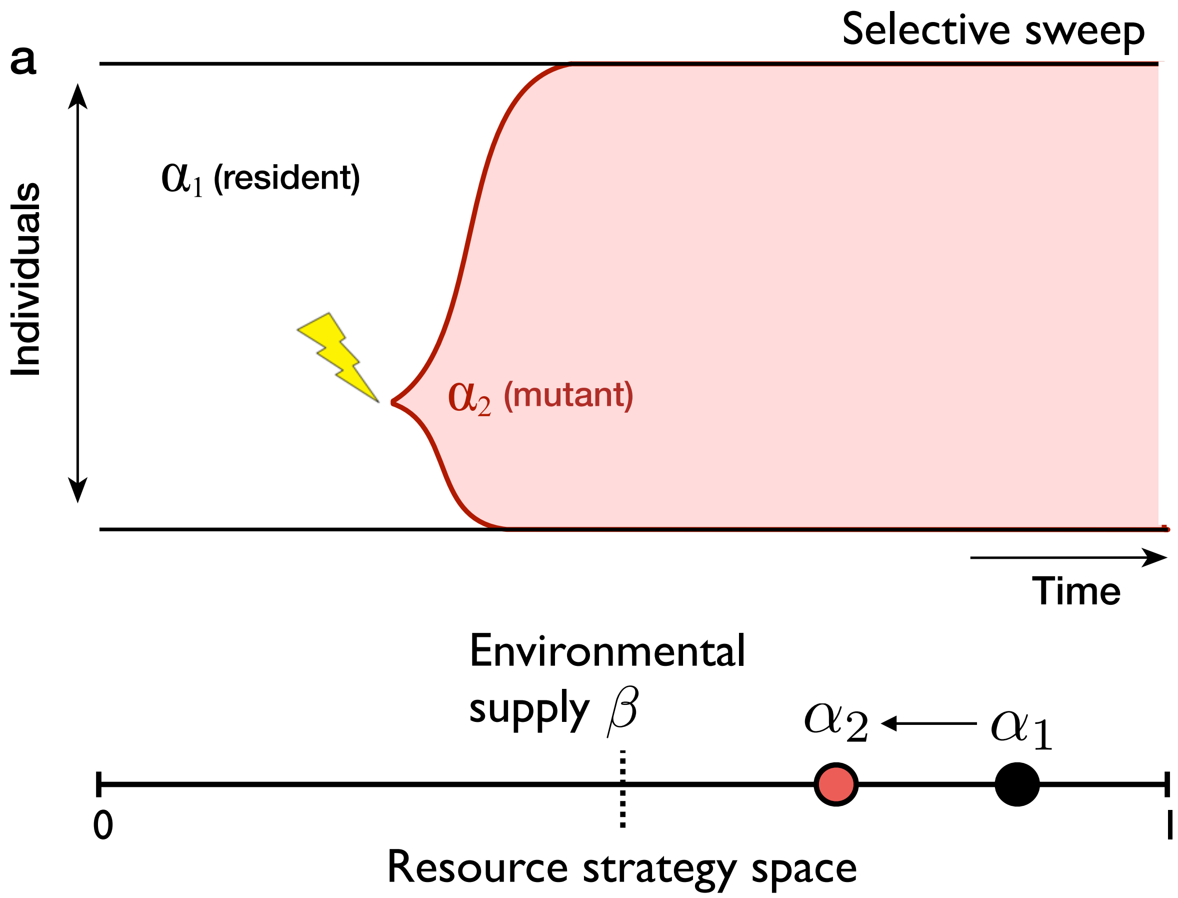

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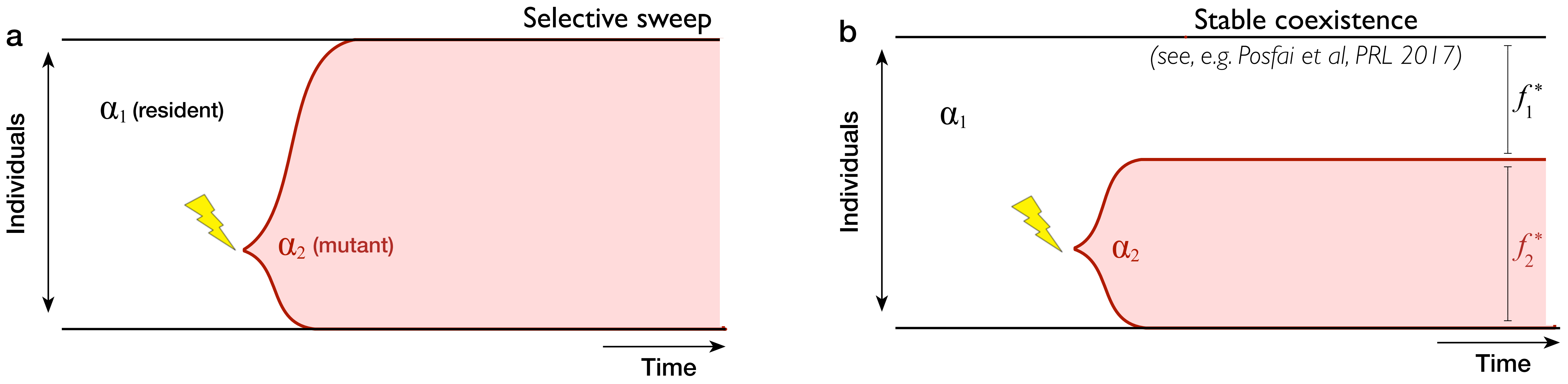

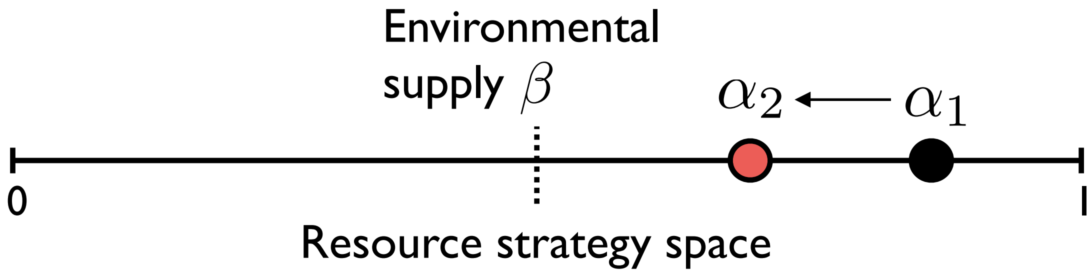

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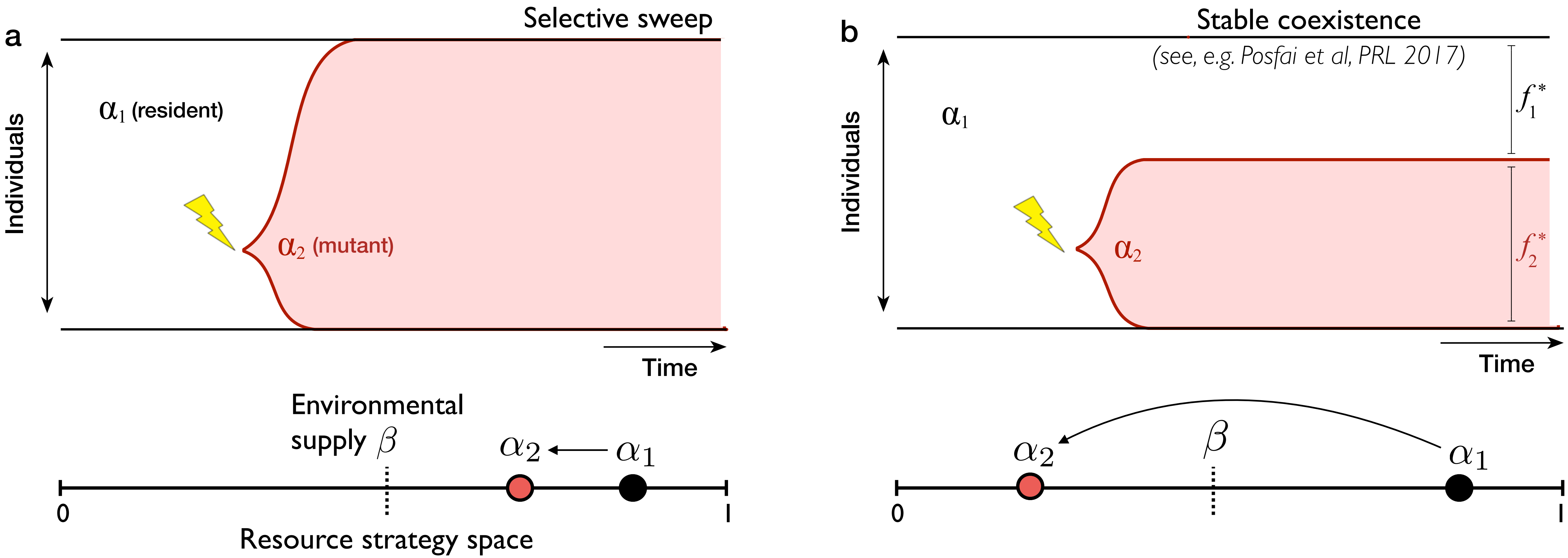

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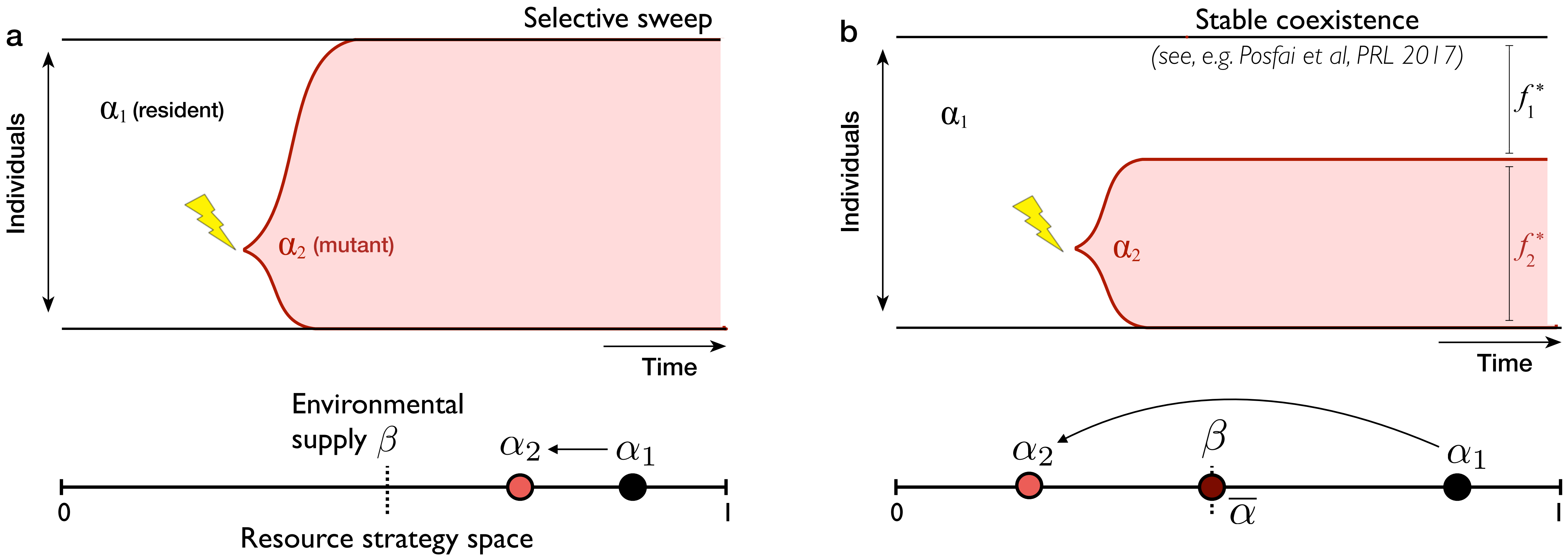

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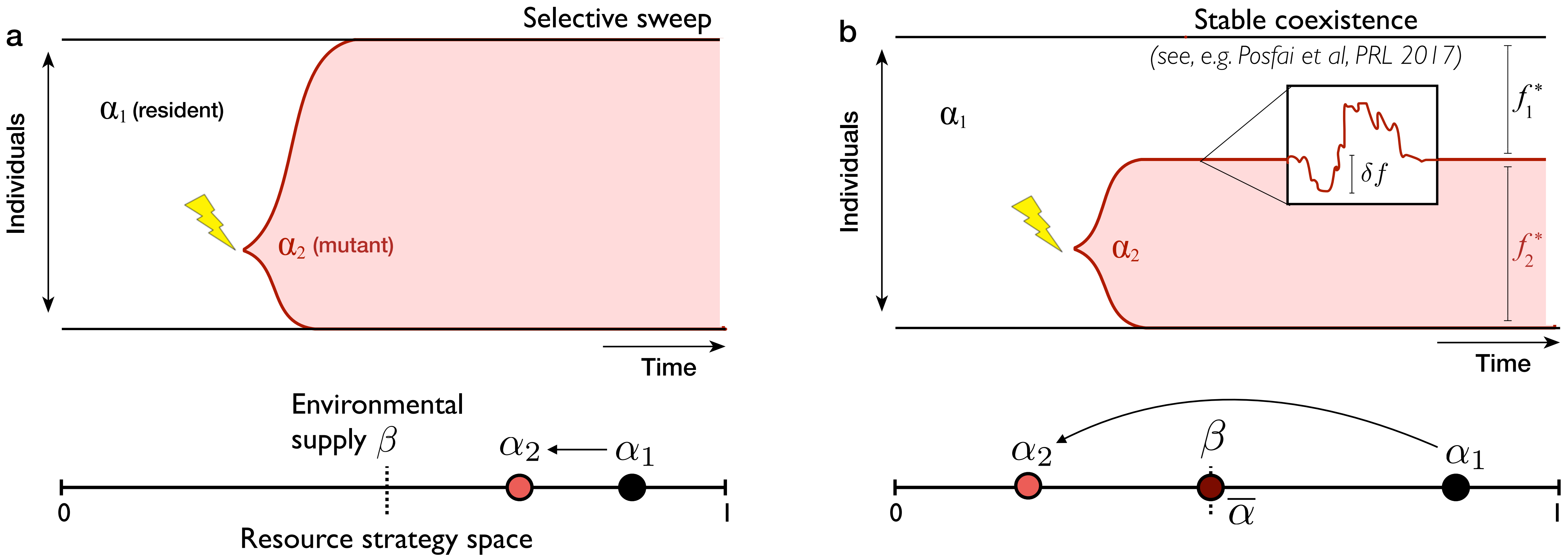

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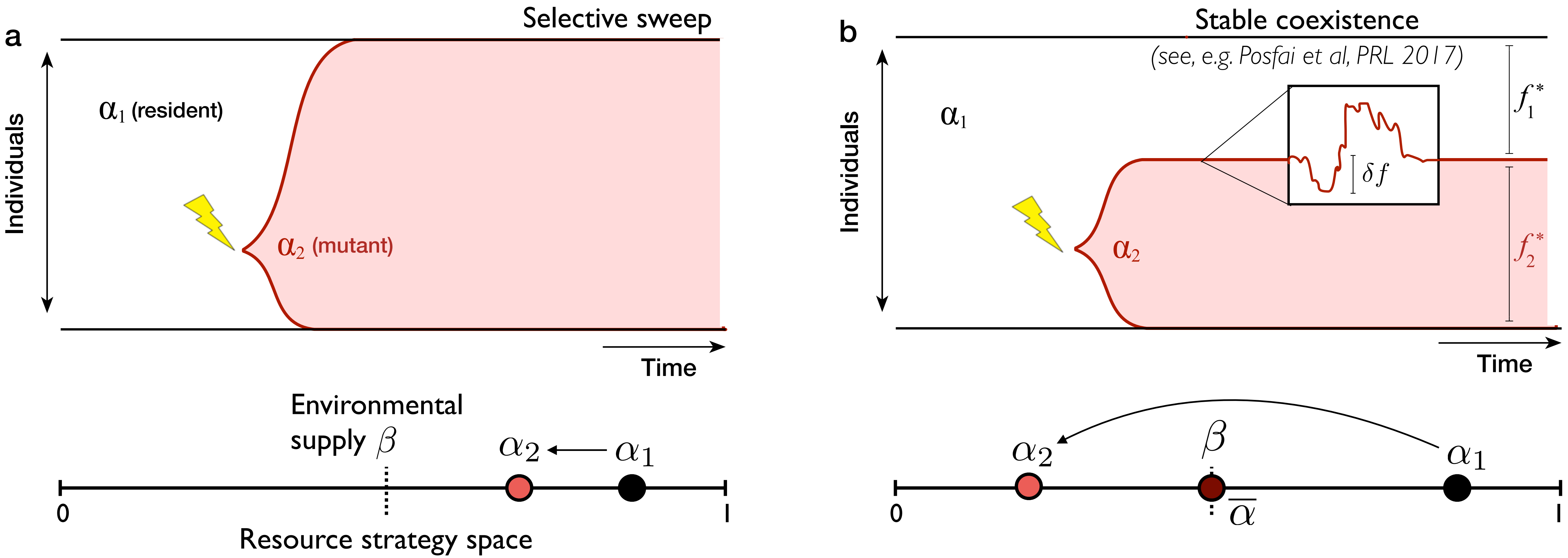

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$$s_{\text{eff}}(\alpha_1 \to \alpha_2) \propto \Delta\alpha(\beta - \alpha_1)$$

Marginal stability against add’l muts

$$s_{\text{eff}}(\alpha_i \to \alpha_3) \sim \mathcal{O}(1/N)$$

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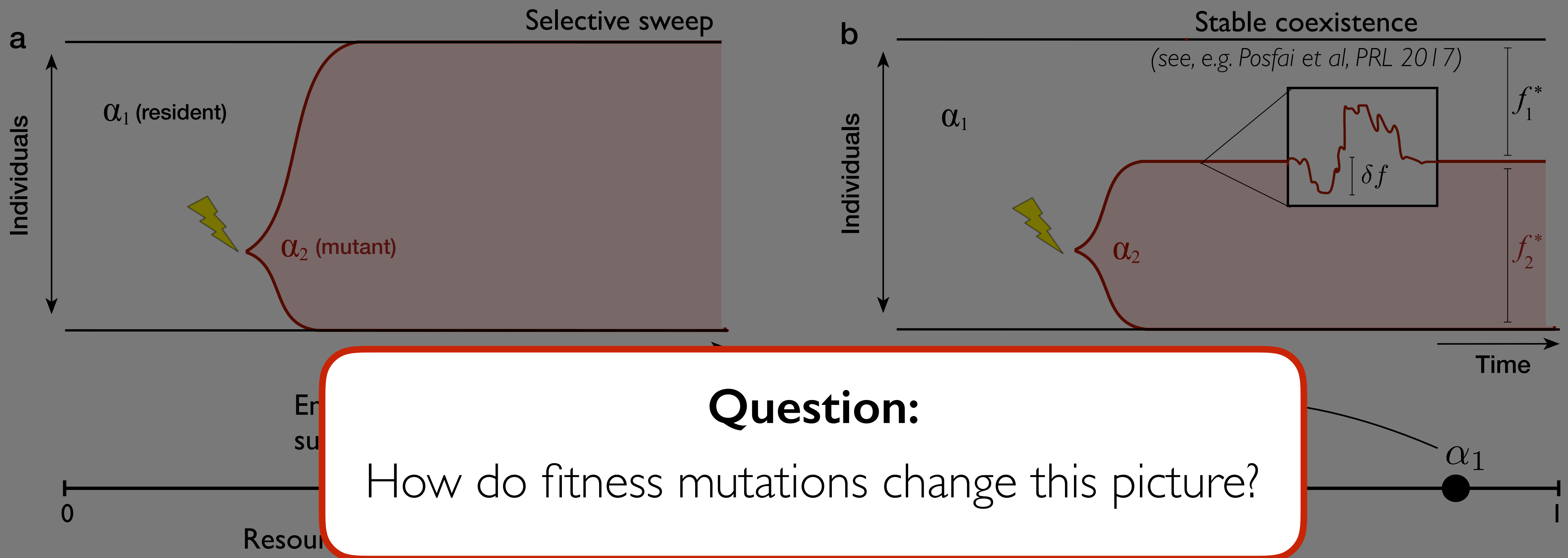

Question:

How do fitness mutations change this picture?

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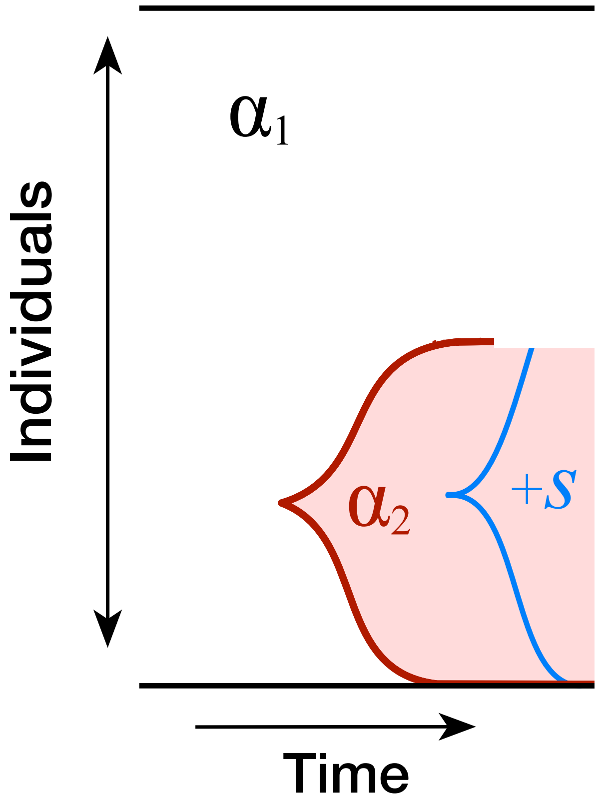
Diversification-selection balance



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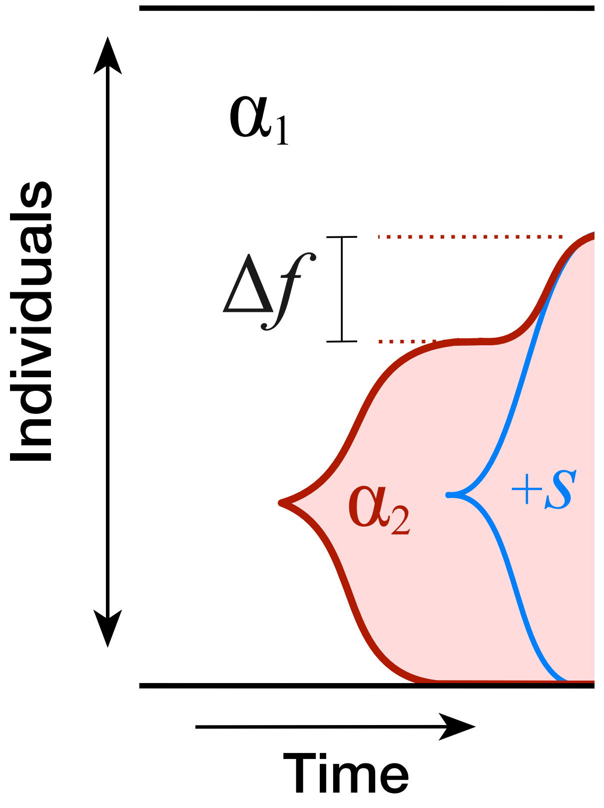

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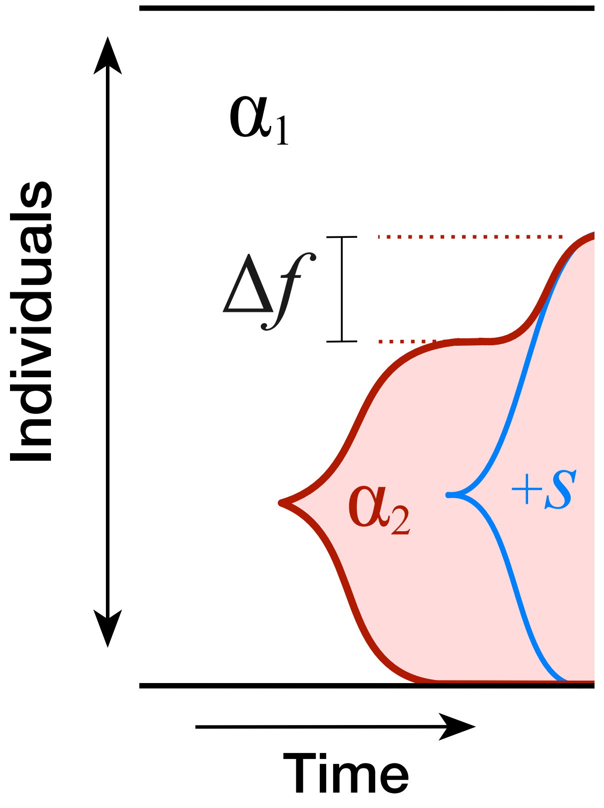

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$$\Delta f \approx \frac{\Delta X}{X^*}; \quad X^* \approx \frac{\Delta\alpha^2}{\beta(1-\beta)}$$

"Evolutionary robustness"

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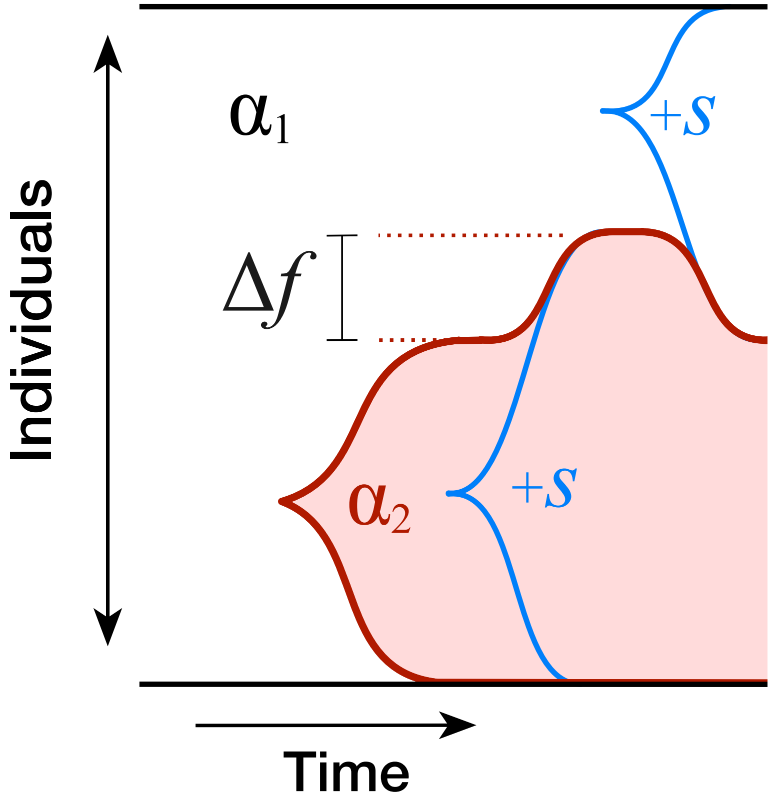

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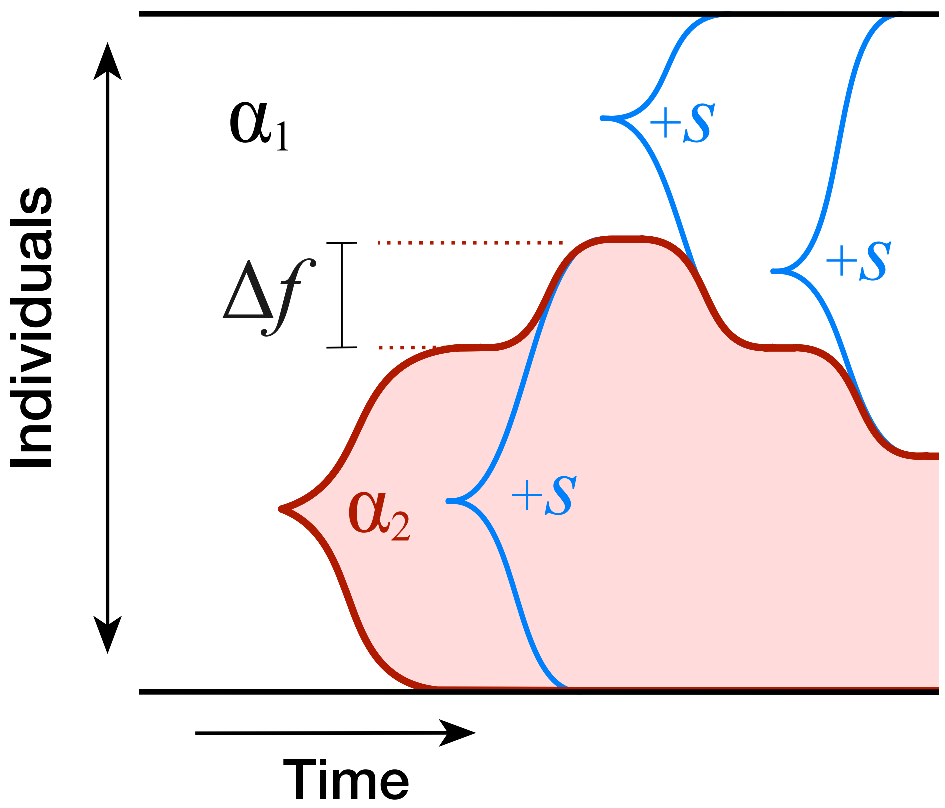

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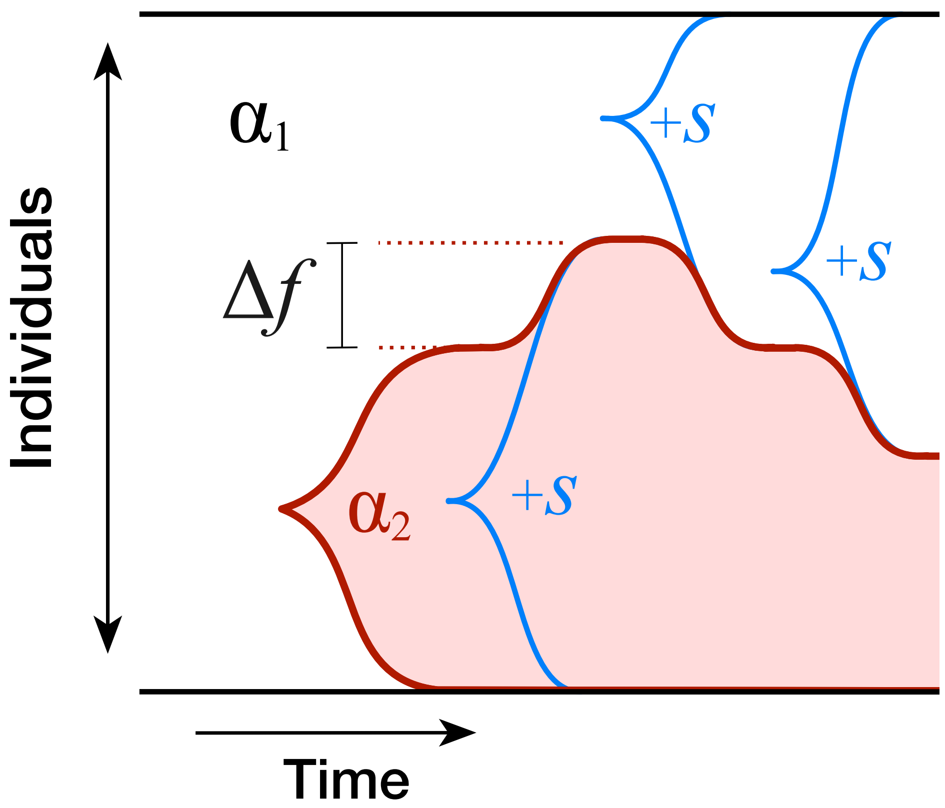

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$$\frac{\partial \Delta X}{\partial t} = N U_X s^2 \left[2 f^*(\Delta X) - 1\right] + \sqrt{N U_X s^3}\,\eta(t)$$

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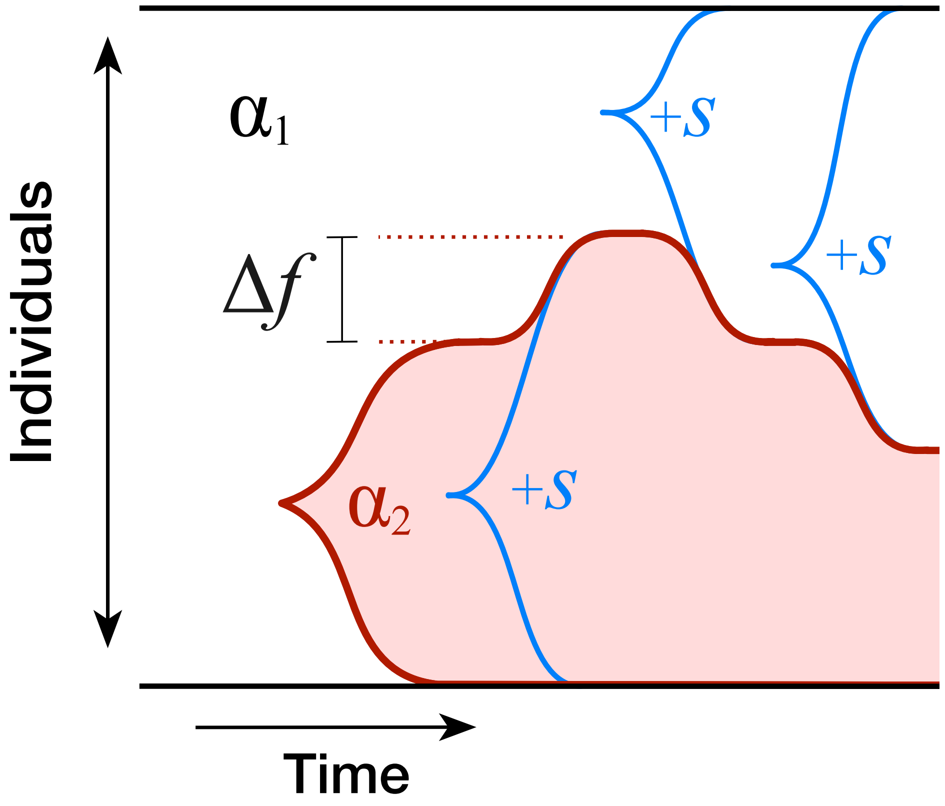

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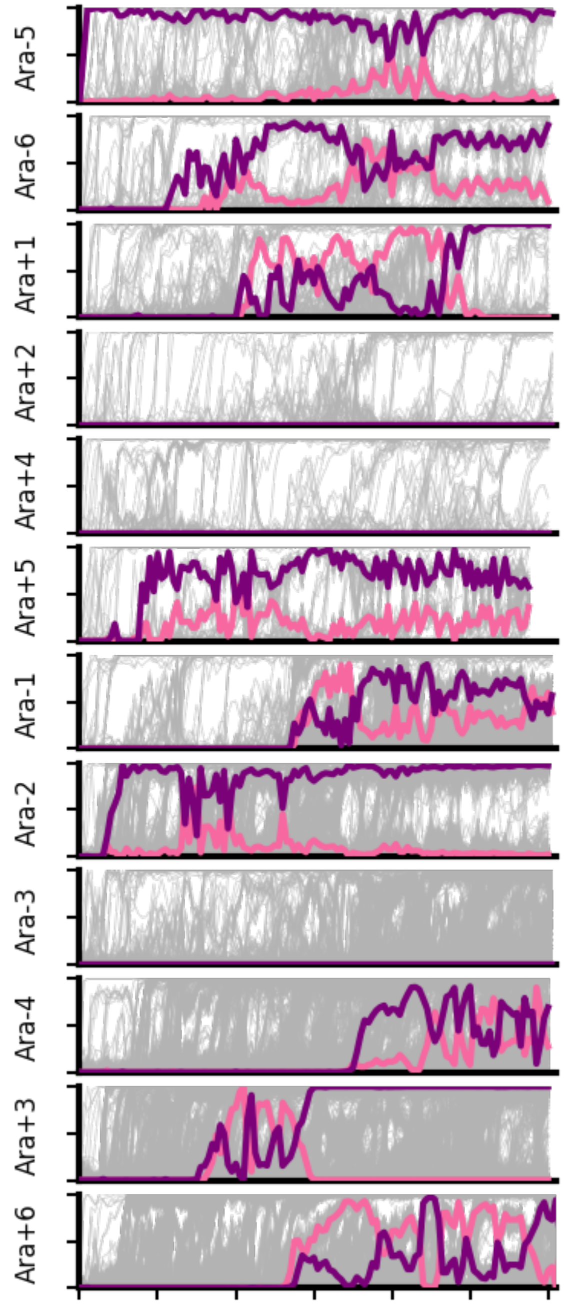
e.g., Lenski lines



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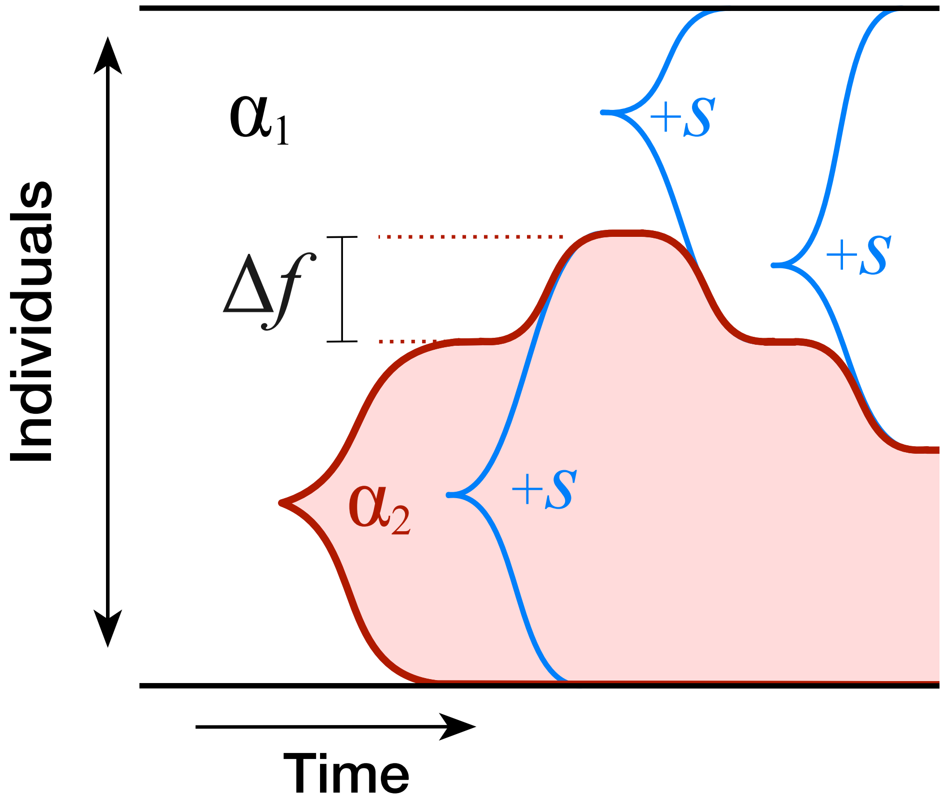

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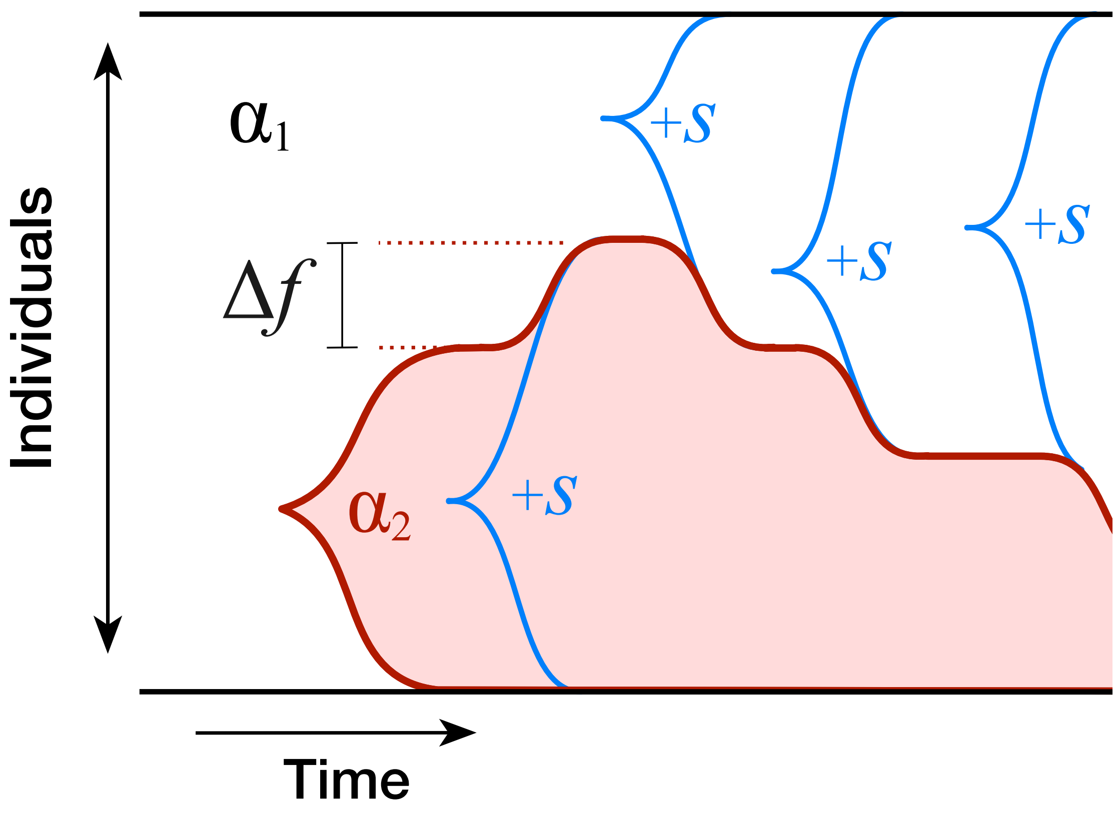

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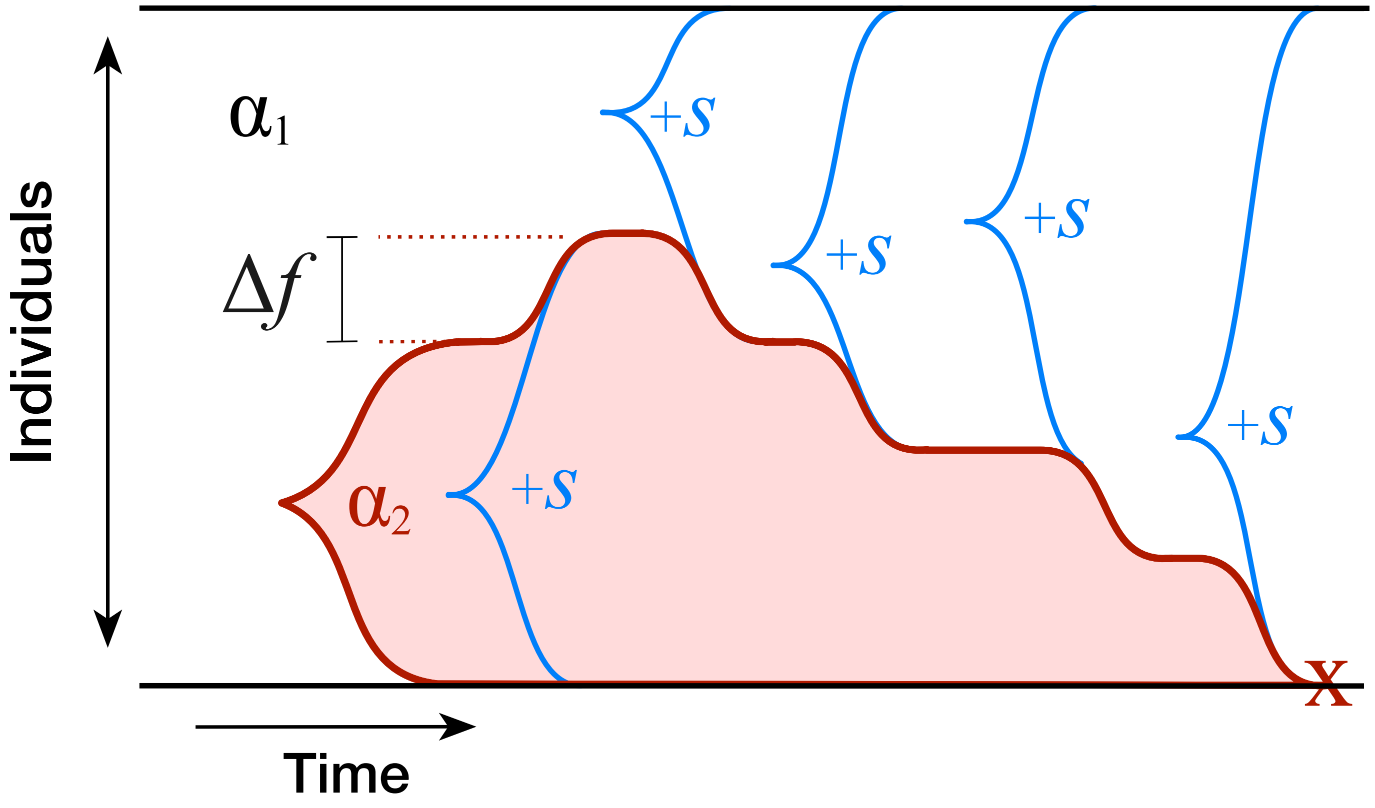

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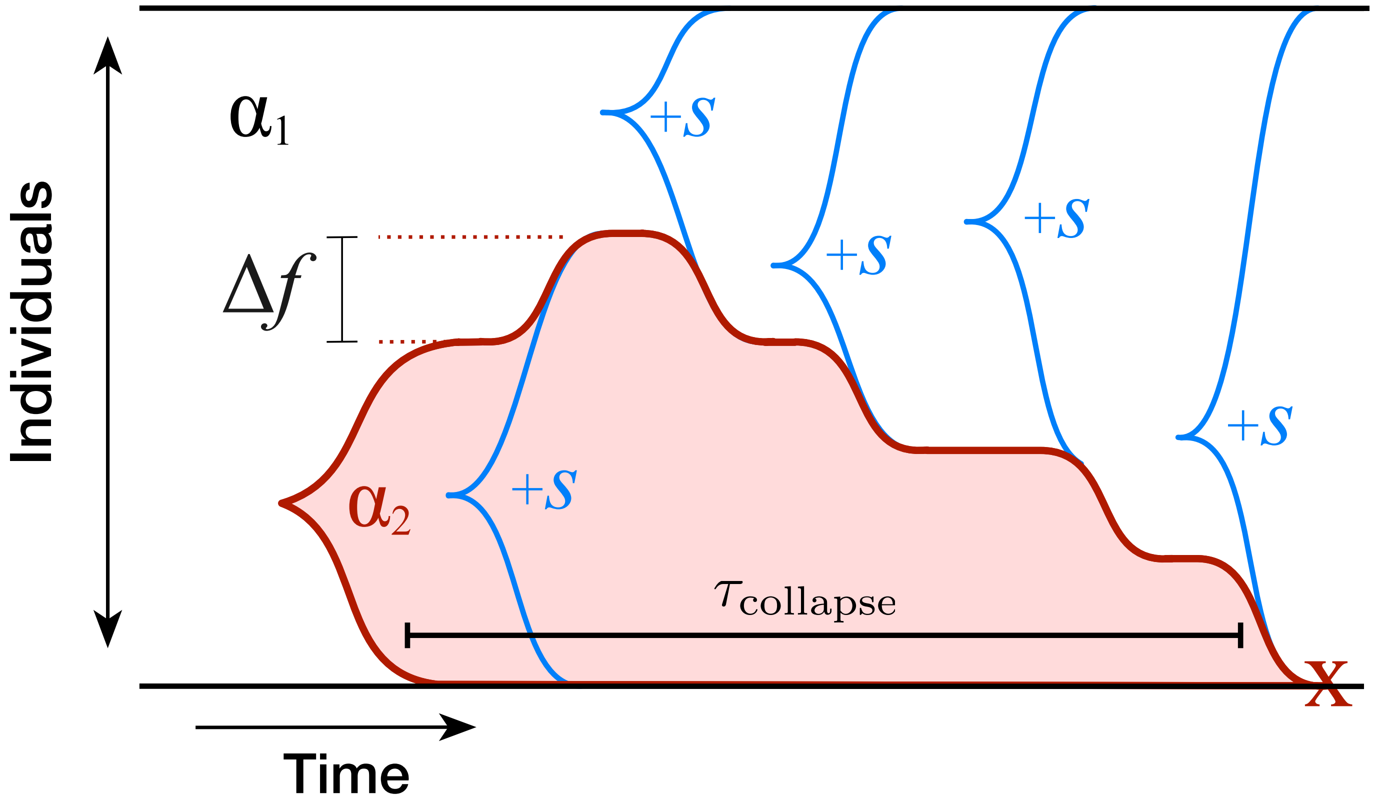

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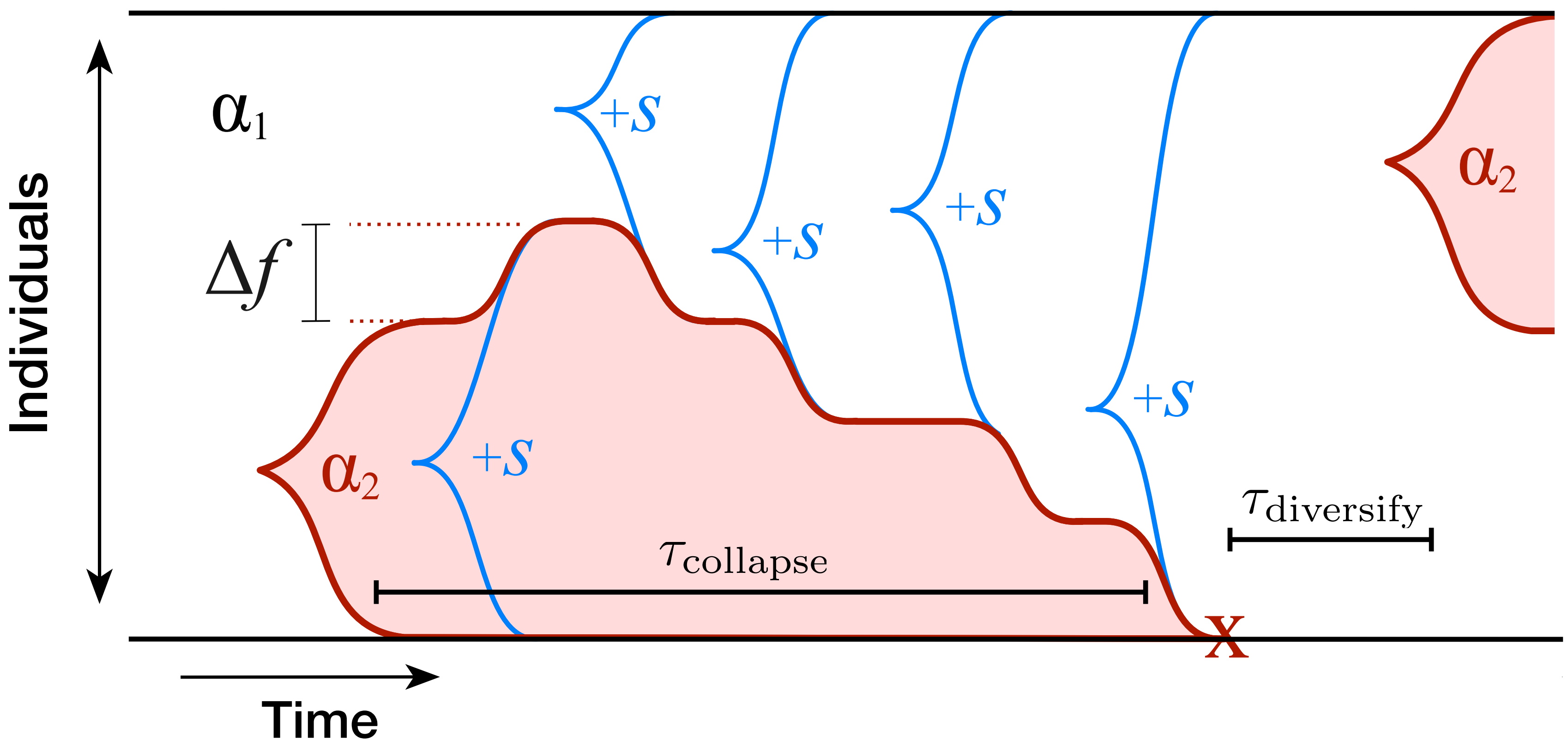

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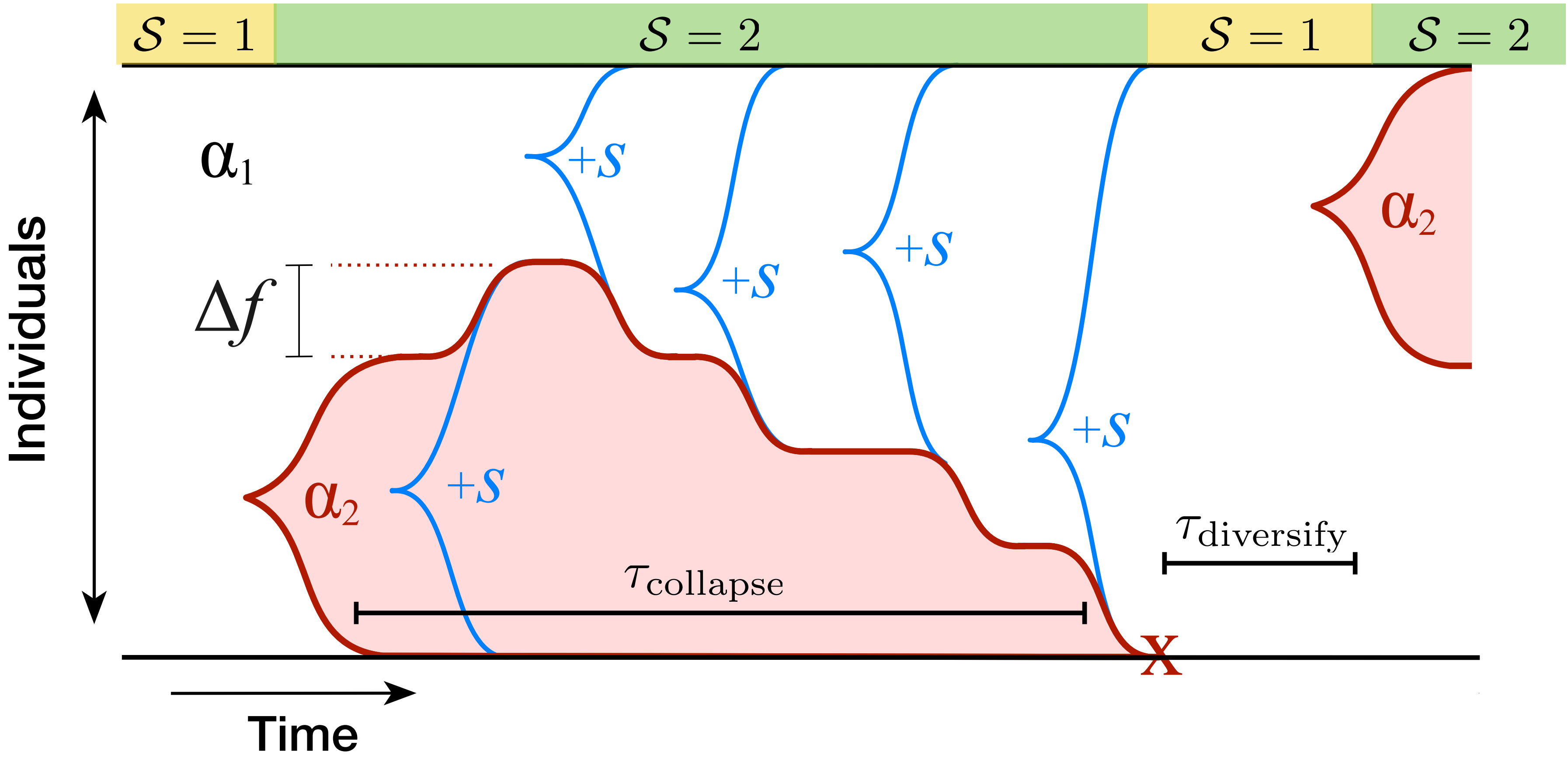

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Diversification-selection balance

$$\frac{\Pr[\mathcal{S} = 2]}{\Pr[\mathcal{S} = 1]} \sim \frac{\tau_{\text{collapse}}}{\tau_{\text{diversify}}}$$

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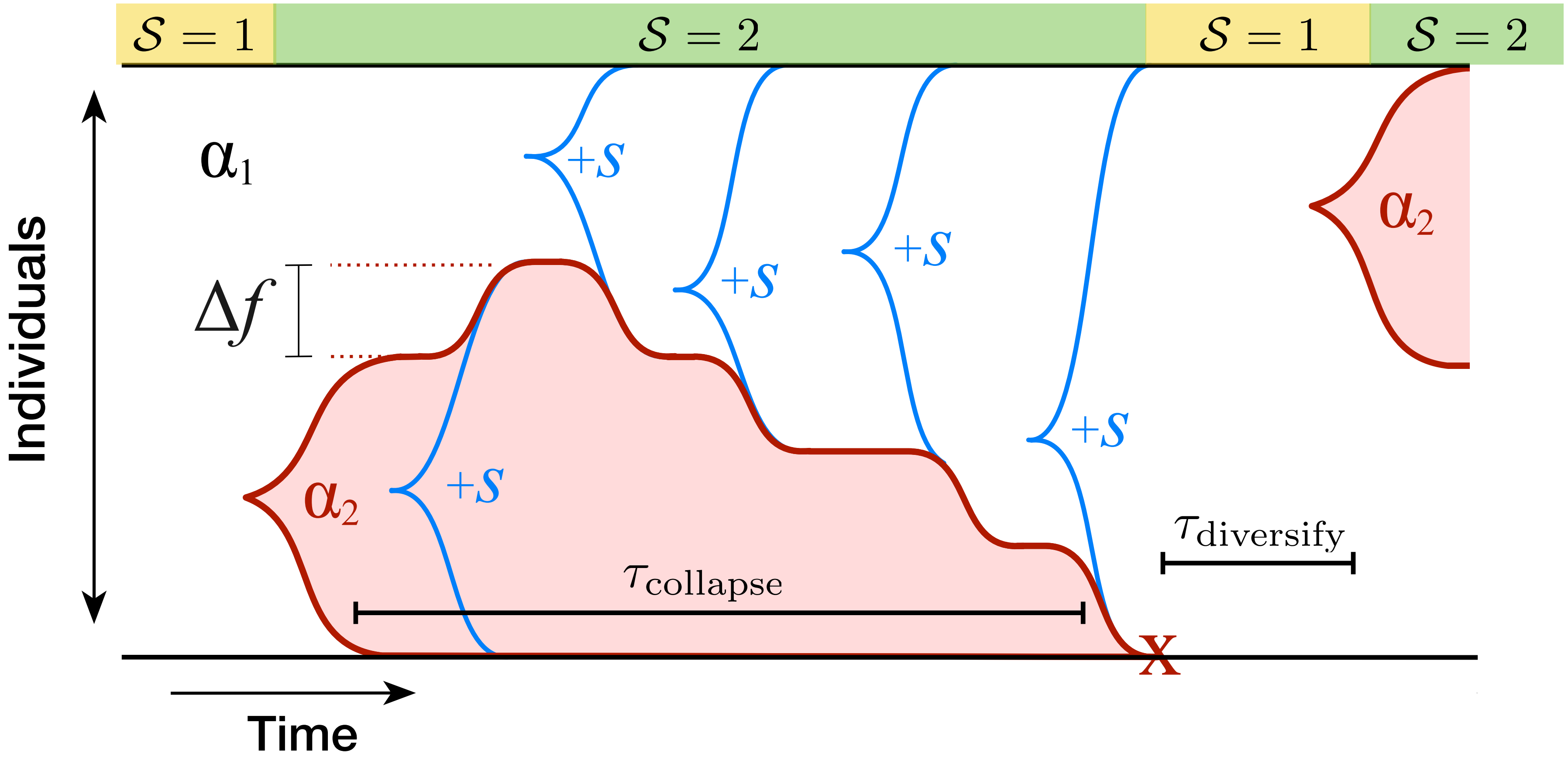

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$$\frac{\Pr[\mathcal{S}=2]}{\Pr[\mathcal{S}=1]} \sim \frac{\tau_{\text{collapse}}}{\tau_{\text{diversify}}}$$

E.g., $$\sim \frac{U_\alpha}{U_X}\left(\frac{X^*}{s}\right)^2 \log\left(\frac{X^*}{s}\right)$$

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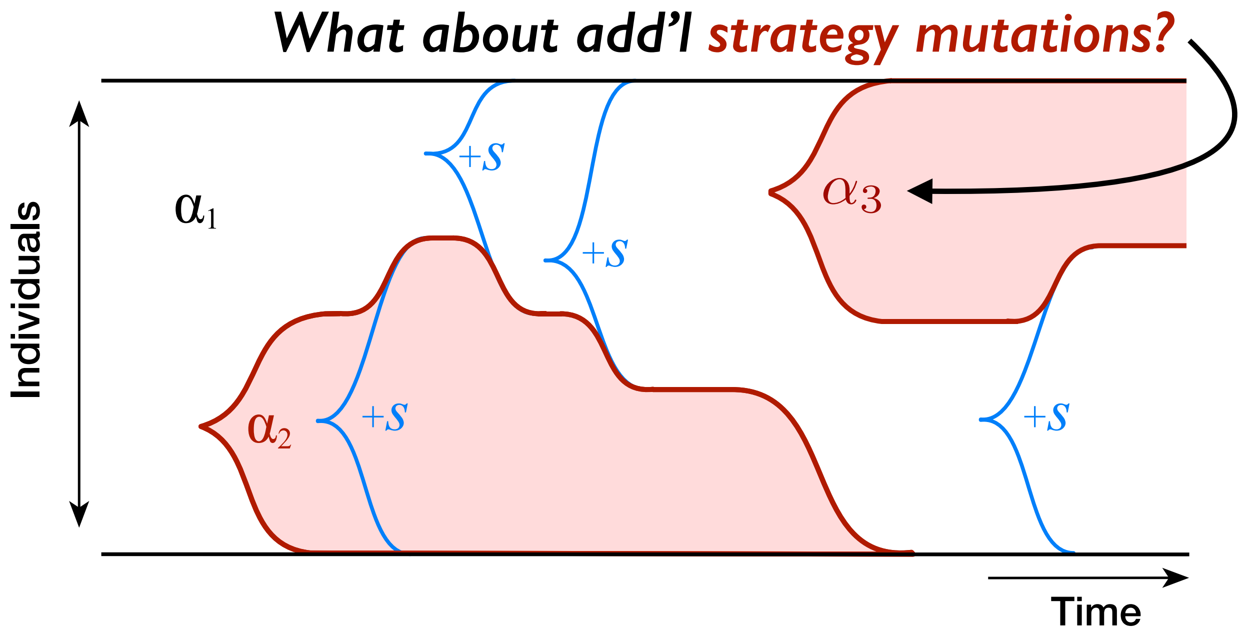
Emergent selection for further ecological tuning



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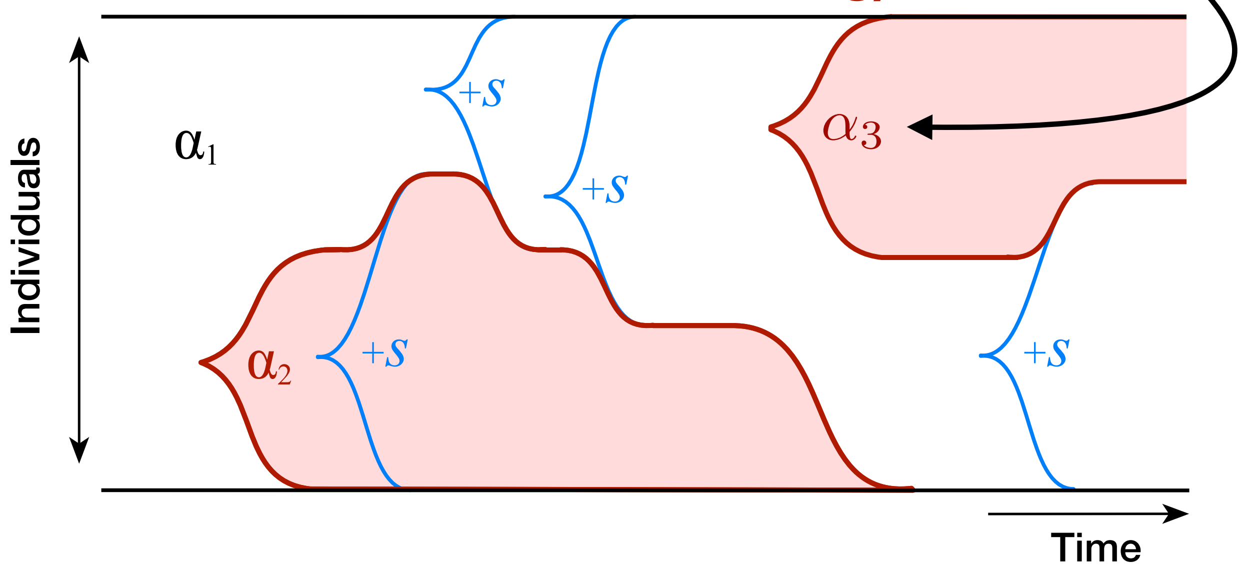
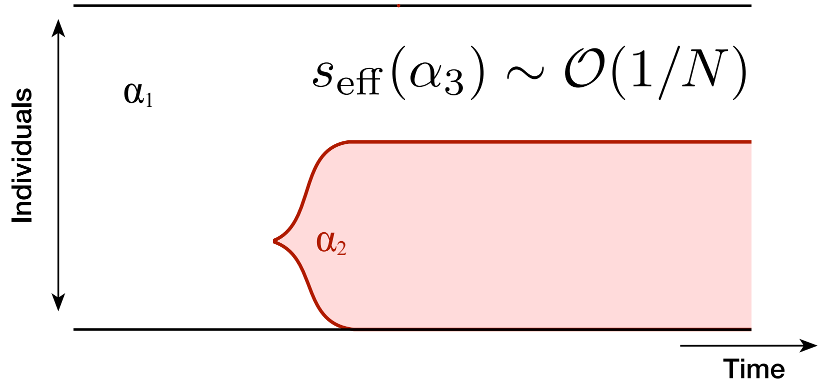
Emergent selection for further ecological tuning

What about add'l strategy mutations?



Recall neutral case: *(Posfai et al 2017)*



$s_{\text{eff}}(\alpha_3) \sim \mathcal{O}(1/N)$

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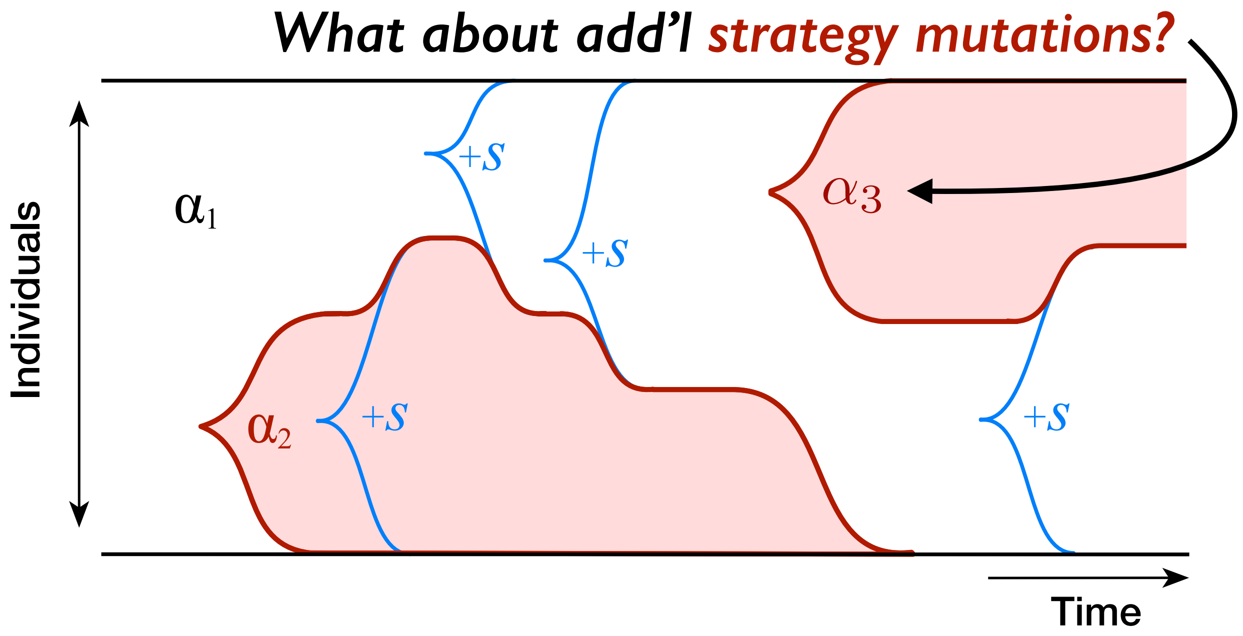

Induced ecological selection pressure:

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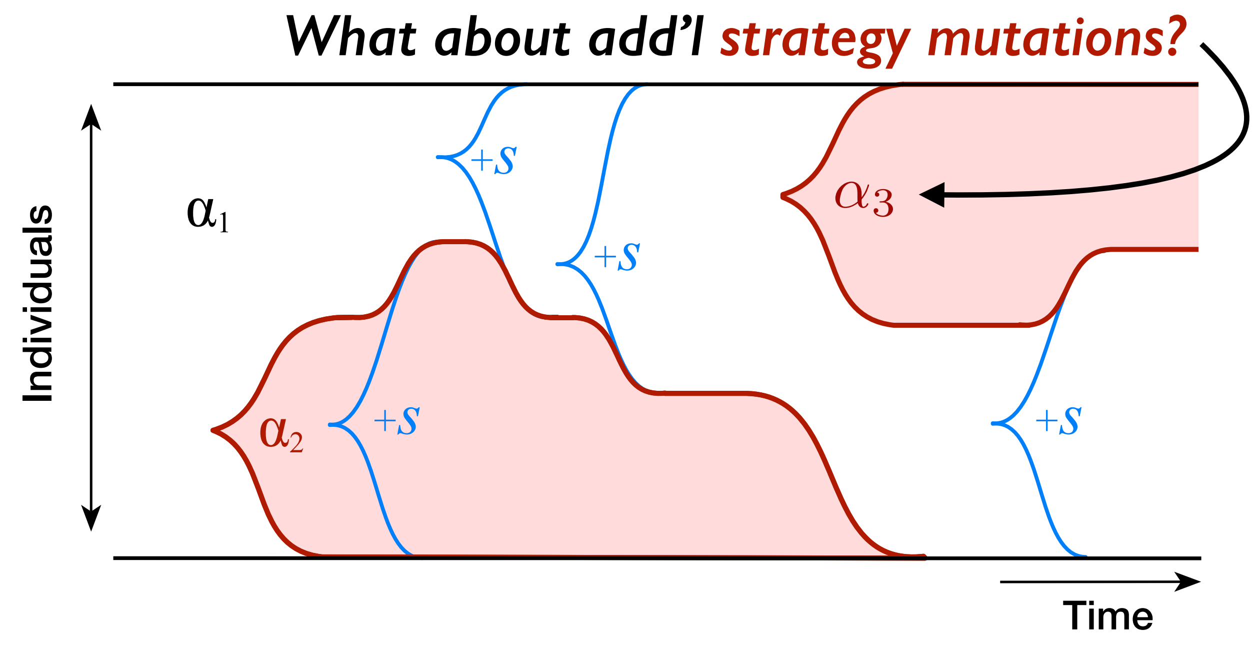

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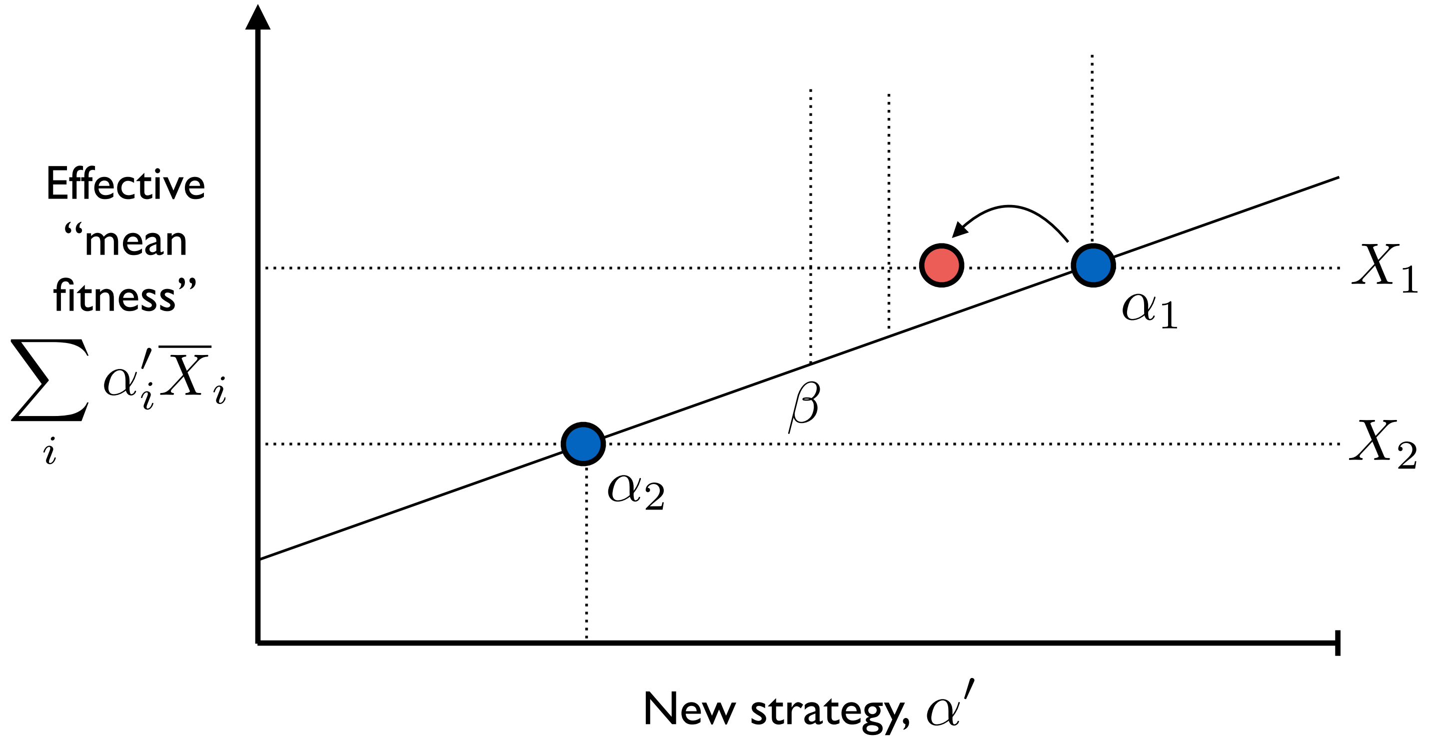
Graphical picture



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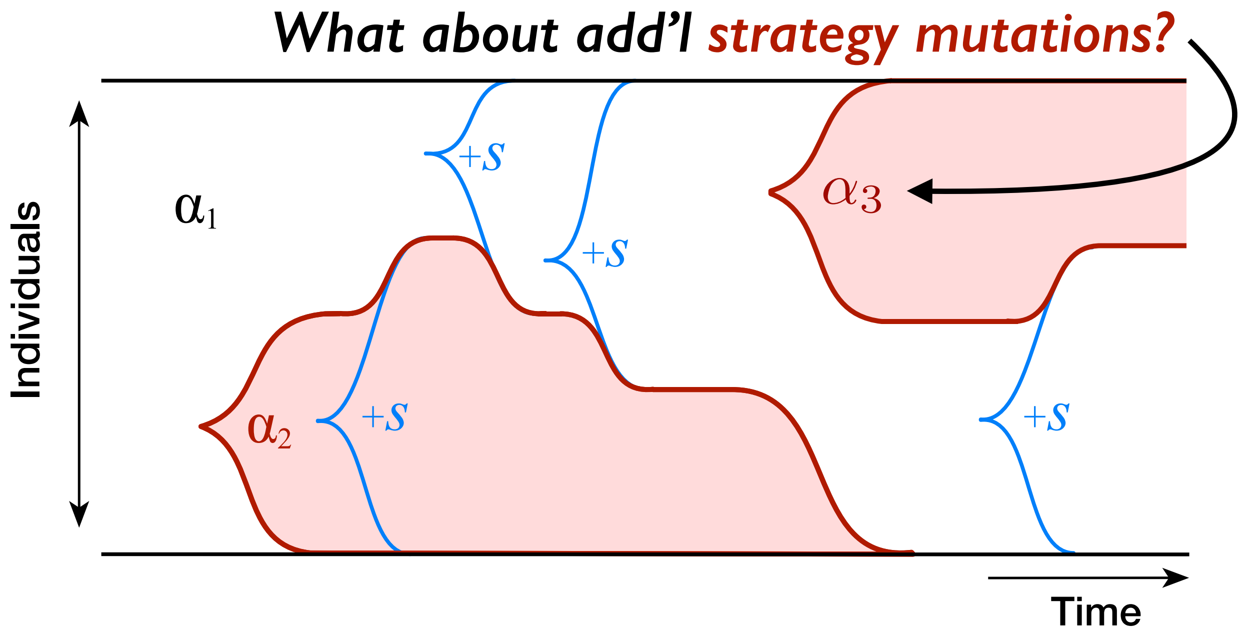

Induced ecological selection pressure:

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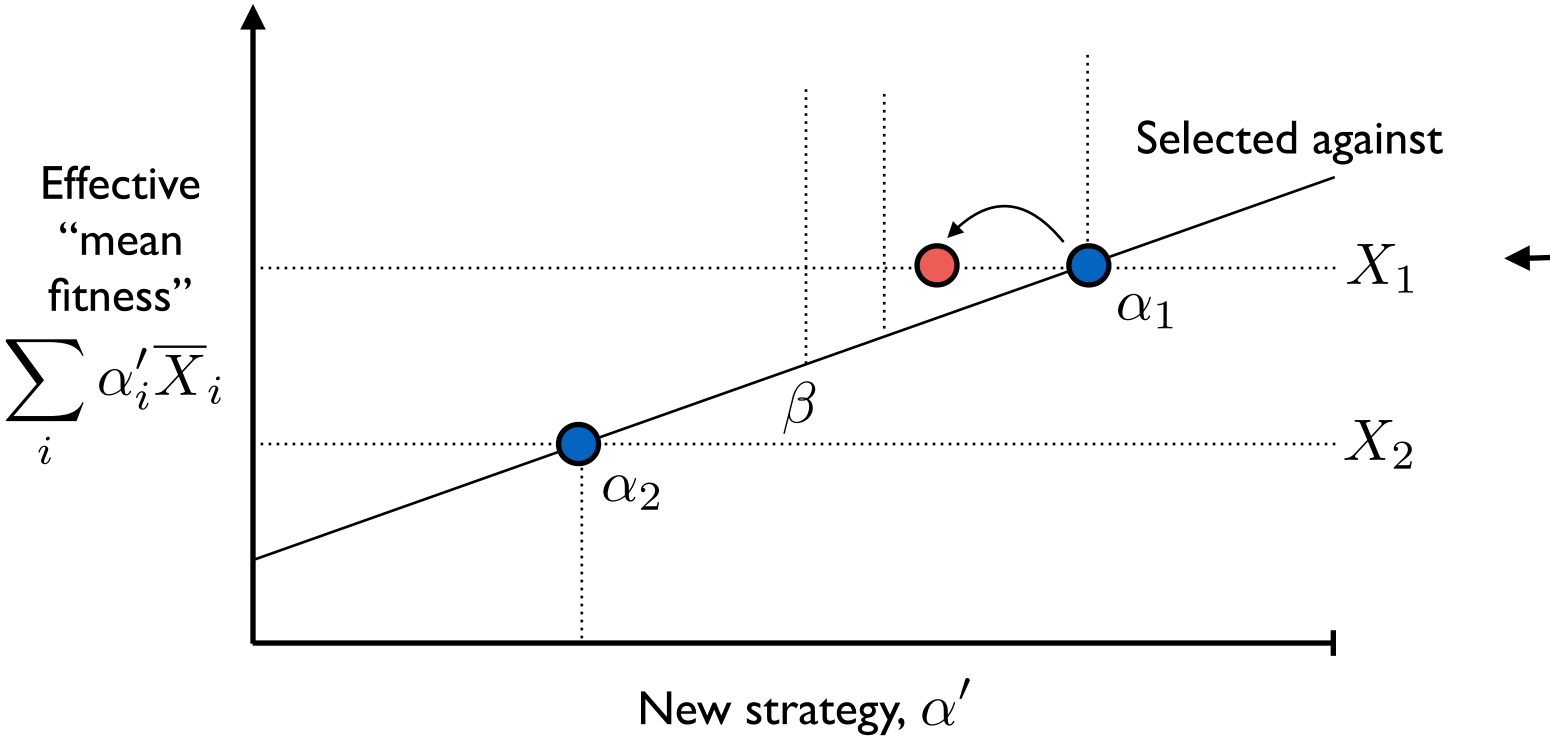
Graphical picture



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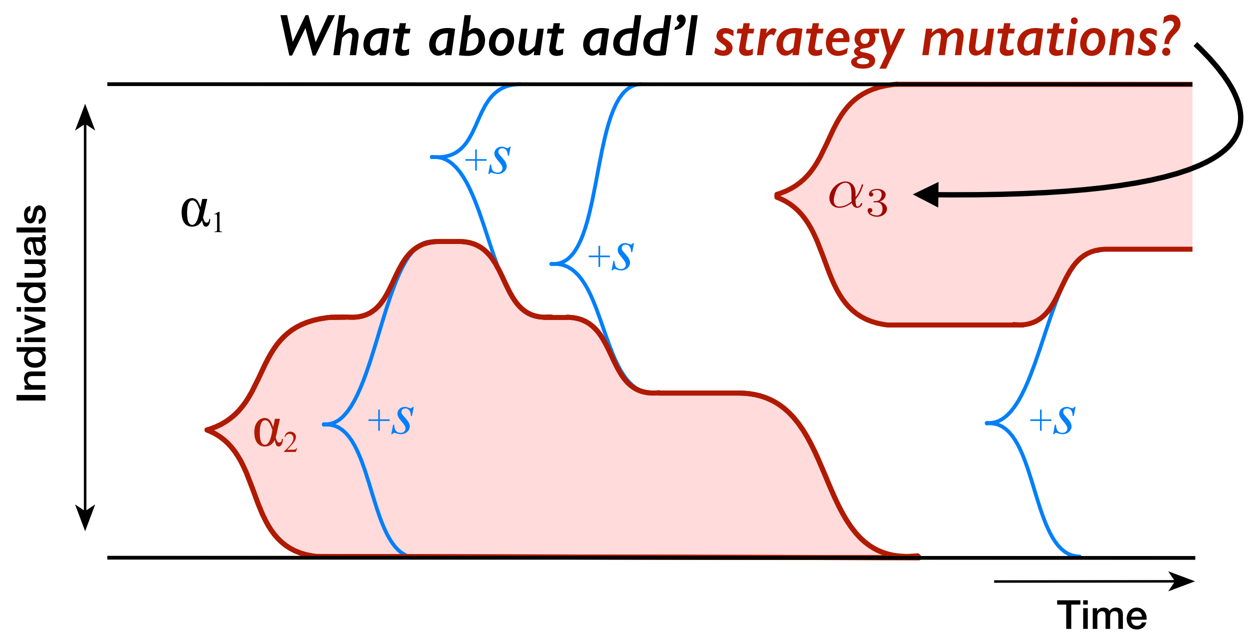

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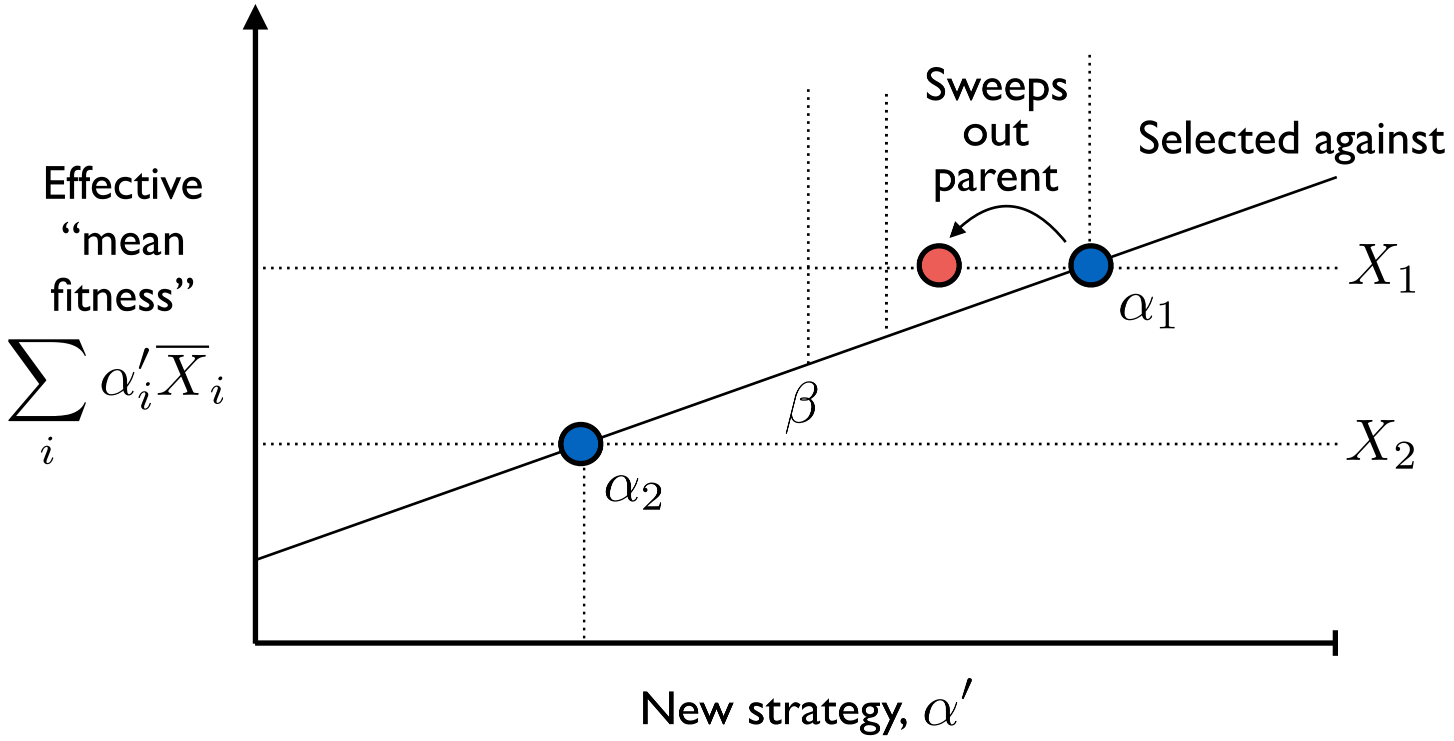

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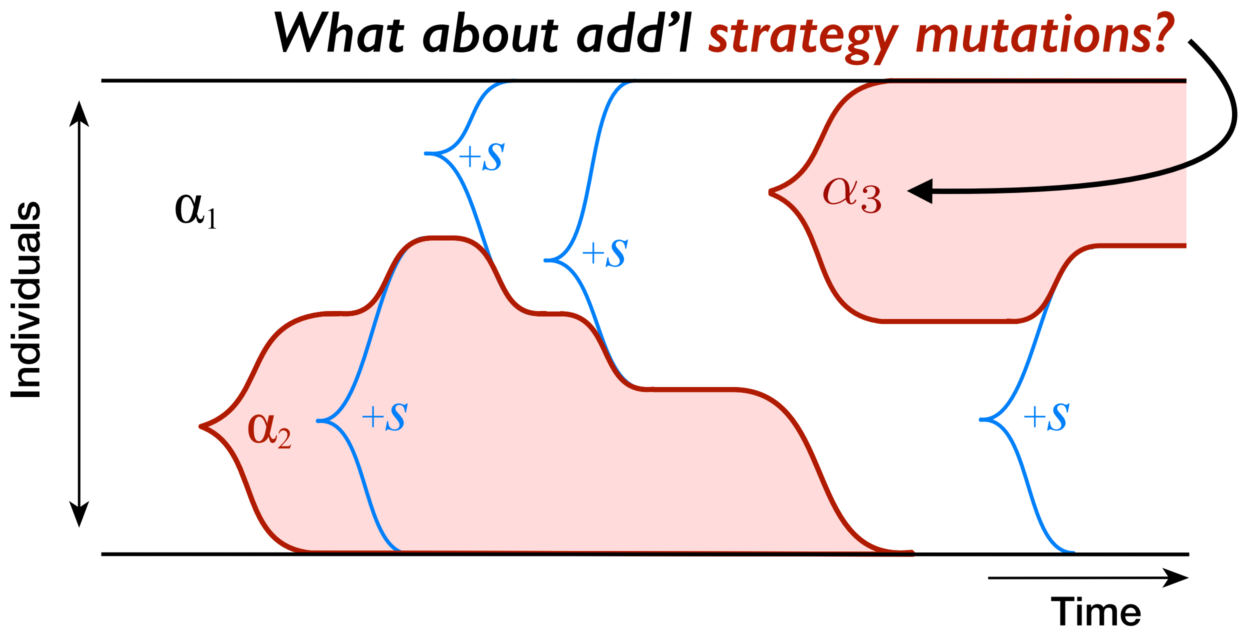

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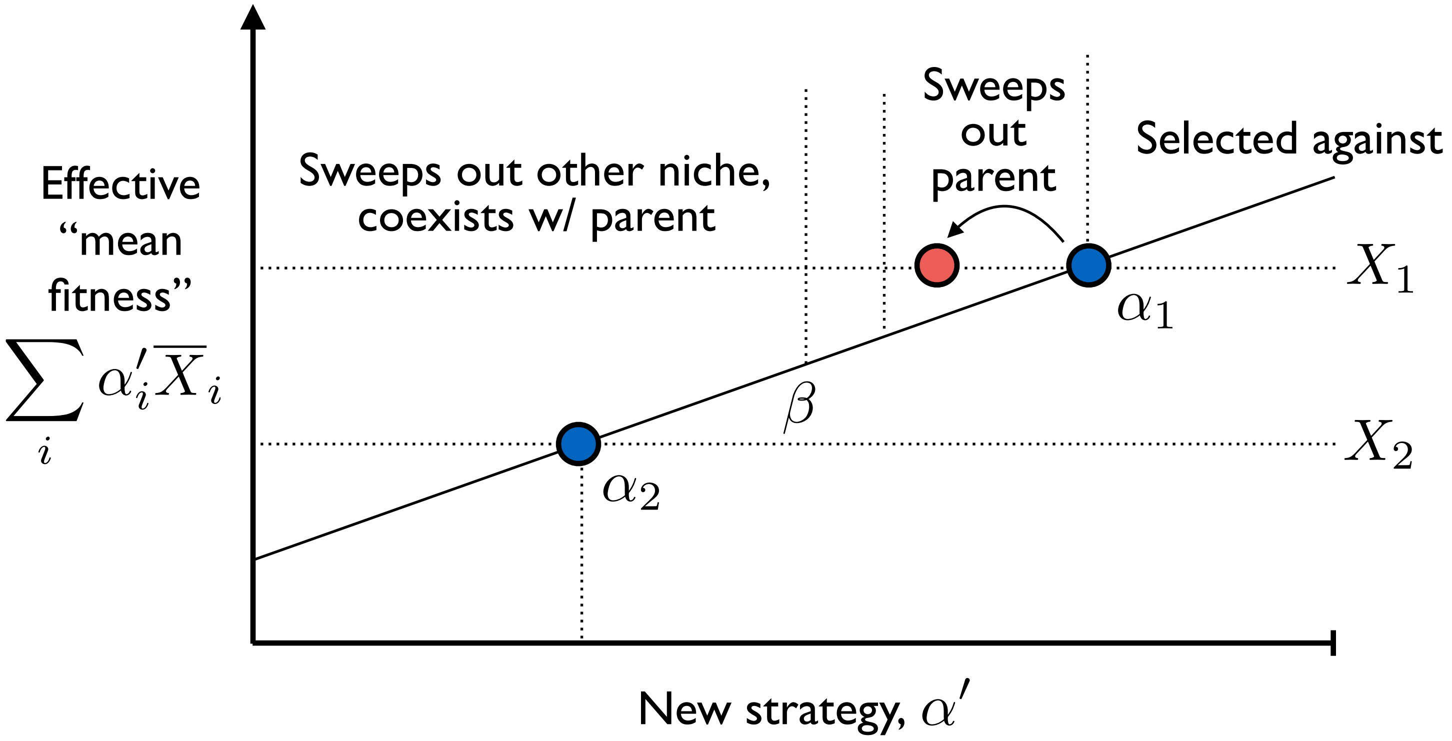

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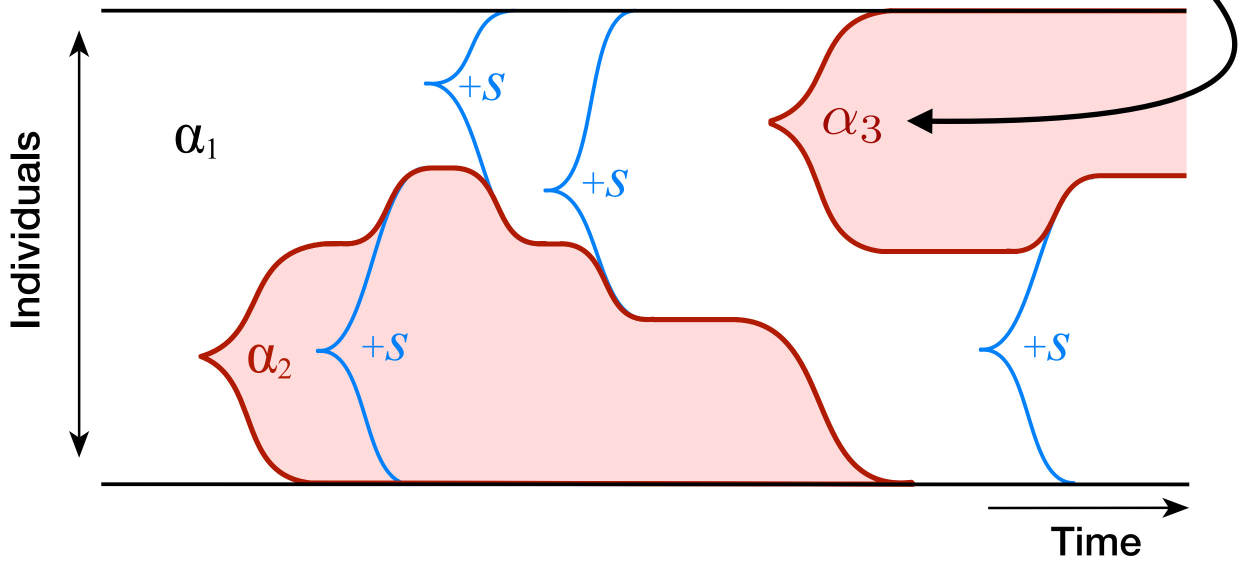

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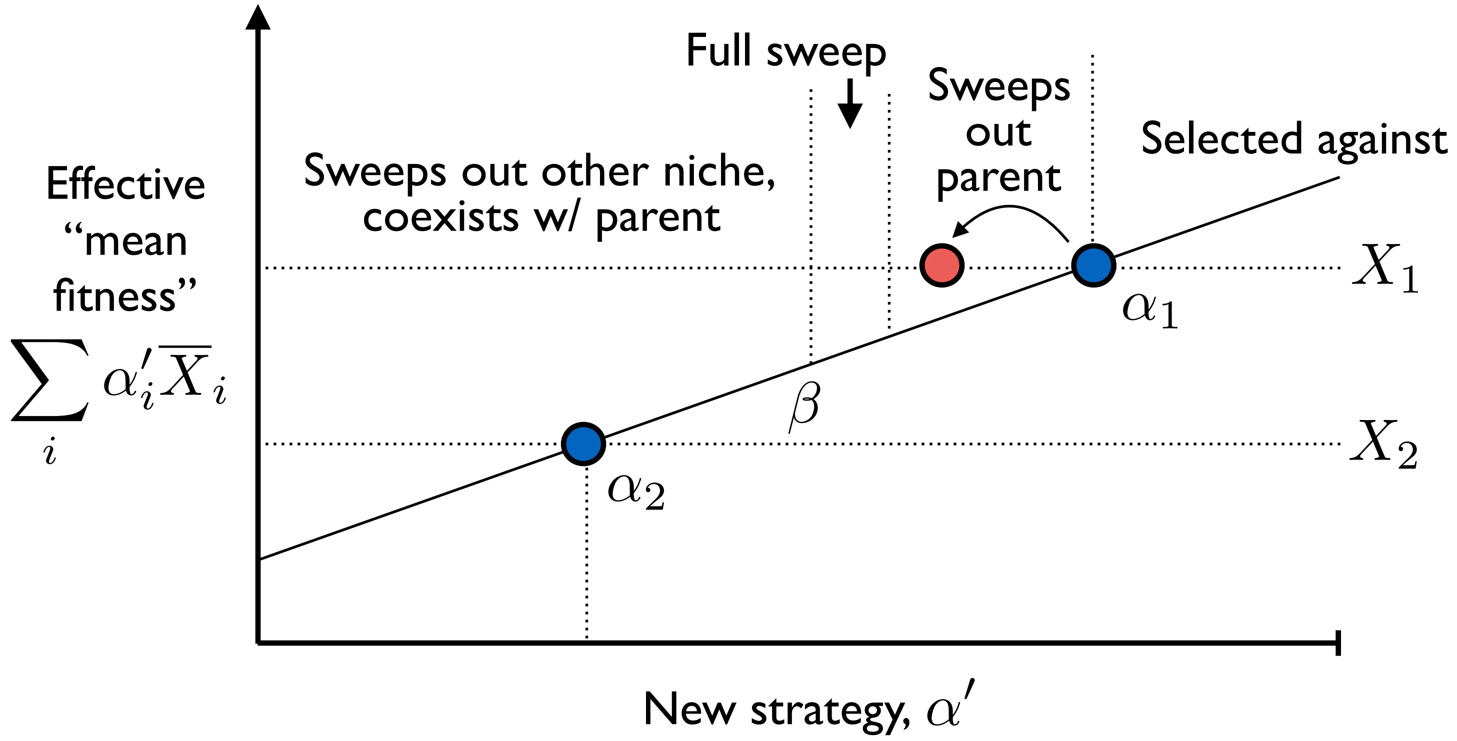

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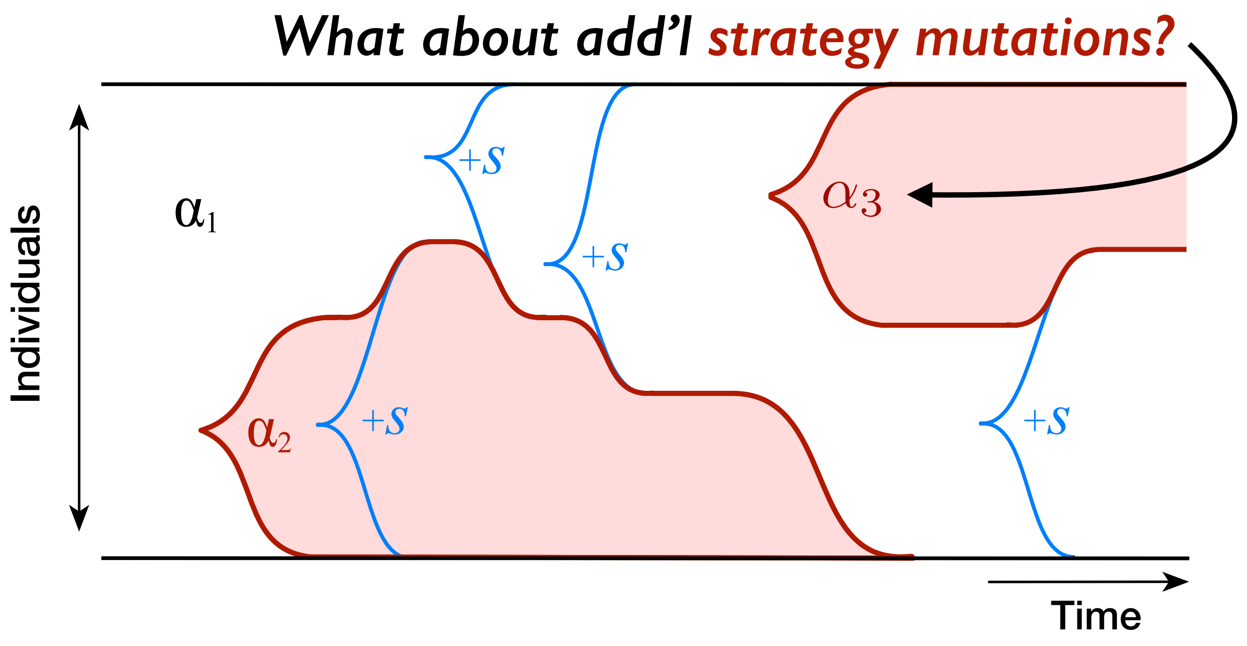

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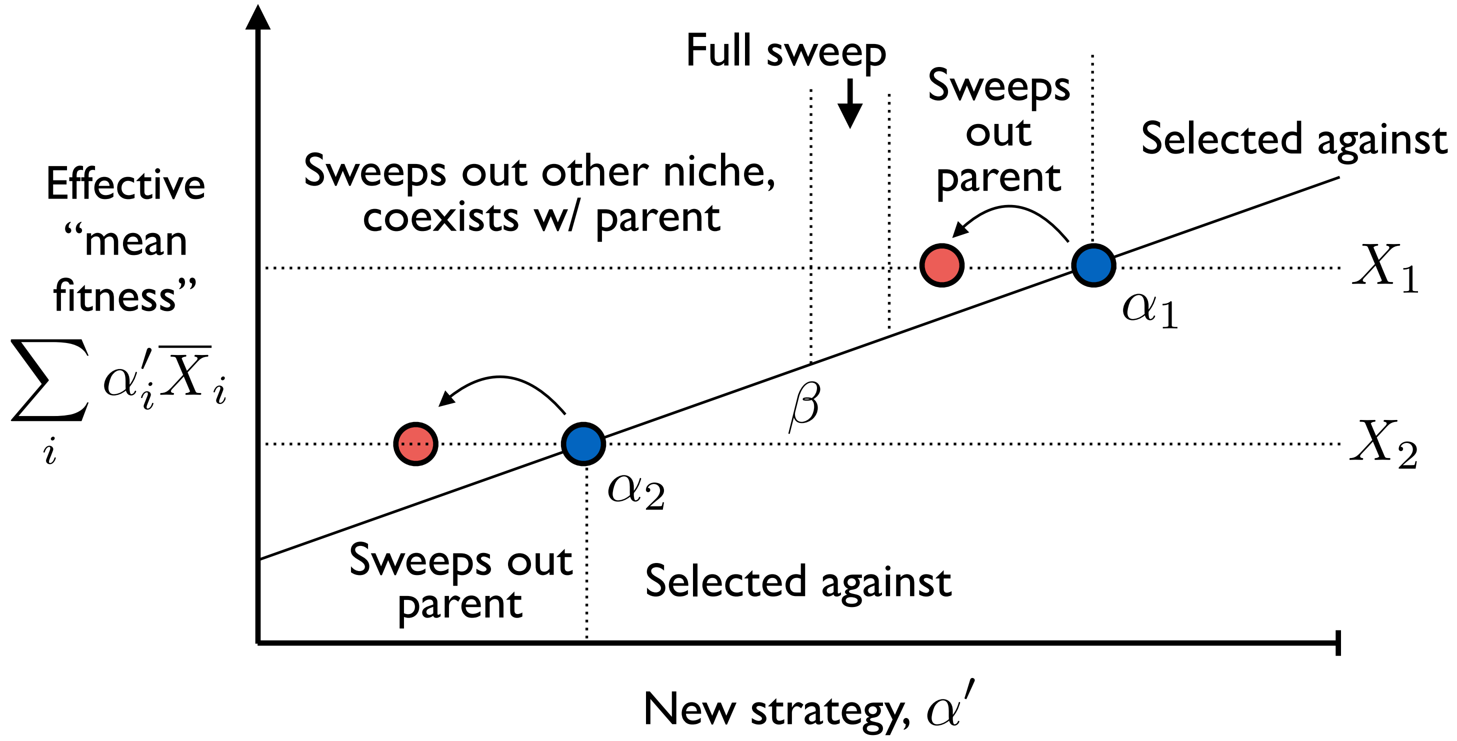

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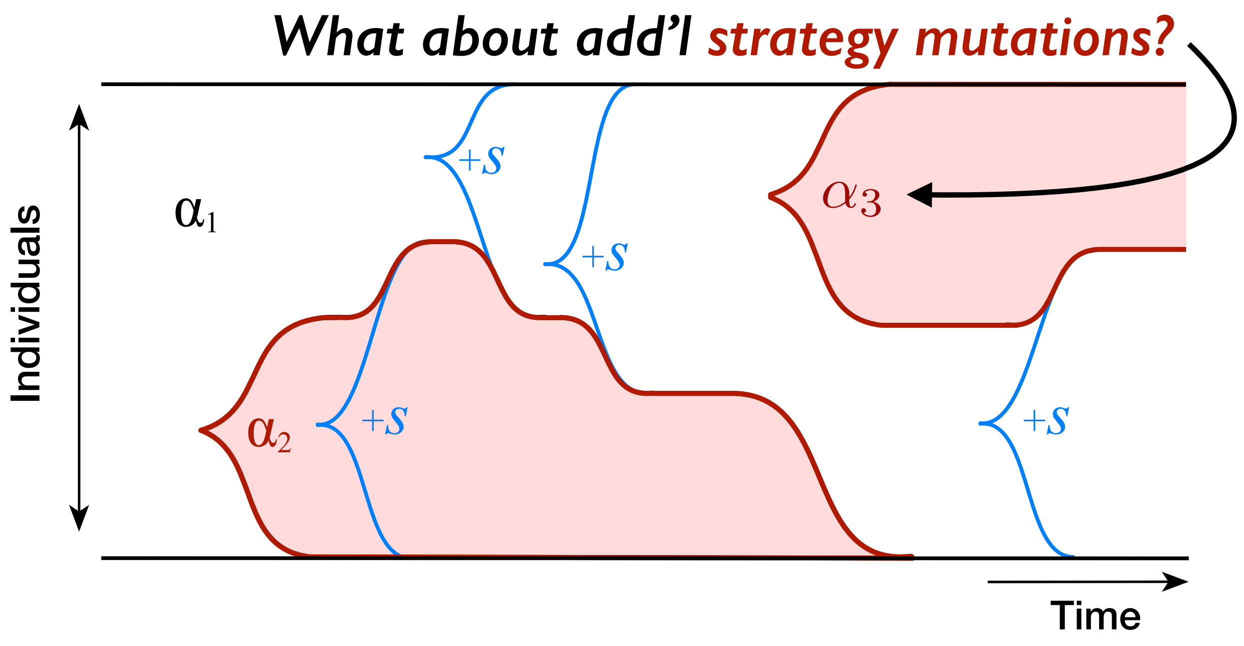

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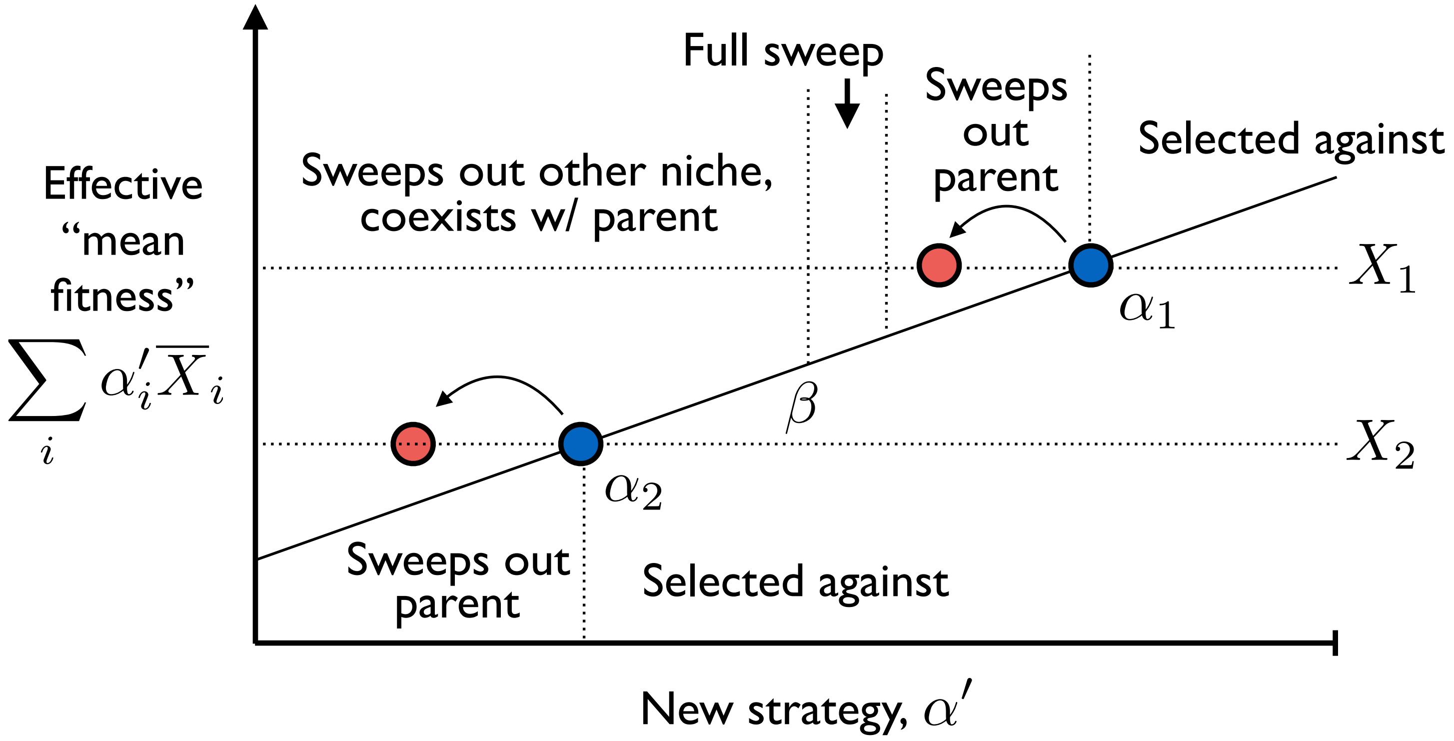

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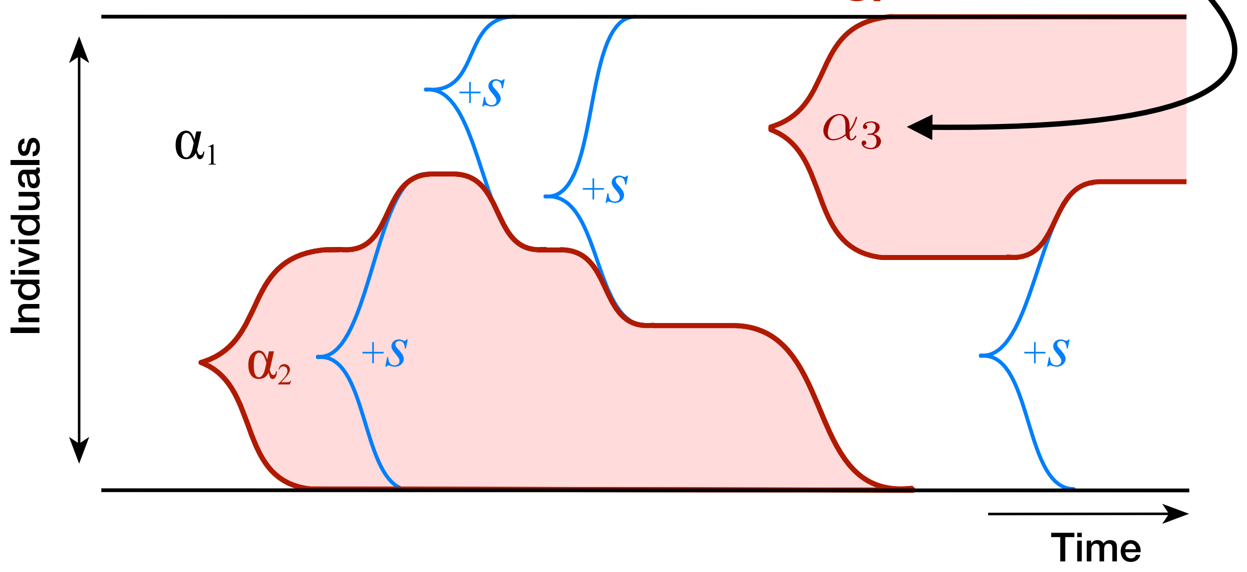

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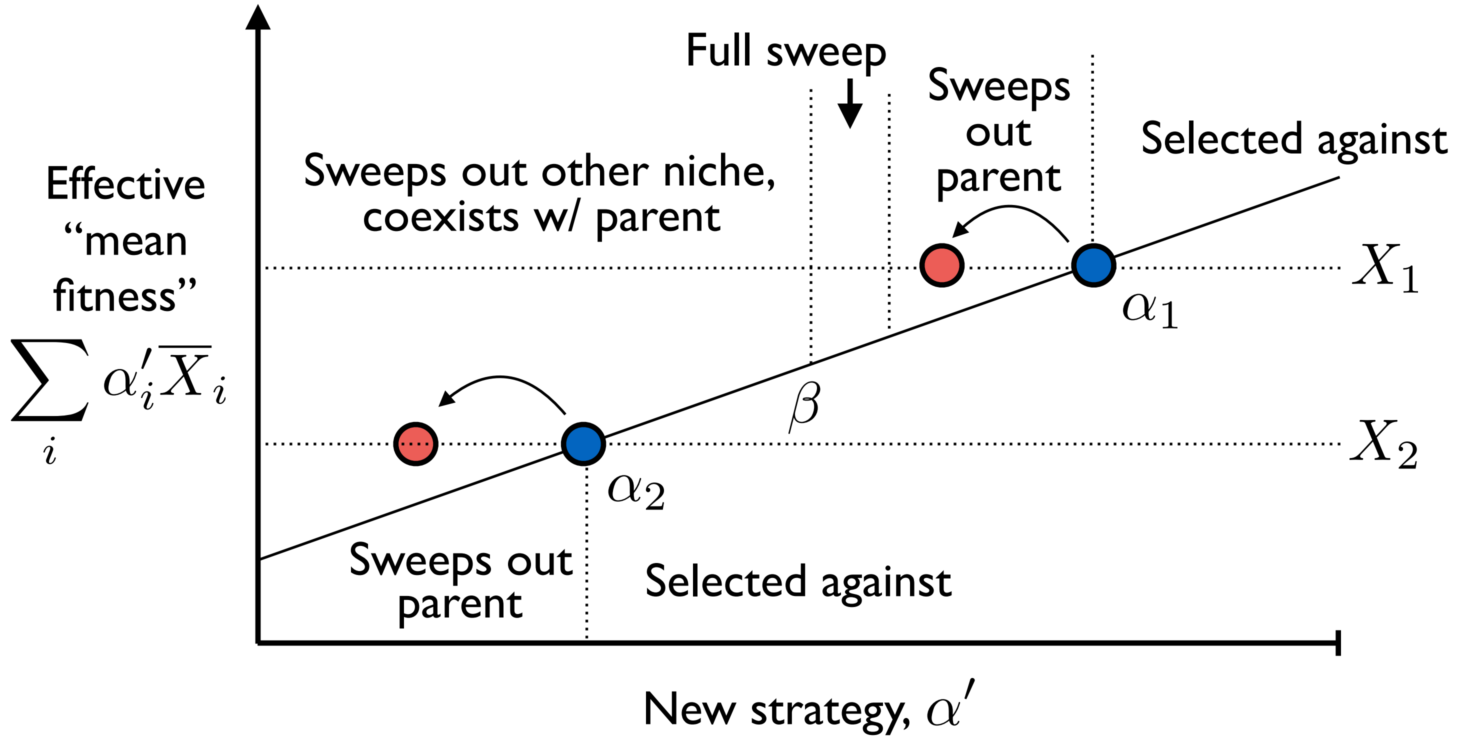

Selection for fit "generalists" and less-fit "specialists"

Test in laboratory experiments?

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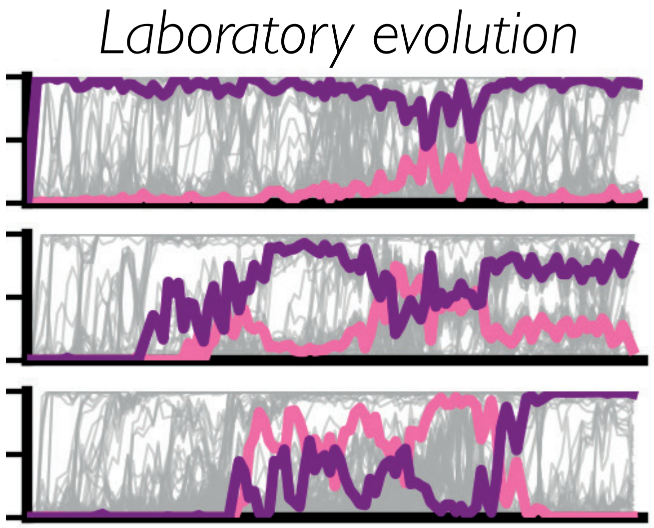
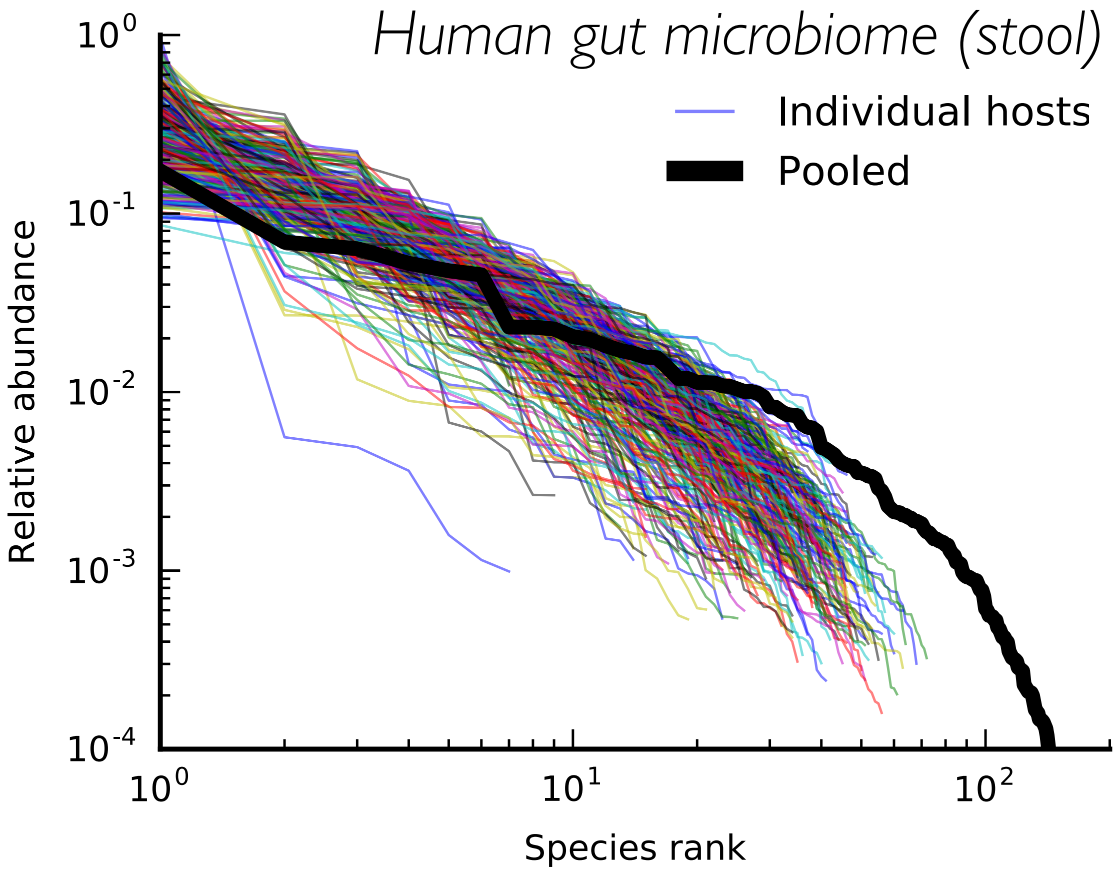
Future directions: evolution in highly diverse ecosystems



VS →



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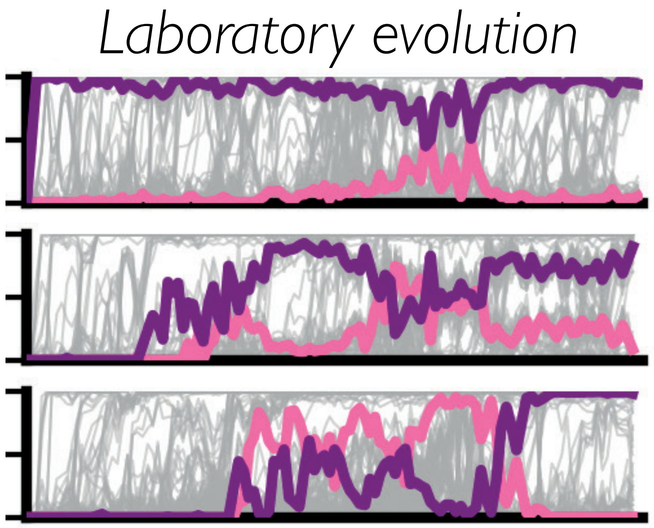

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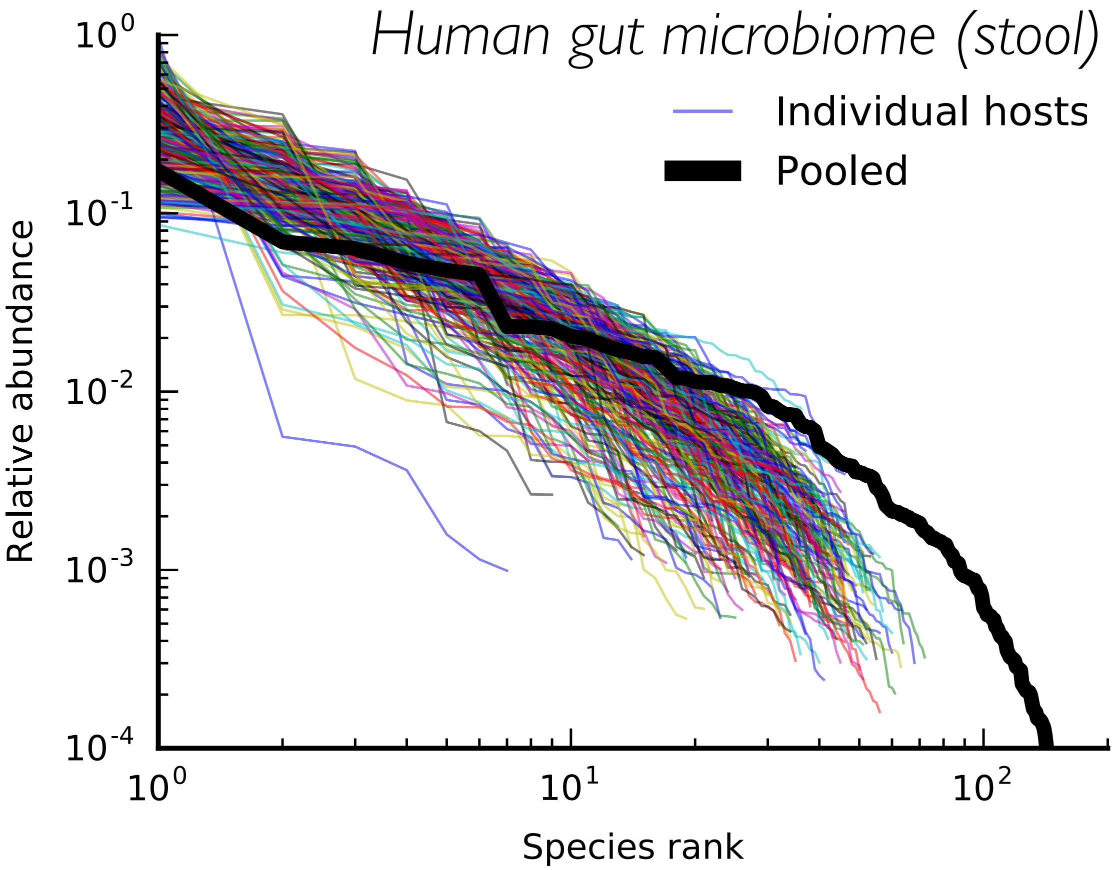
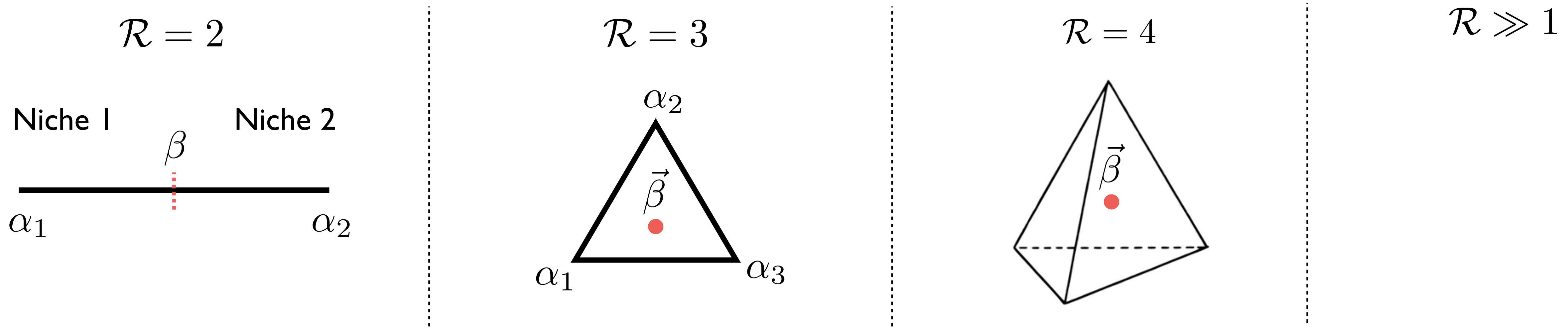


Questions: *How does evolution alter community structure?*
How does the community alter evolutionary dynamics?
Can we make connections to sequence data?

Future direction 1: highly diverse consumer-resource models



increasing # of coexisting strains ⟶

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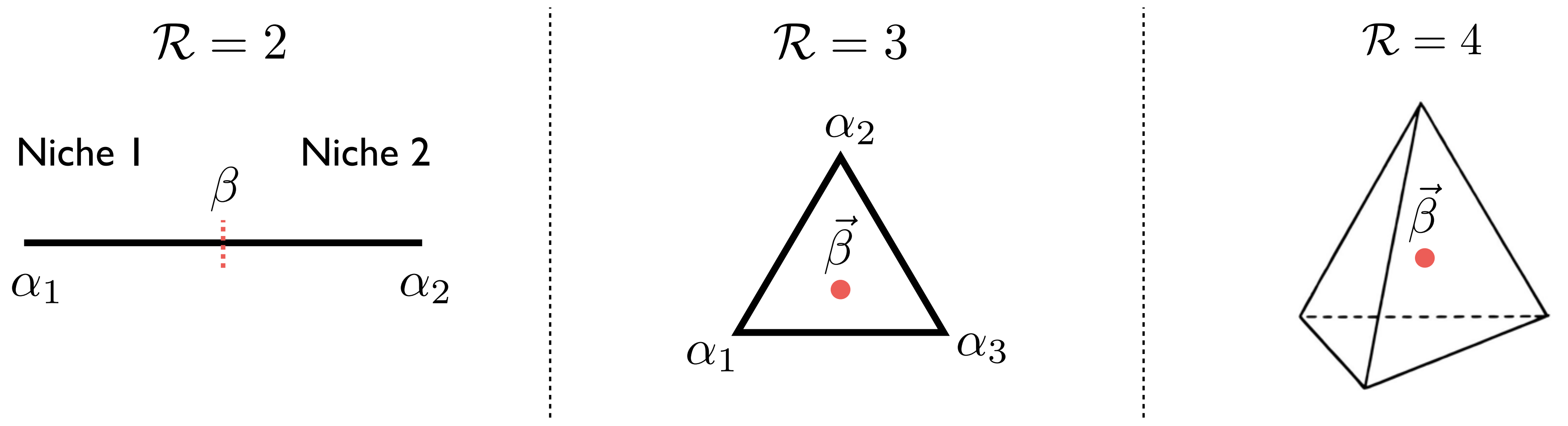

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New behavior?

or just
harder math?

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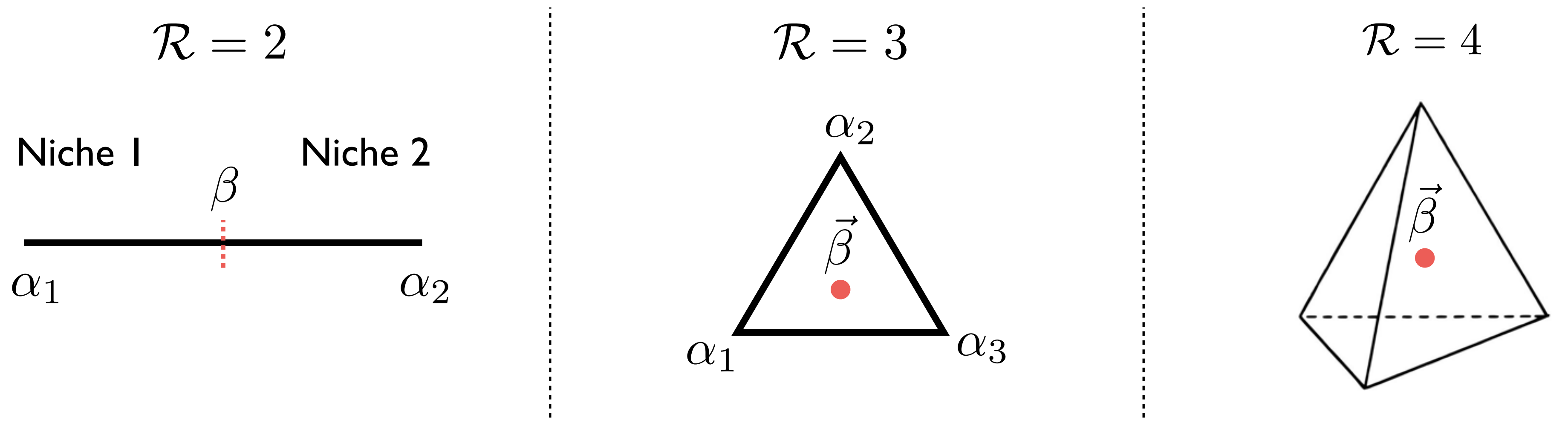

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In ***"saturated"*** ecosystems ($\mathcal{S} = \mathcal{R}$)

Future direction 1: highly diverse consumer-resource models

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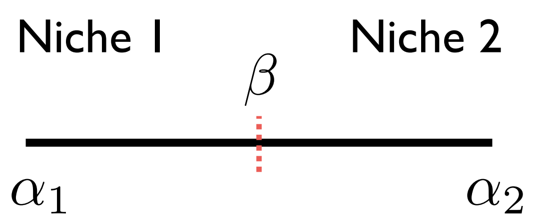

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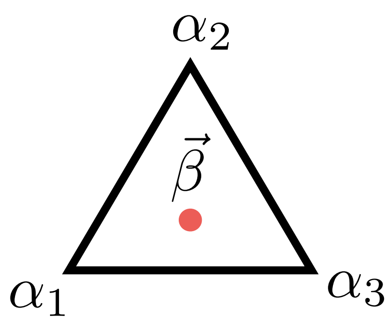

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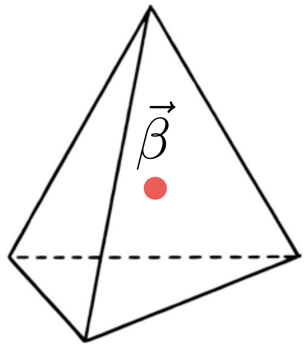

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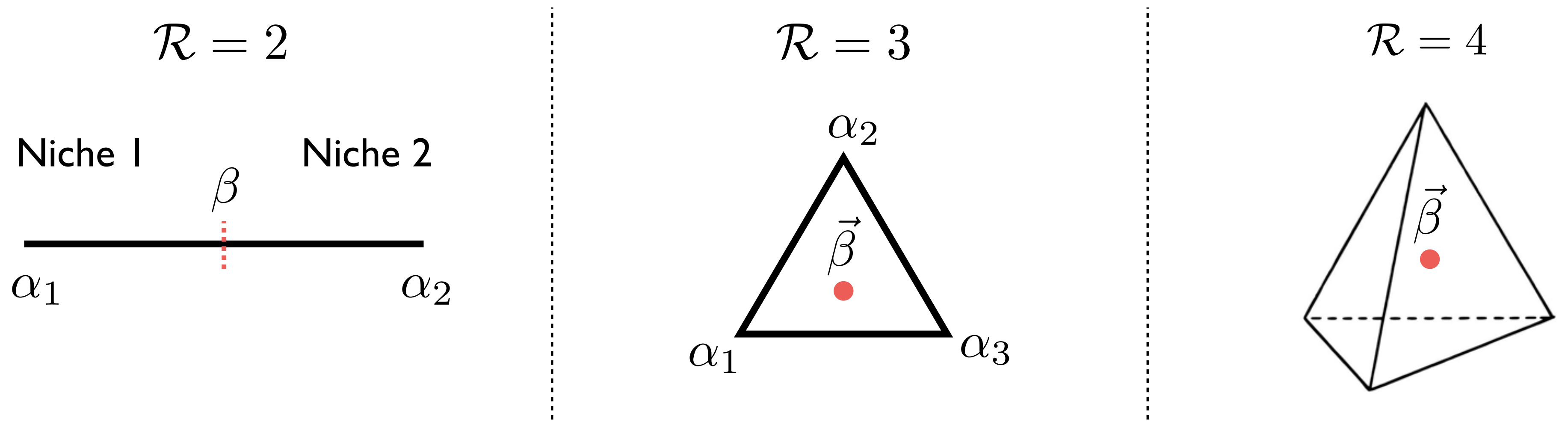

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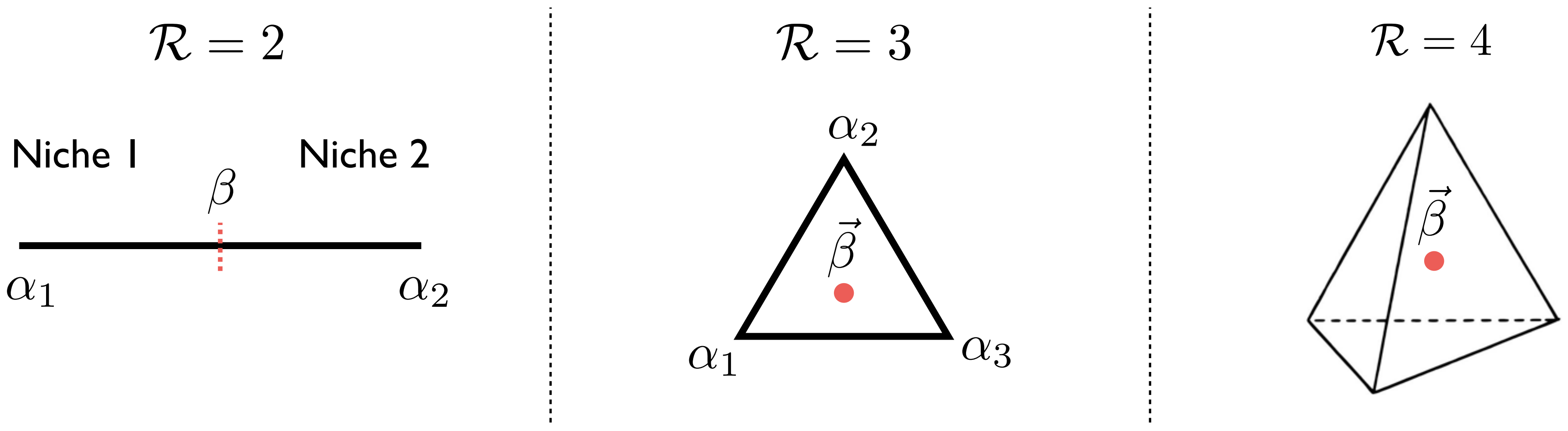

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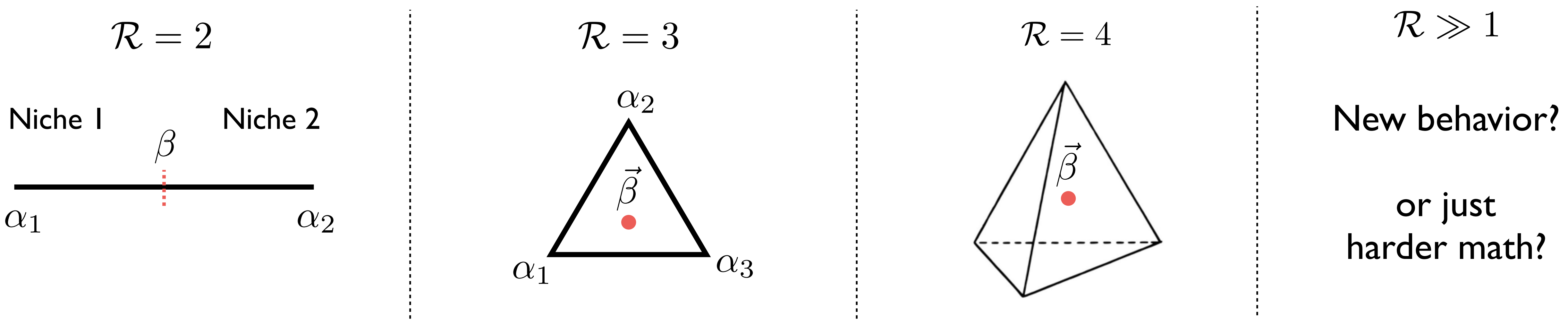

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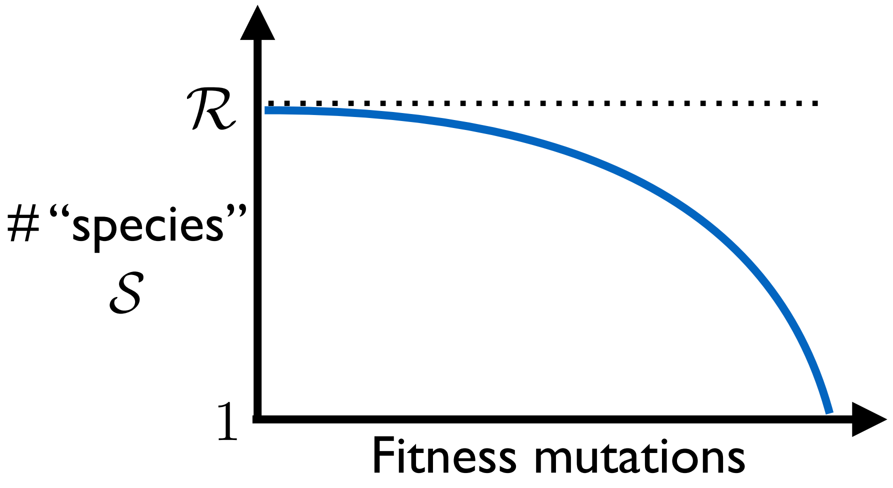

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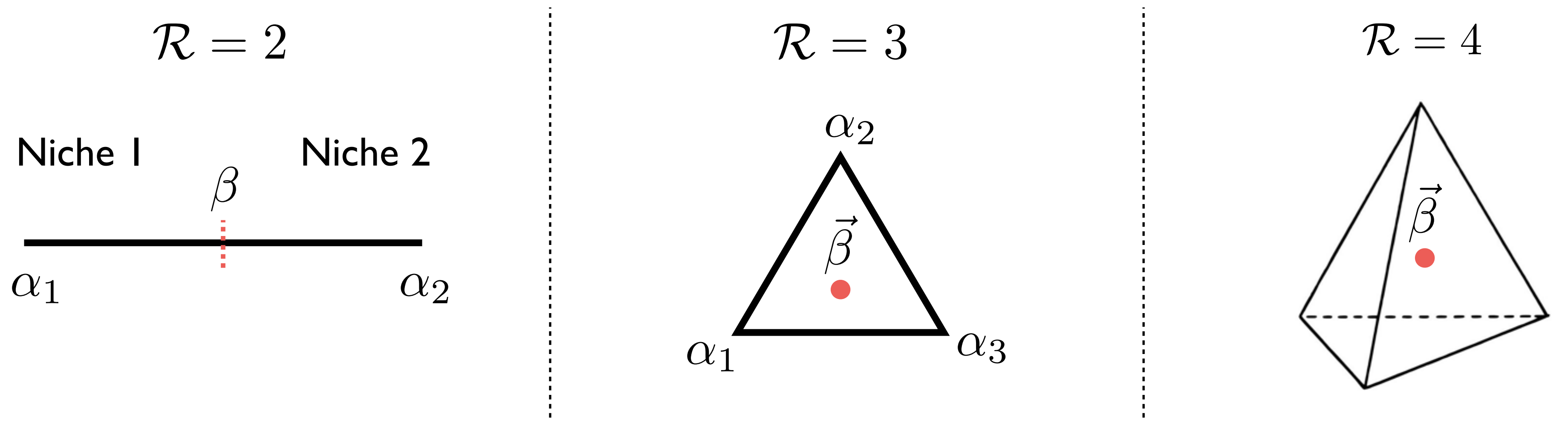

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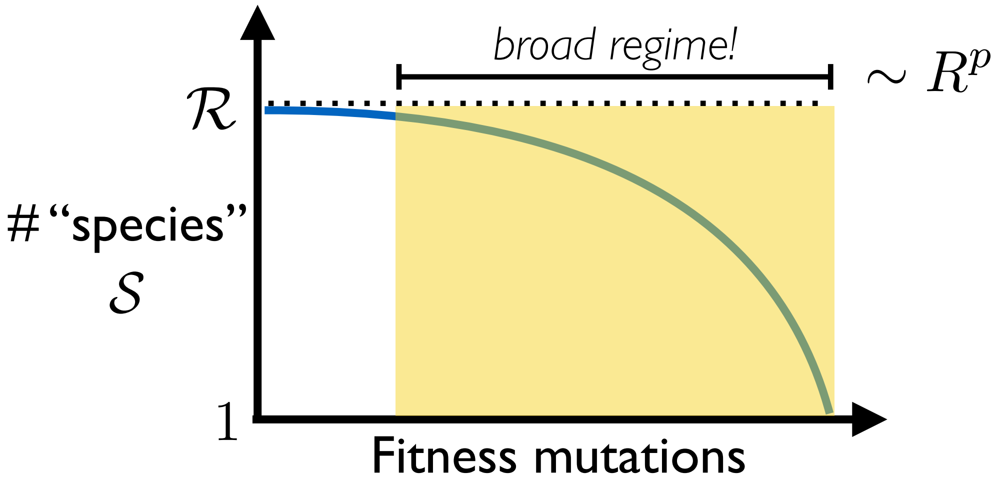

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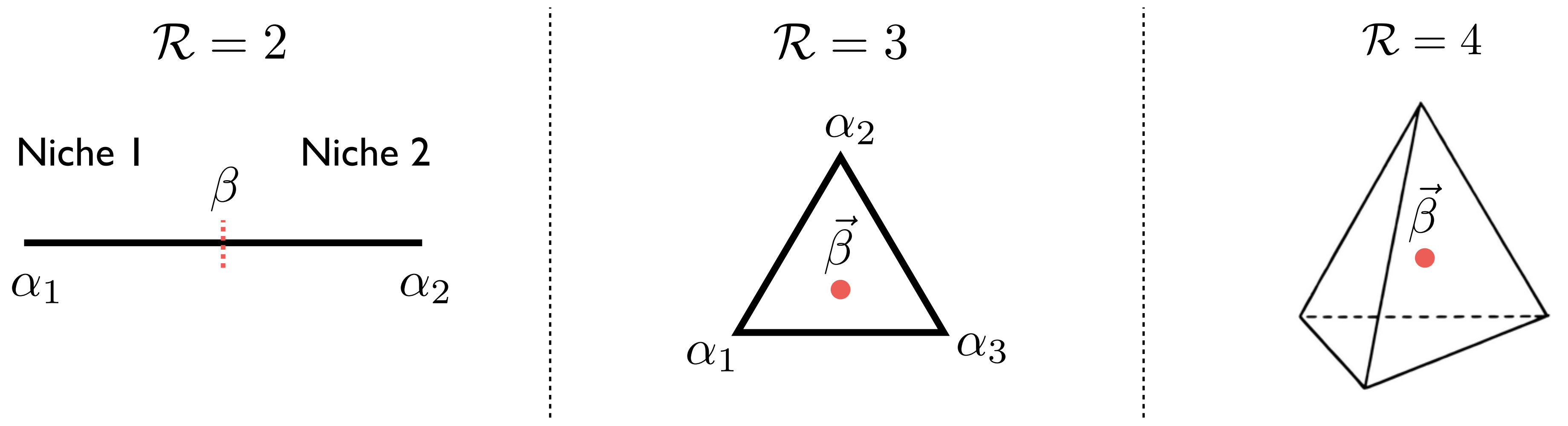

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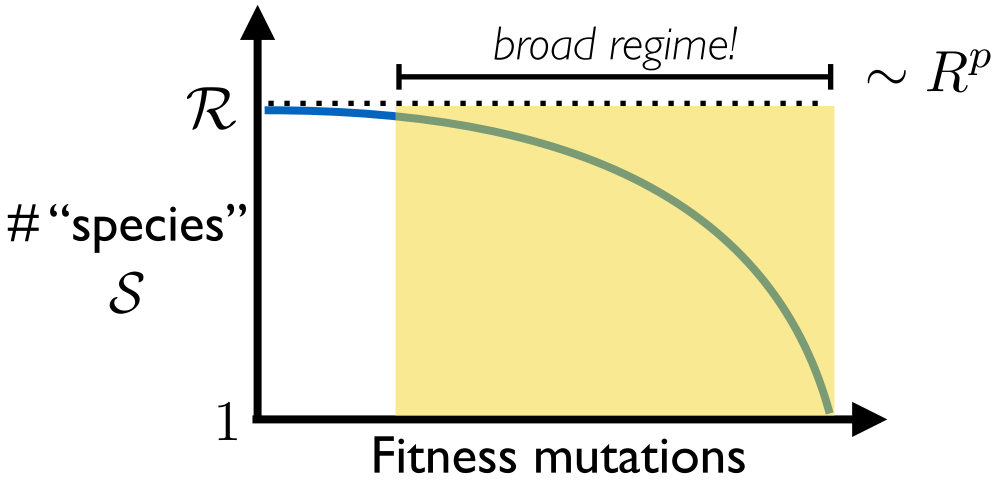

Typical structure of steady-state ecosystem?

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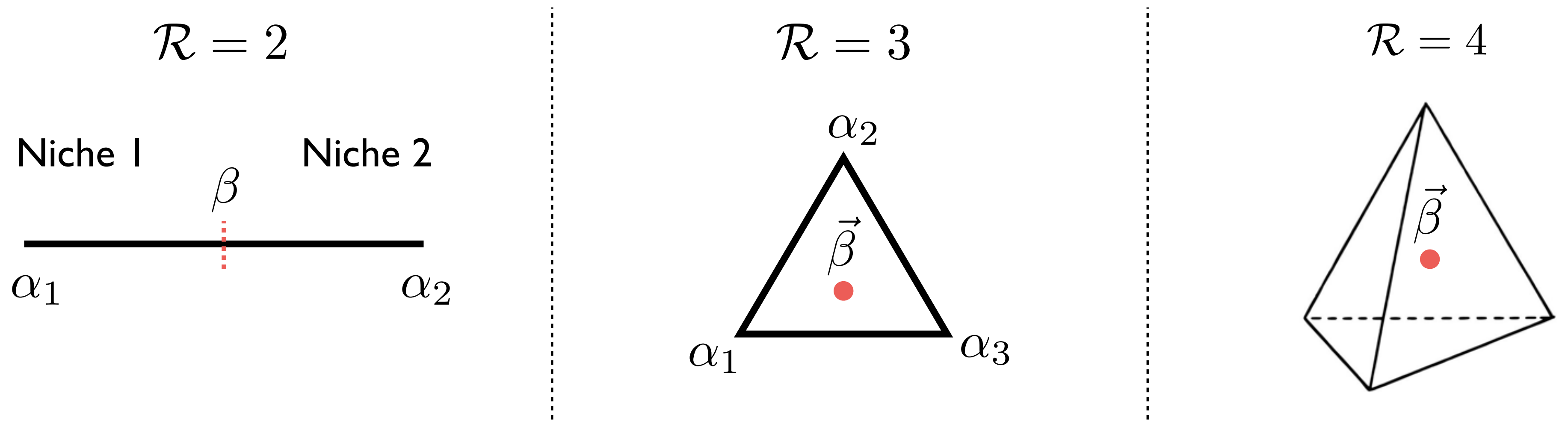

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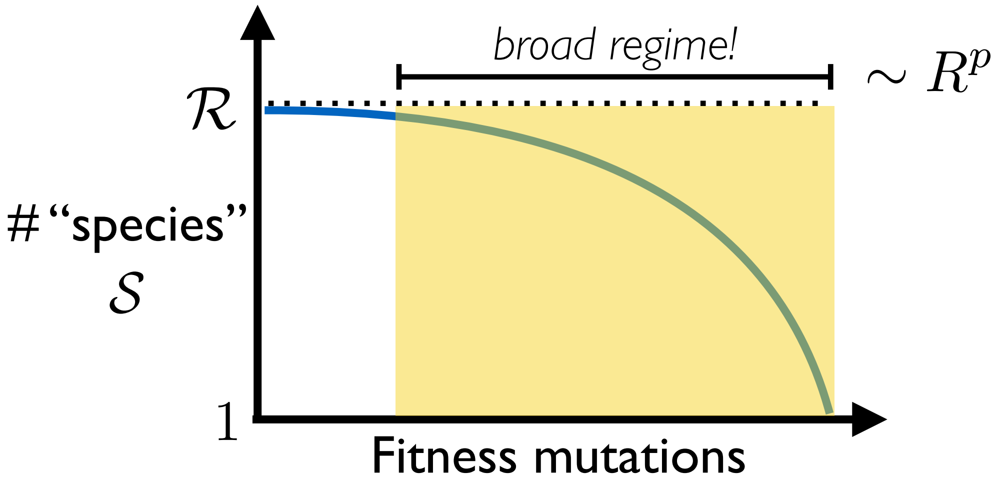

Typical structure of steady-state ecosystem?

Statistical structure of genealogies?

Lots of ***potential*** models… how do we choose?

↓

empirical data from ***natural microbial communities***

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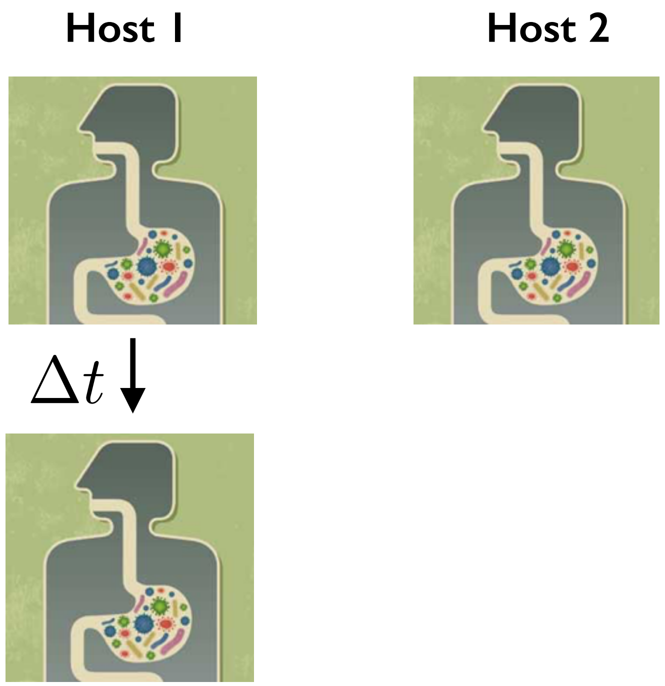
But few observations of evolution so far

Future direction 2: evolution in the gut microbiome



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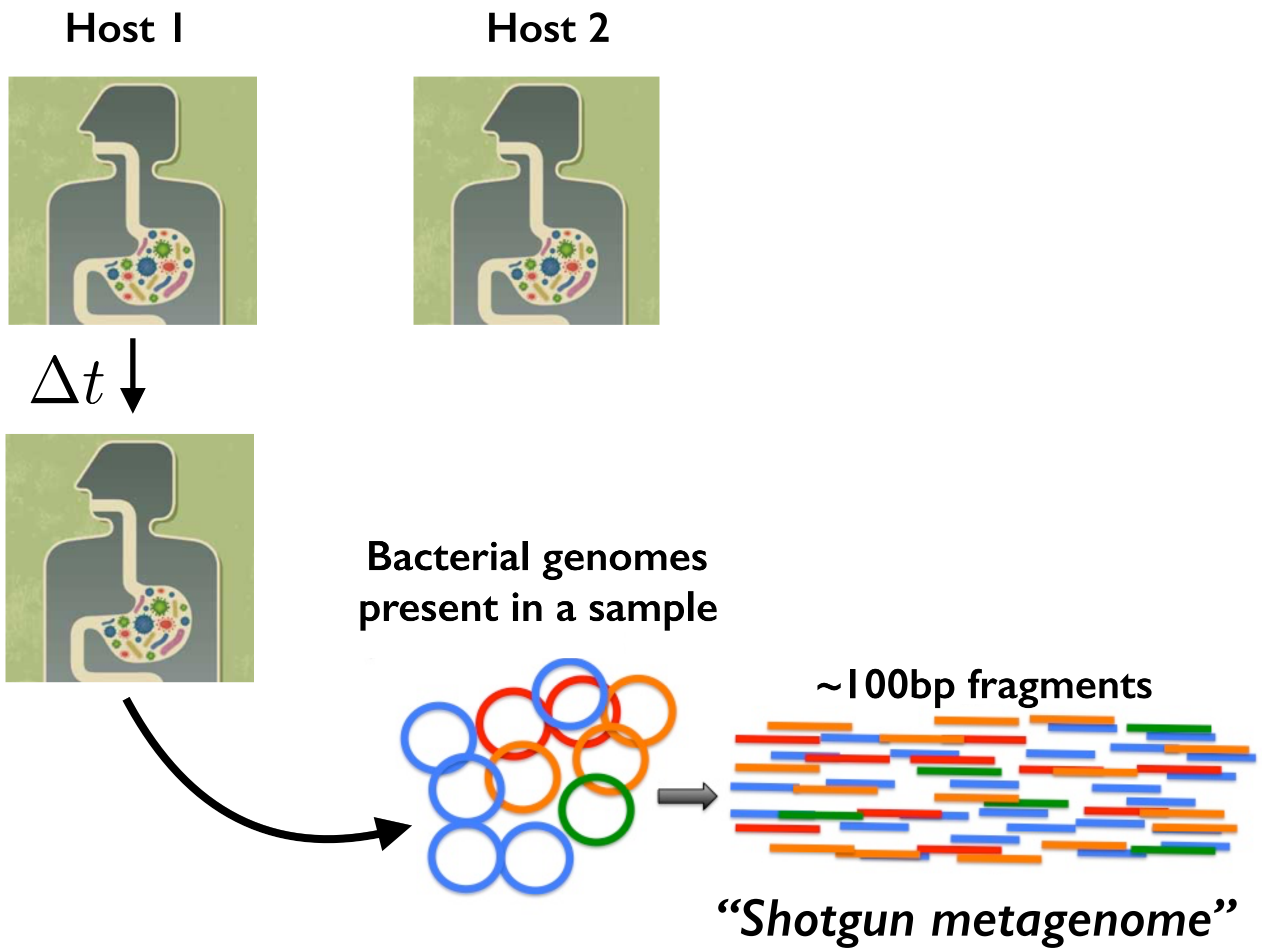

Host 1

Host 2

Δt

Bacterial genomes present in a sample

~100bp fragments

"Shotgun metagenome"

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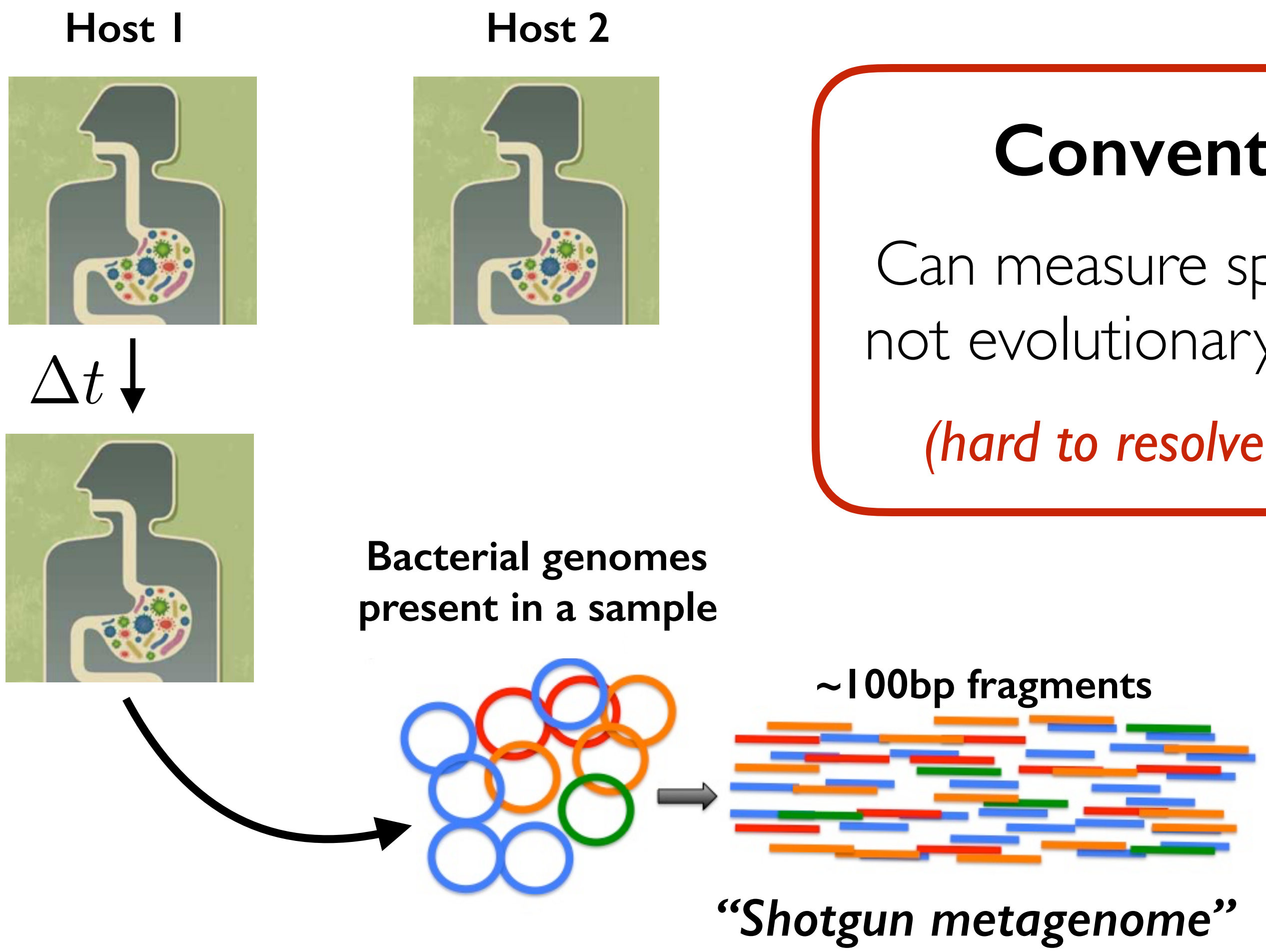

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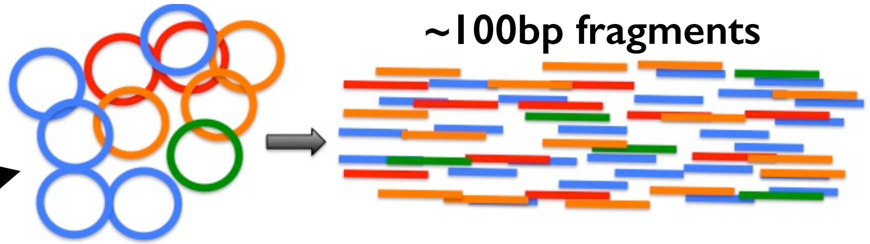

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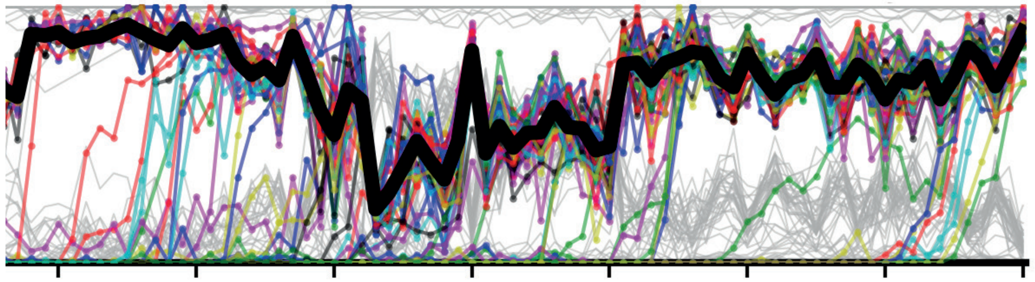
Evolution in LTEE "community"



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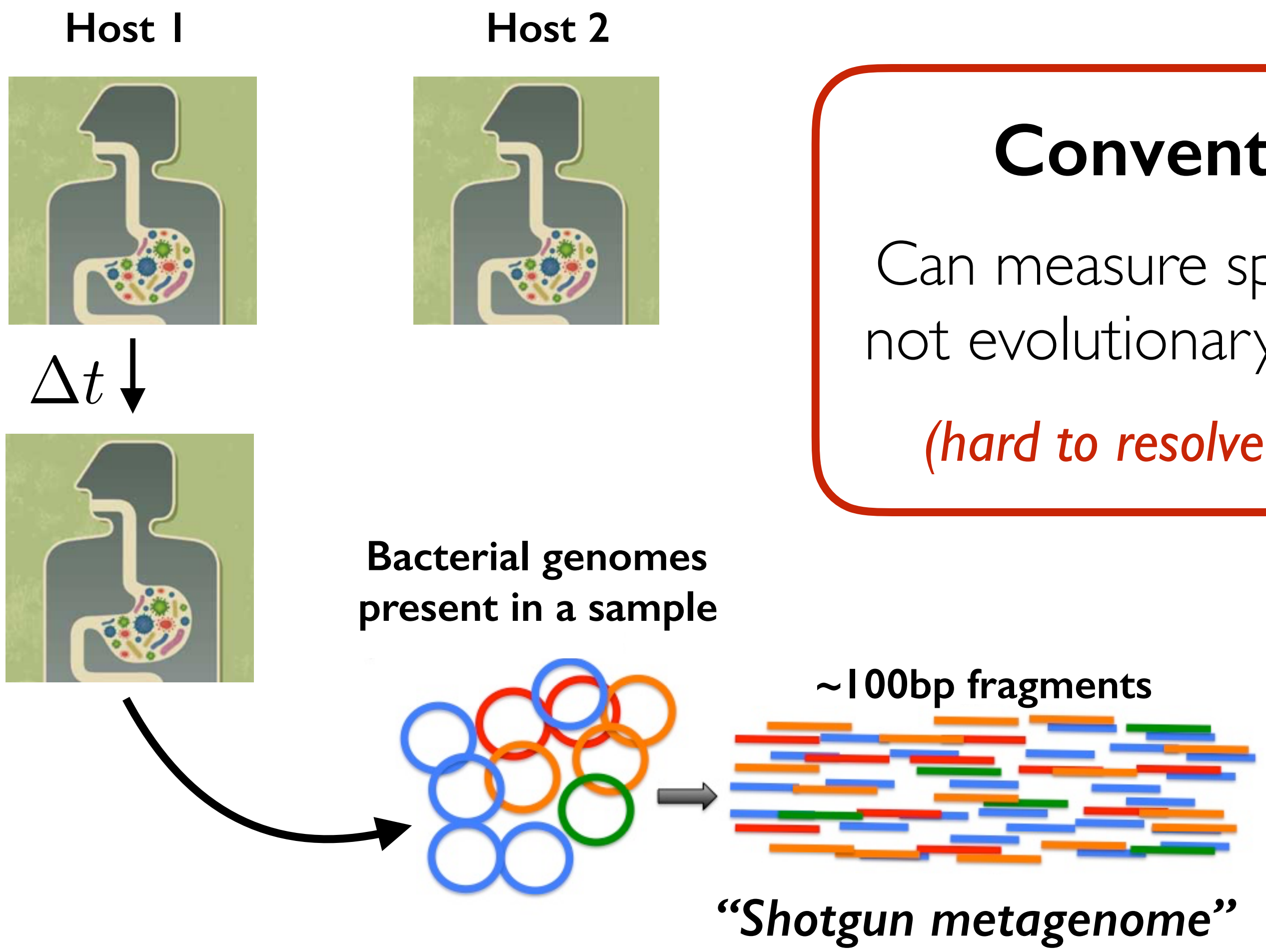

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w/ **Nandita Garud**
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Proof of principle, see: Garud, Good*, et al (biorXiv, 2017)*

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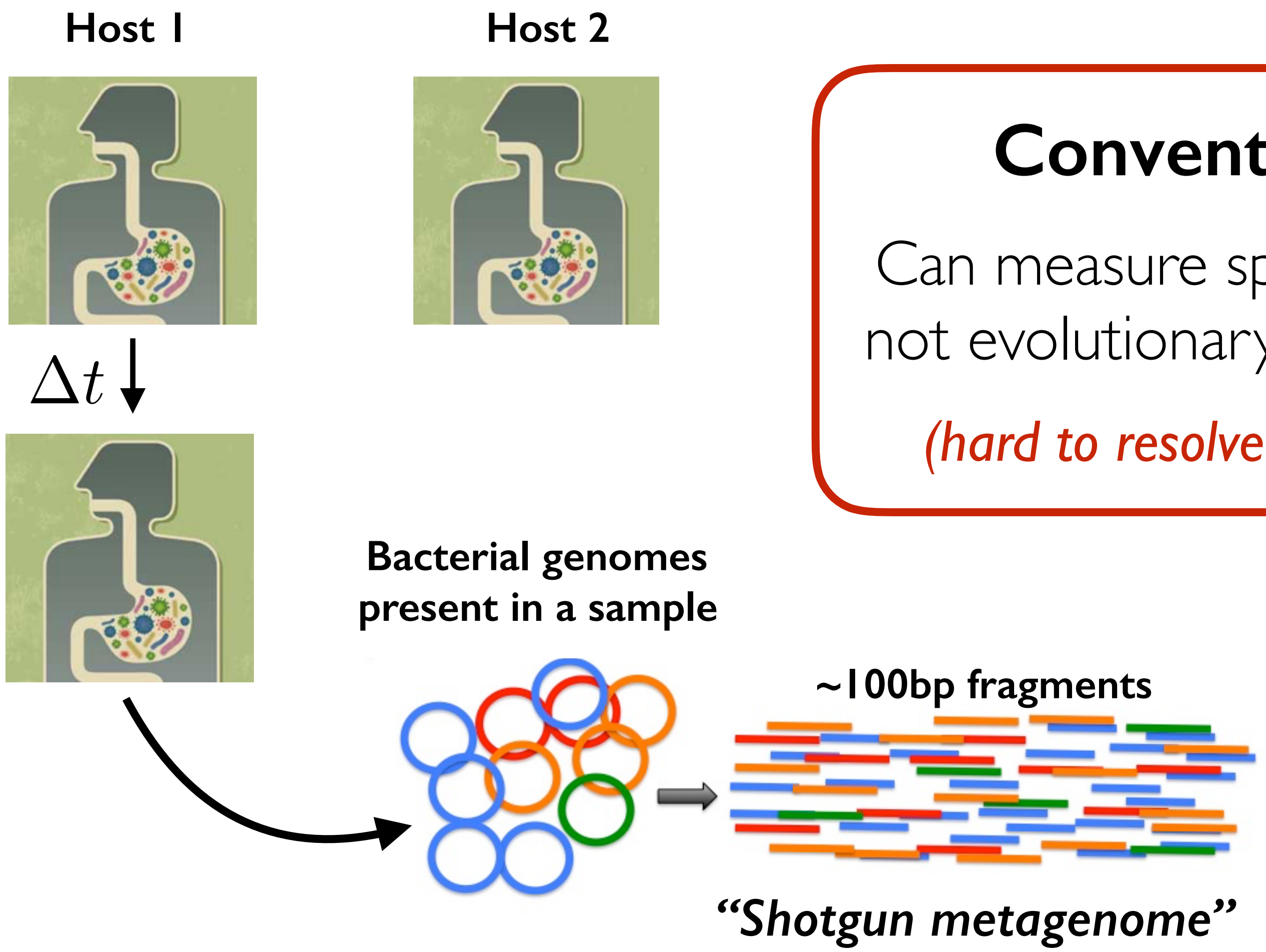

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Methods for measuring evolutionary changes within and across hosts in ~30 gut species

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Preliminary findings and future questions

1. **Across-host genealogical signatures challenge existing pop gen models**

   What models can produce these patterns?

   Global signatures of adaptation? or stasis?

Preliminary findings and future questions

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Is linkage as important as in experimental evolution?

Correlations w/ changes in species abundance? w/ evolution in co-colonizing species?

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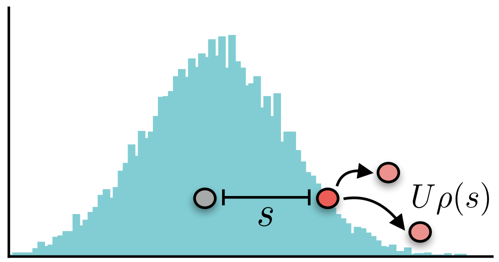
3. Bacterial recombination plays greater role

Will require new theoretical models of selection + linkage + recombination / HGT

Summary

In rapidly evolving populations, fates of mutations are strongly influenced by ***dynamical processes***, in addition to their ***inherent biological effects***.



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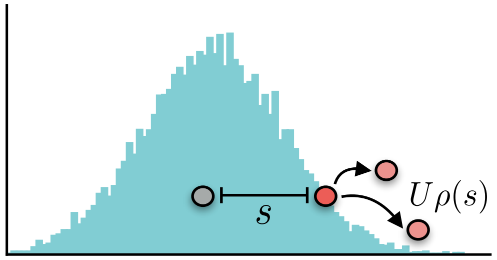
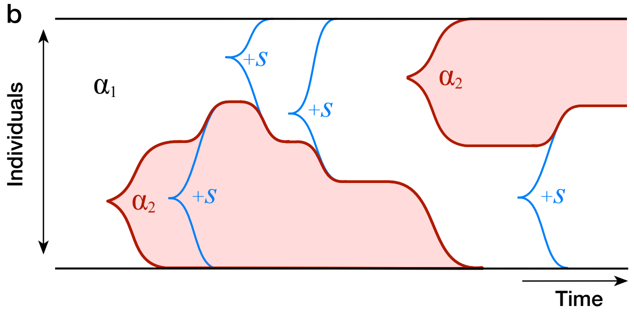


In simple ecological settings, ***rapid evolution*** can also play a important role in determining the ***structure of the community***, and vice versa.



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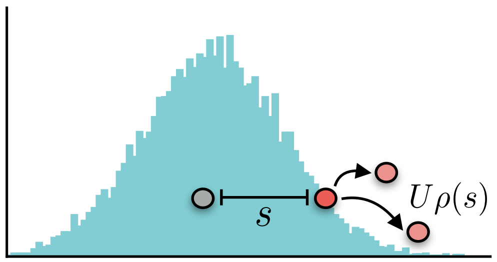

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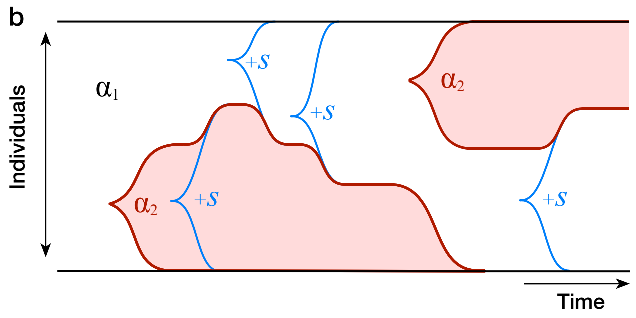
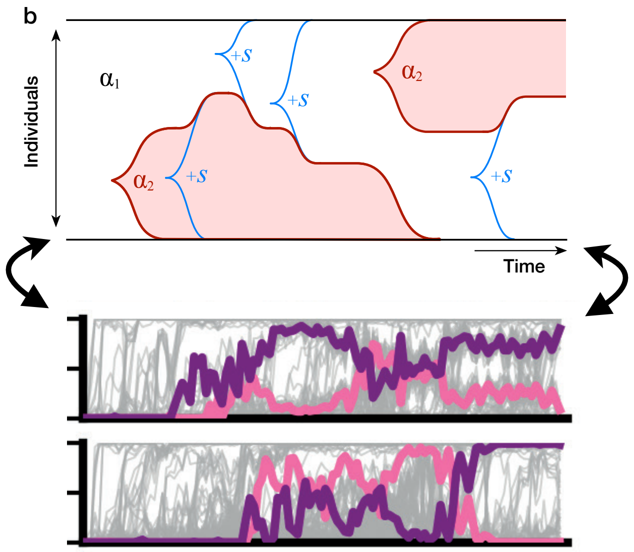
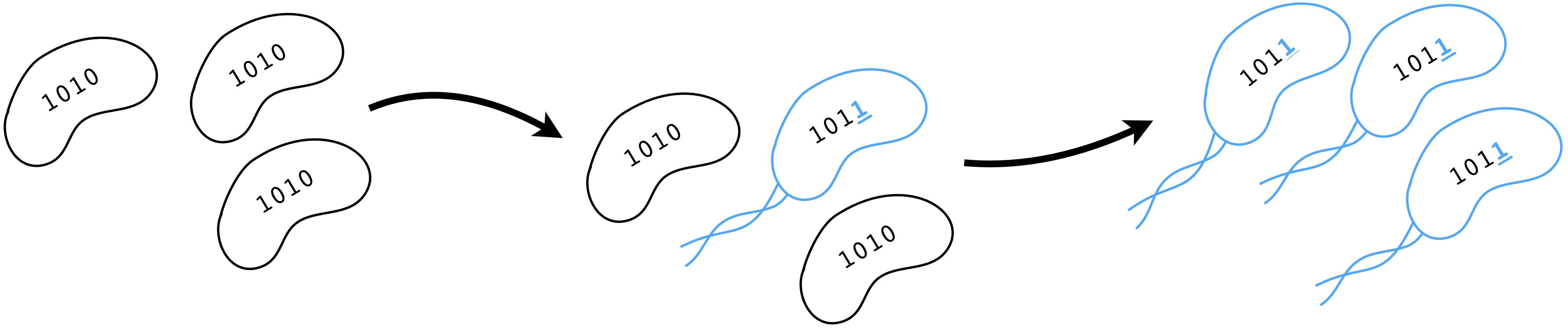


Integrated approach of ***empirically-guided theory*** and ***theoretically-motivated data analysis*** and ***experimental design*** is a promising path toward understanding these processes.



Thanks!



LTEE Sequencing

Mike McDonald (Monash)
Jeff Barrick (UT)
Rich Lenski (MSU).
Michael Desai (Harvard)

Good*, McDonald* et al
(*Nature*, 2017)

Eco-evolutionary theory

Stephen Martis,
Oskar Hallatschek
(UC Berkeley)

Good et al, (in prep)

Evolution in the microbiome

Nandita Garud, Katie Pollard (UCSF)
M. Roodgar, M. Snyder (Stanford)

Garud*, Good*, et al
Evolutionary dynamics of bacteria in the gut microbiome within and across hosts
(*biorXiv* 210955)

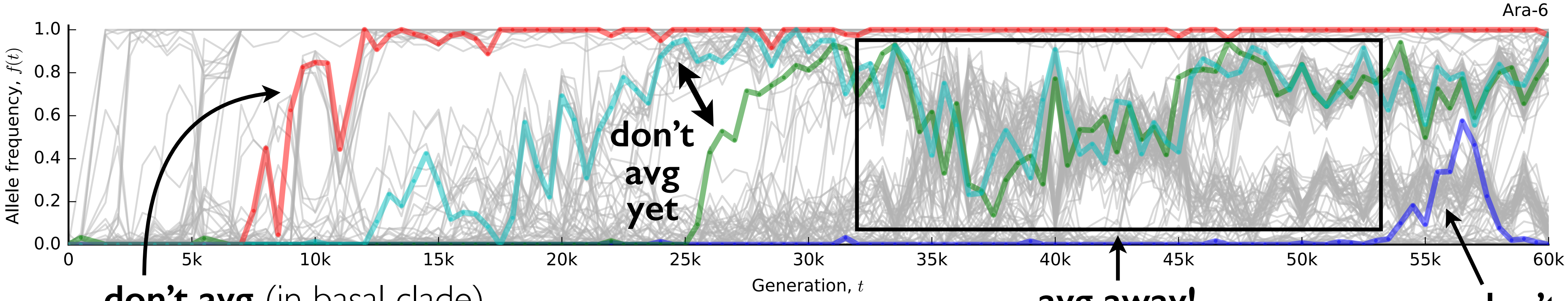
Other collaborators: Ivana Cvijovic (Harvard), Matt Melissa (Harvard), Genya Frenkel (Whitehead), Dan Rice (Chicago), Elizabeth Jerison (Stanford), Daniel Balick (HMS), Richard Neher (Biozentrum), Aleksandra Walczak (ENS), Igor Rouzine (Gladstone)

Miller Institute for Basic Research in Science, University of California, Berkeley

Inferring clade dynamics with hidden Markov models

Basic idea: individual mutations noisy ⟶ avg together to measure clade freq

Problem: which mutations to average, which times to average?



don't avg yet

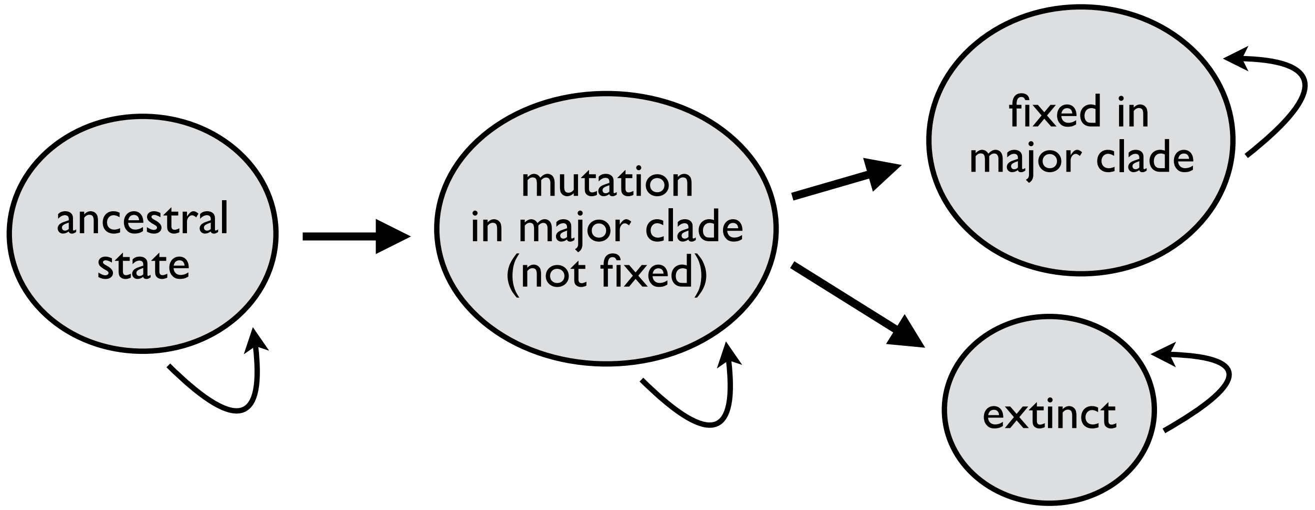
don't avg (in basal clade)

avg away!

don't avg (goes extinct)

Solution: infer with custom hidden Markov model (***cladeHMM***)
⟶ like clustering, but phylogenetically-aware

E.g.



ancestral state

mutation in major clade (not fixed)

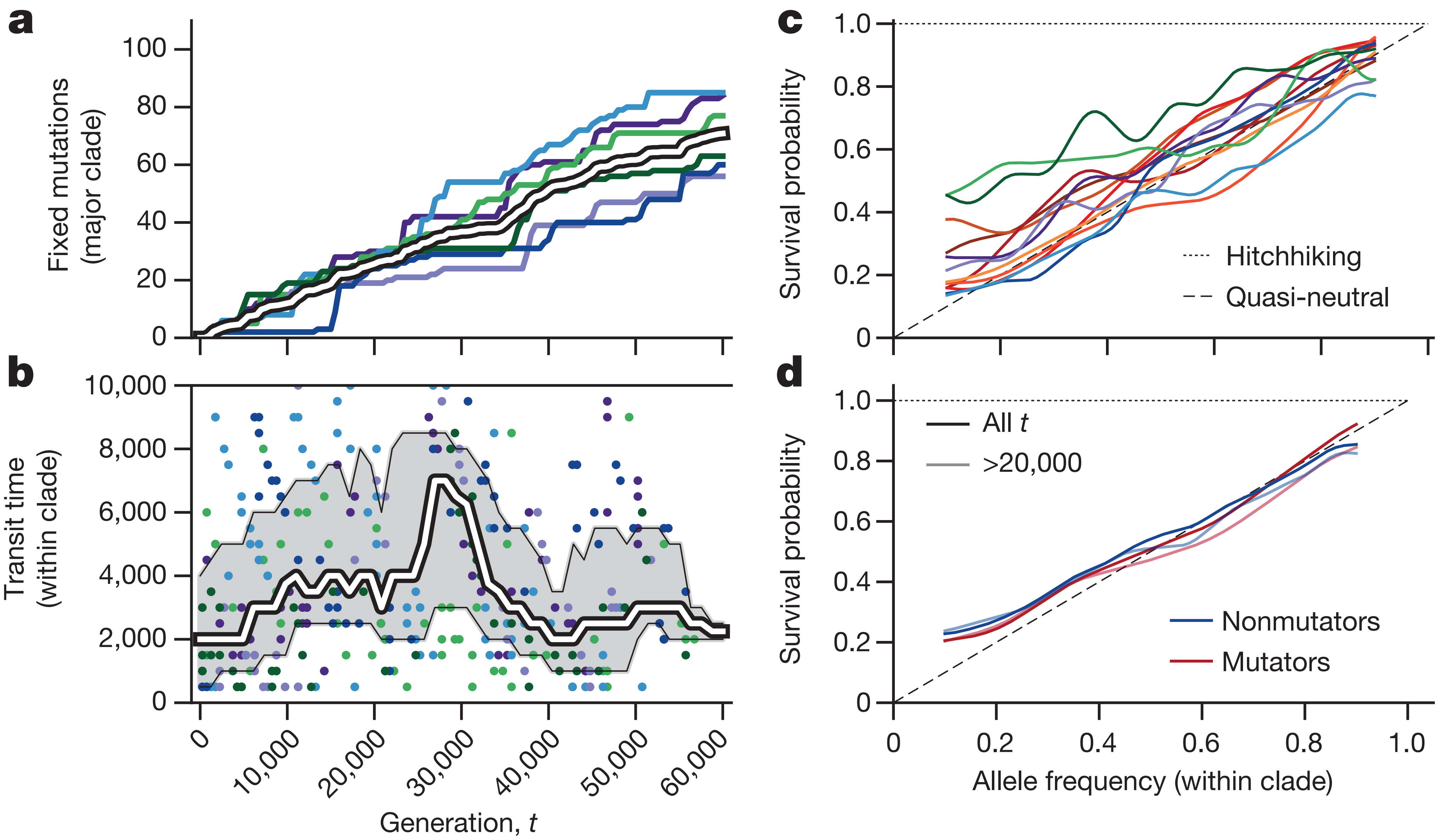
fixed in major clade

extinct

\+ etc.

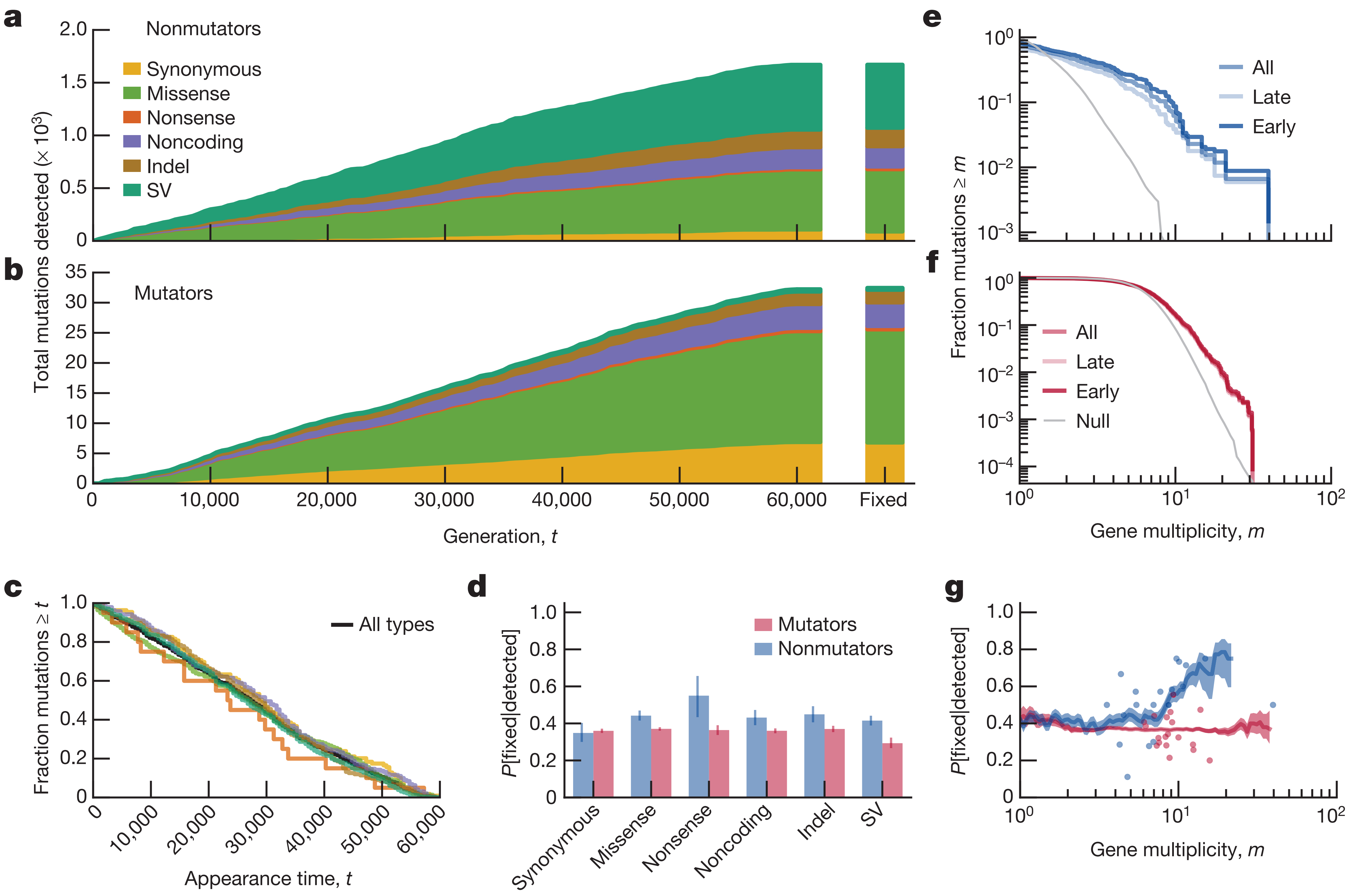
Good, McDonald* et al (Nature, 2017)*

Rapid adaption and clonal interference within clades



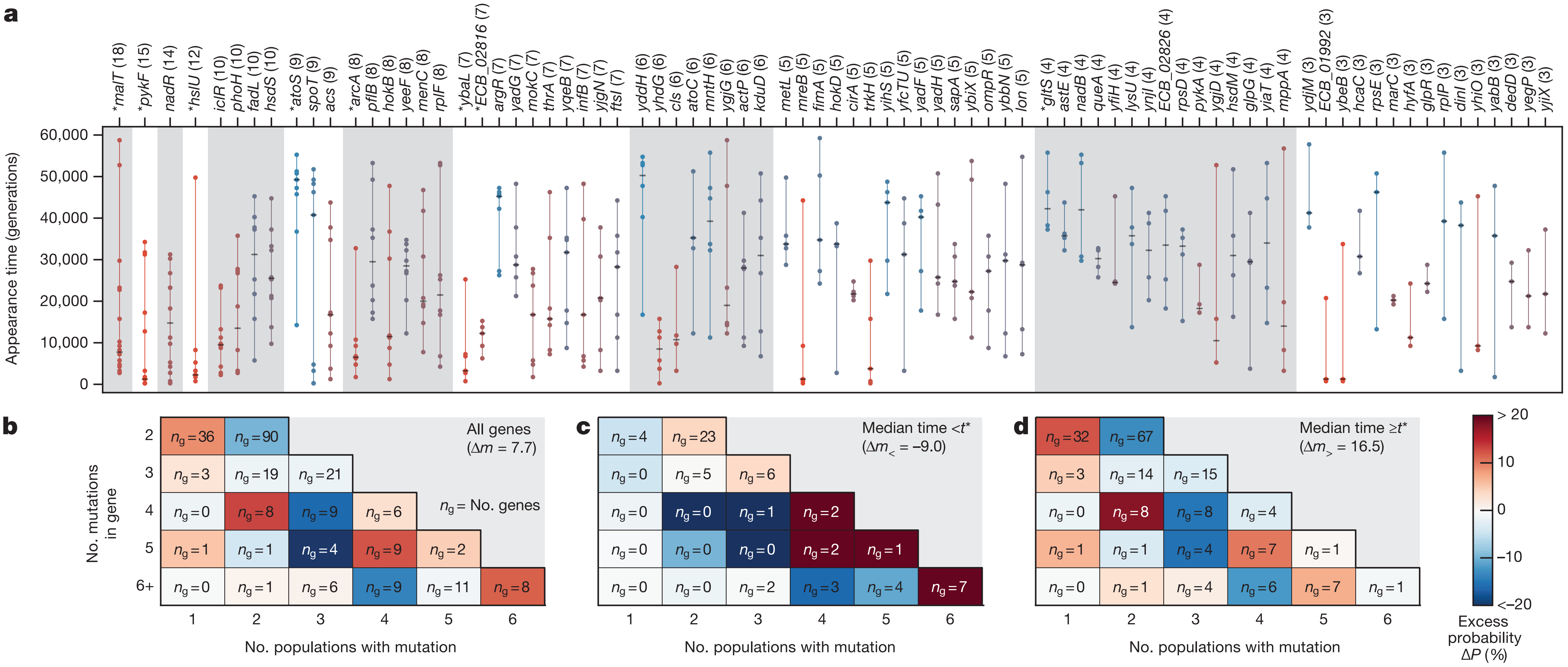
Good, McDonald* et al (Nature, 2017)*

Parallelism at the genetic level



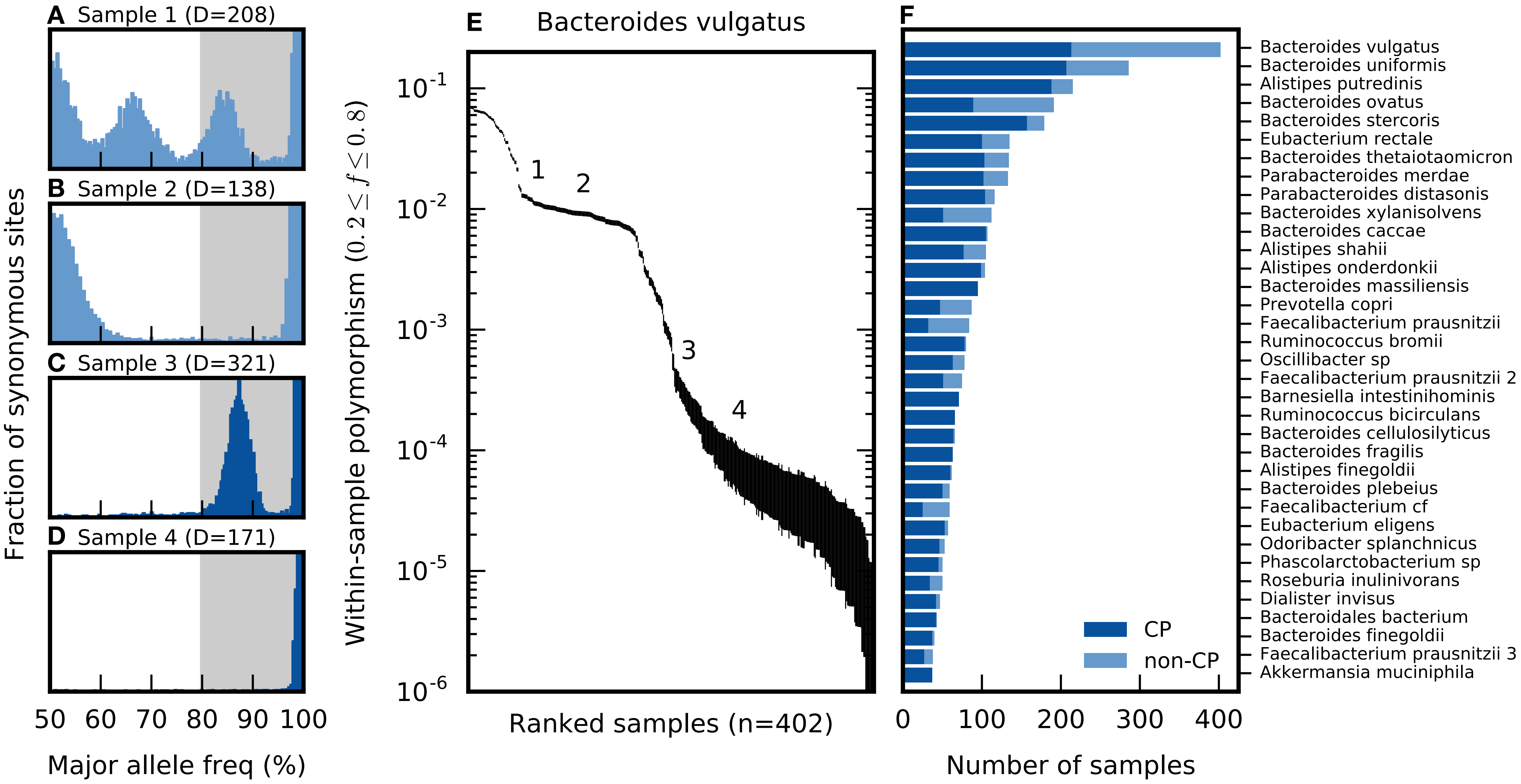
Good, McDonald* et al (Nature, 2017)*

Patterns of epistasis and contingency at the gene level



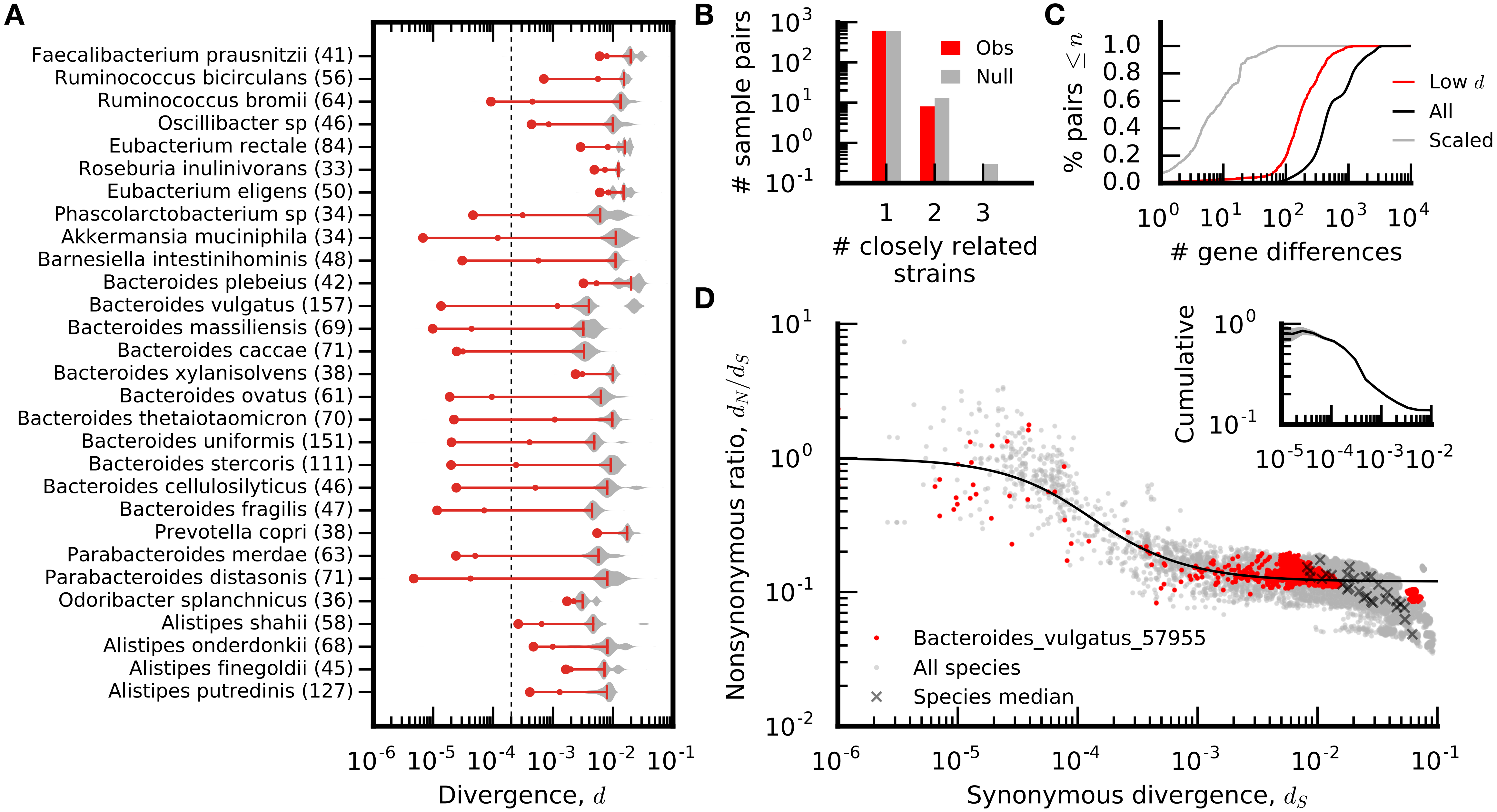
Good, McDonald* et al (Nature, 2017)*

Patterns of genetic diversity within hosts



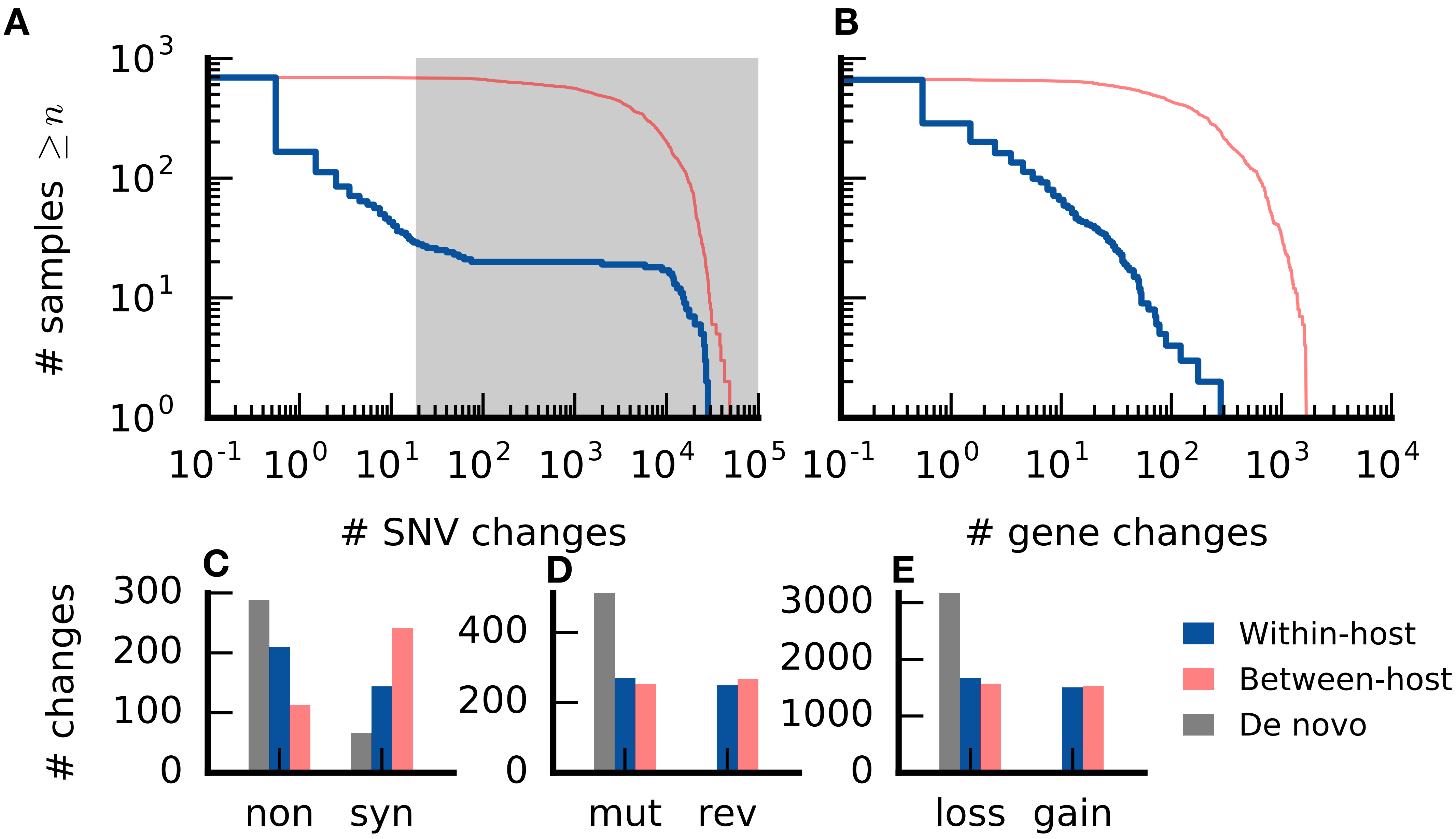
Garud, Good*, et al (biorxiv 2017)*

Patterns of genetic divergence across hosts



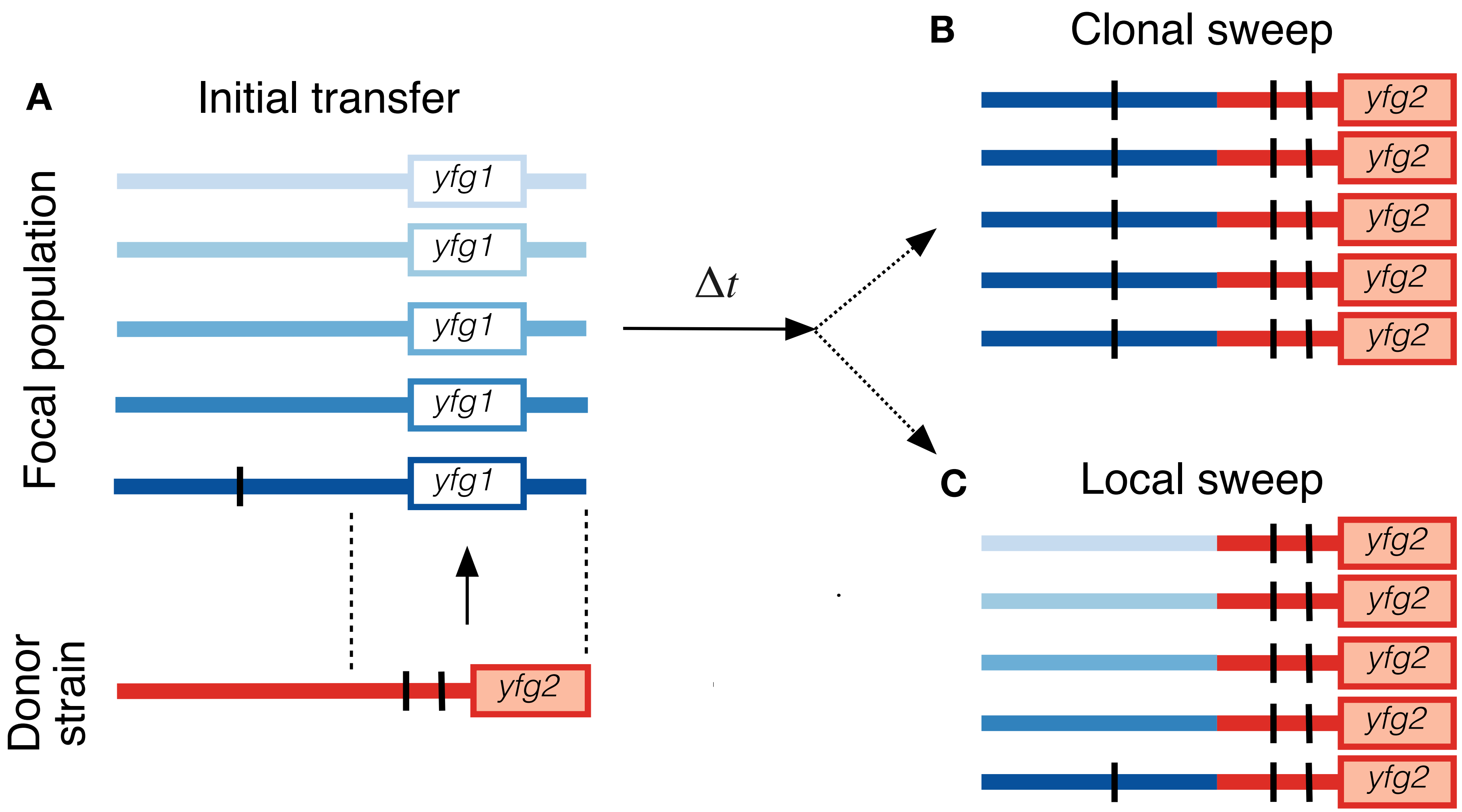
Garud, Good*, et al (biorxiv 2017)*

Short-term succession within hosts



Garud, Good*, et al (biorxiv 2017)*

Putative model of within-host evolution



Garud, Good*, et al (biorxiv 2017)*