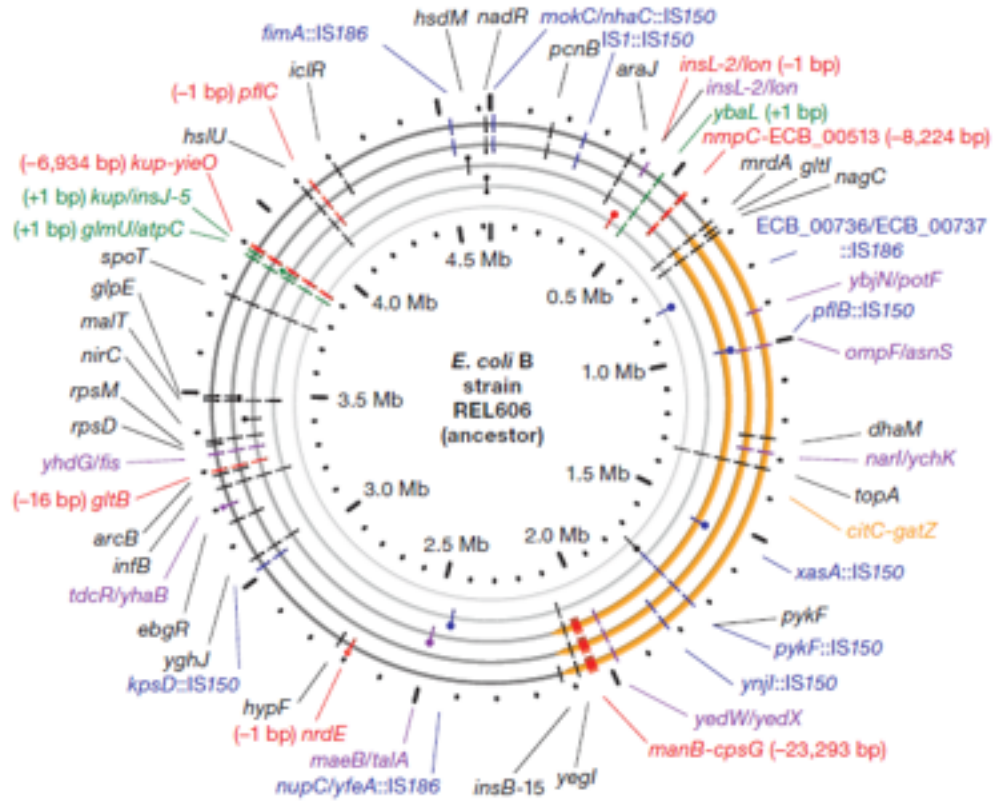
Evolution as a Stochastic Algorithm

Set of Possibilities
Mutations and Fitness Effects

Evolutionary Dynamics:
Mutations, Selection, Drift

Set of Outcomes
Fixed Mutations, Patterns of Variation, etc.



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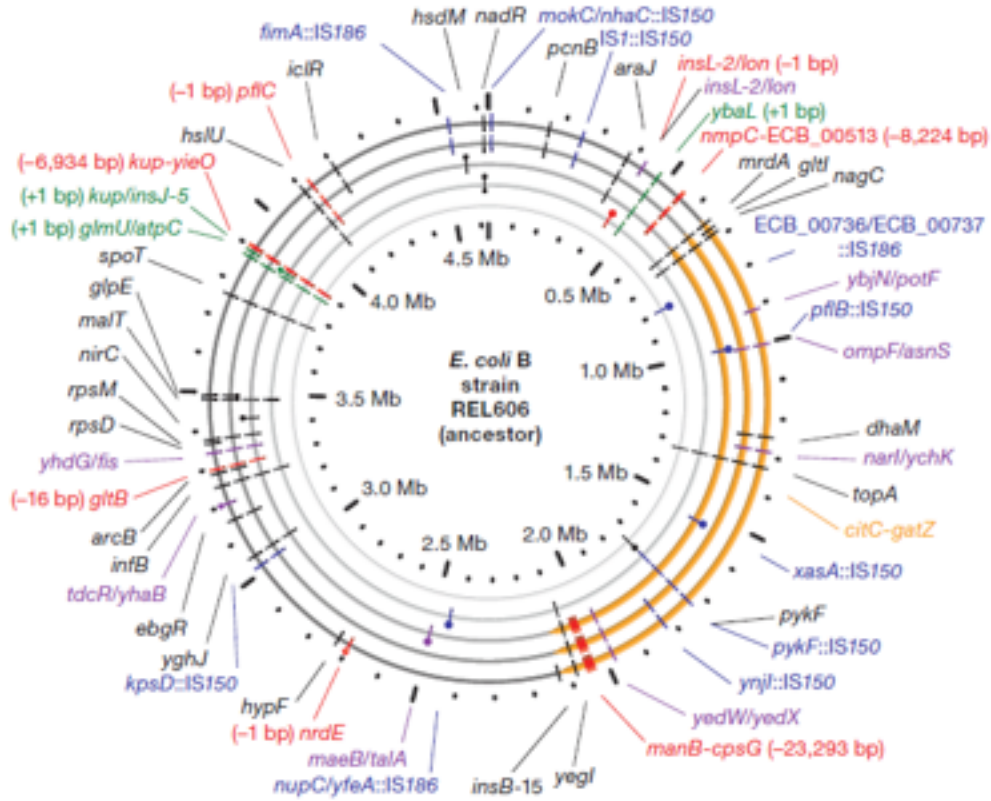

Set of Outcomes
Fixed Mutations, Patterns of Variation, etc.

The rules are well known:
Mutations generate variation. Drift, selection, recombination etc. alter frequencies of variants

The quantitative consequences are not understood, even in very simple situations!

Acknowledgements

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Lucy Colwell
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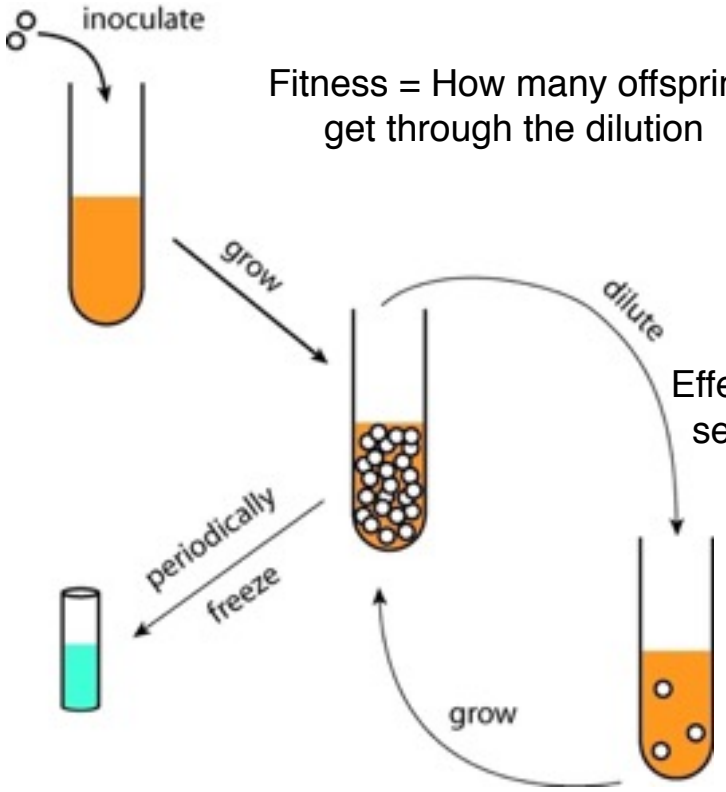
Sebastian Akle
Lauren Nicolaisen
Genya Frenkel

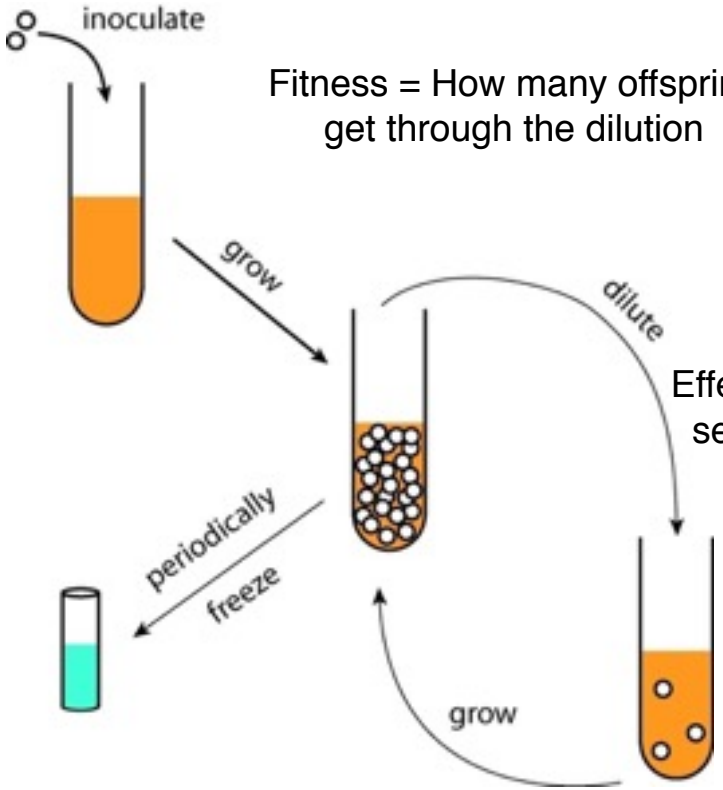
Evolution in Laboratory Yeast Populations



Fitness = How many offspring get through the dilution

Effective population size set by bottleneck size

Evolution in Laboratory Yeast Populations



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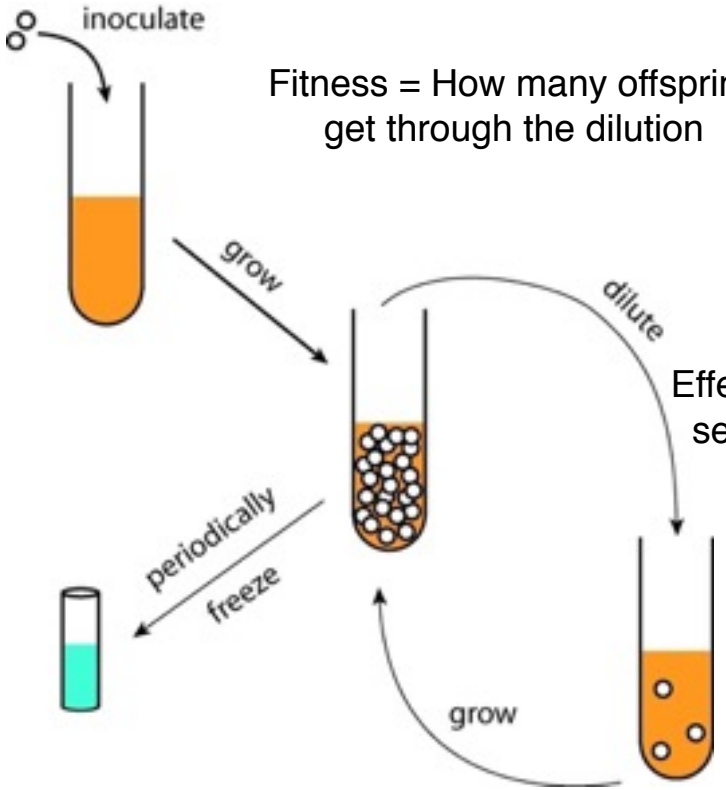

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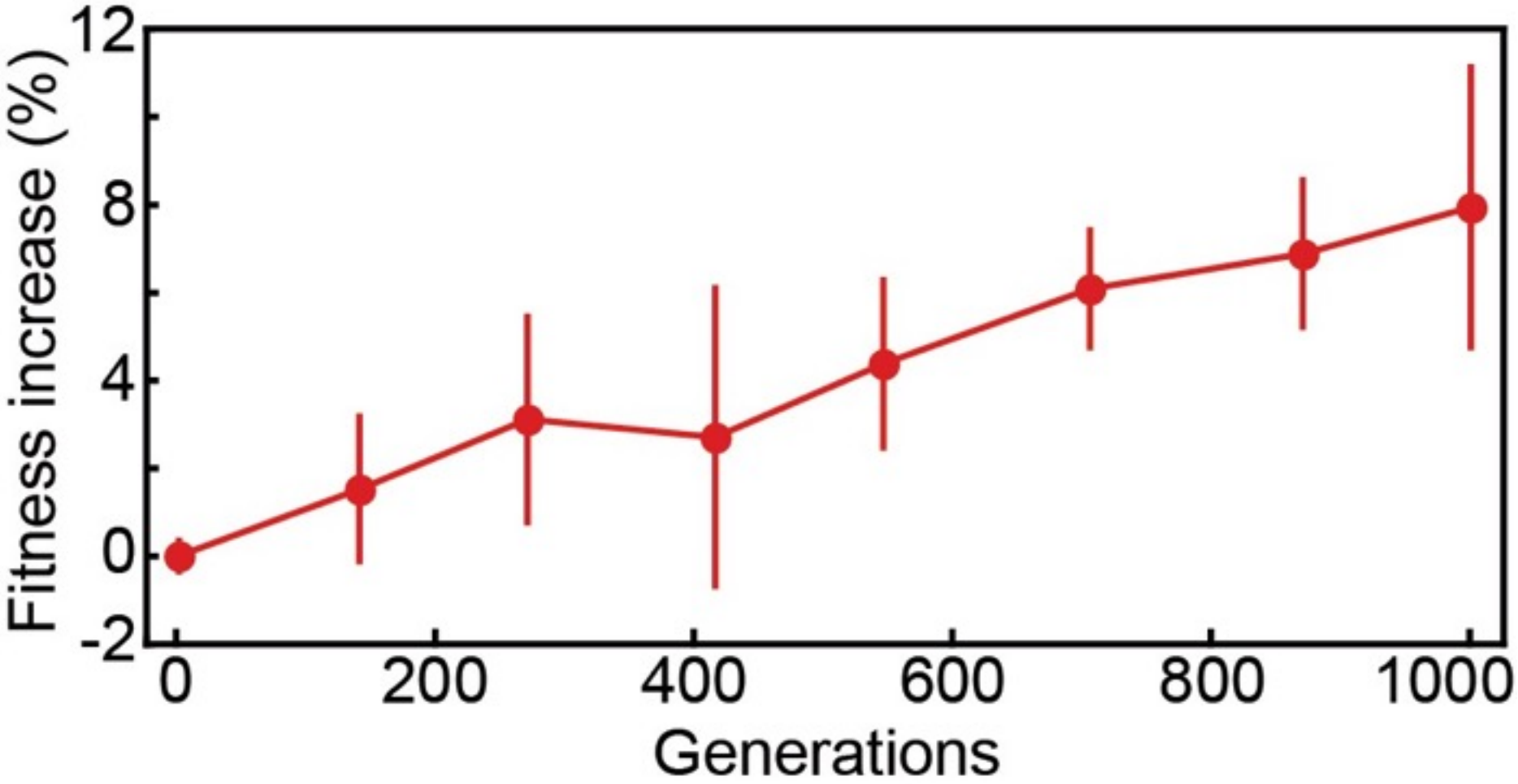
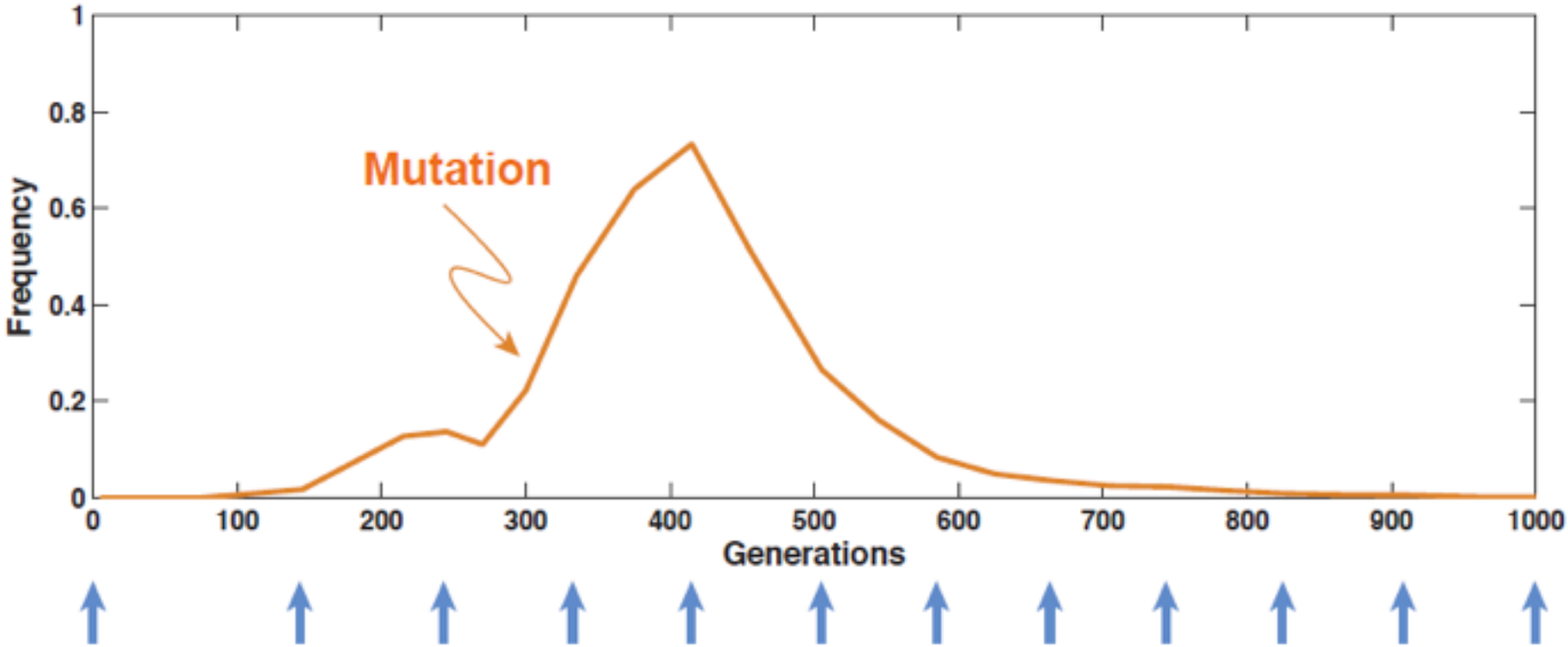
Haploid Asexual Budding Yeast in Rich Laboratory Media: *A completely artificial system!*

Can we understand evolution in the simplest possible settings?

Populations adapt in response to selective pressures



Sequencing to Observe Evolutionary Dynamics



Sequencing:

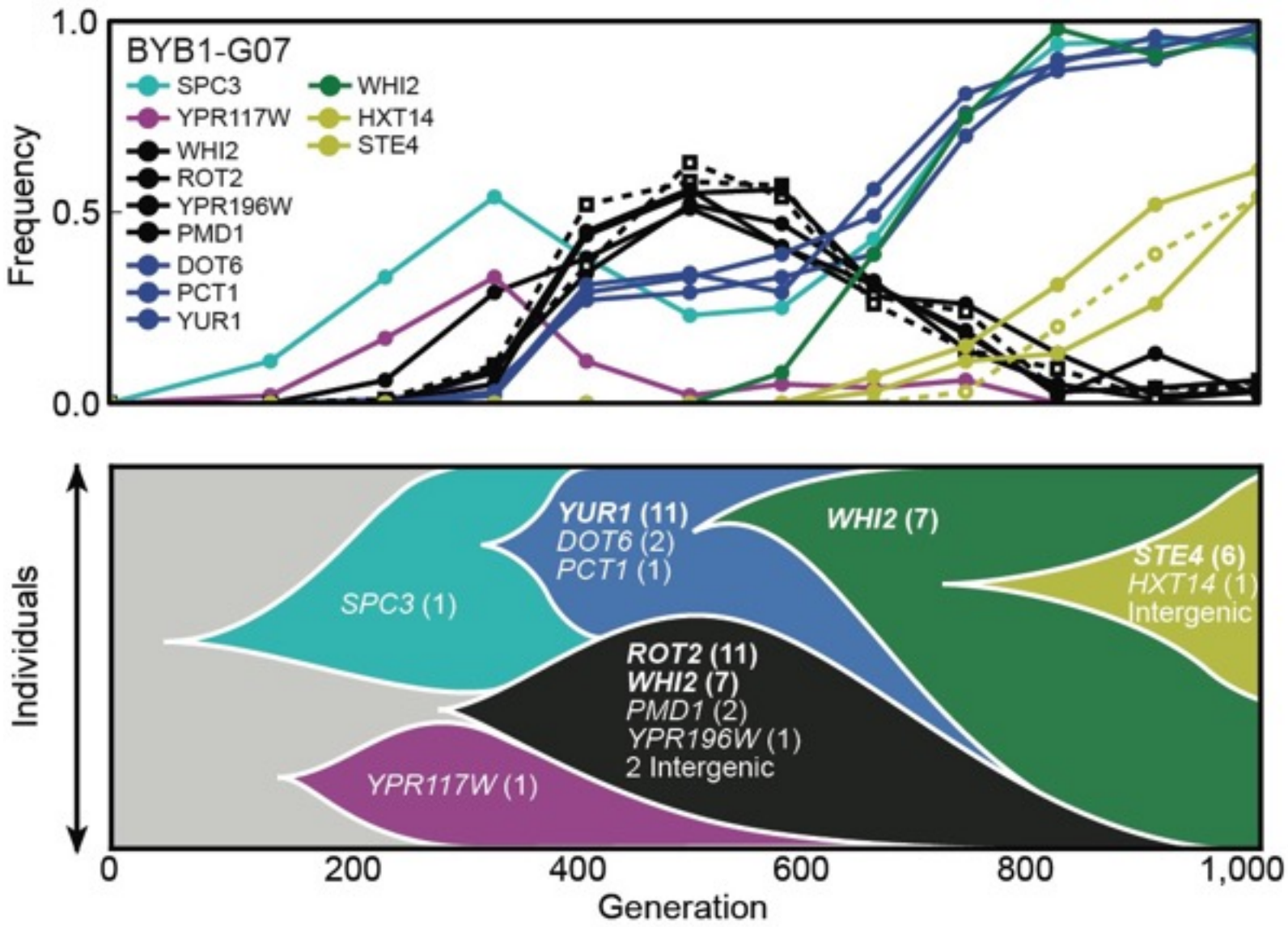
Population (“metagenomic”) whole-genome sequencing at multiple timepoints through the evolution

Leverage entire timecourse simultaneously to distinguish true mutations from sequencing errors.

More generally, build error model from all the data. Find true mutations by looking for deviations from the error model that obey the known genealogy.

We identify mutations that reach a frequency of at least ~10% at some point during the timecourse.

Interference and Hitchhiking Determine Outcomes



Long-Term Evolution in a Constant Environment

Our results show that rapid adaptation to a new environment on relatively short timescales are characterized by pervasive selection, clonal interference, and hitchhiking

Does long-term evolution in a constant environment look different?

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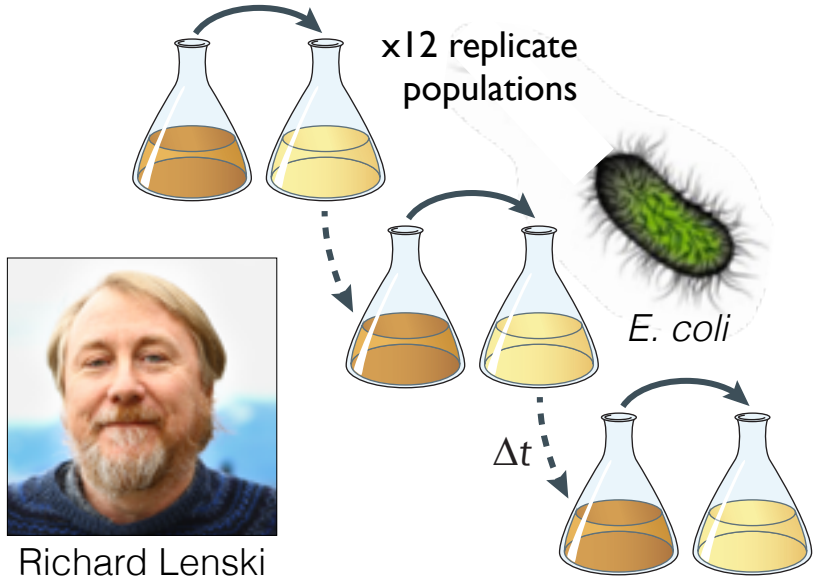

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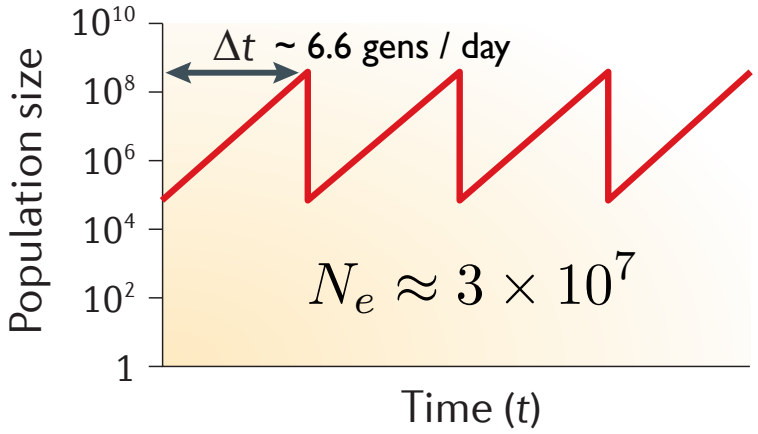

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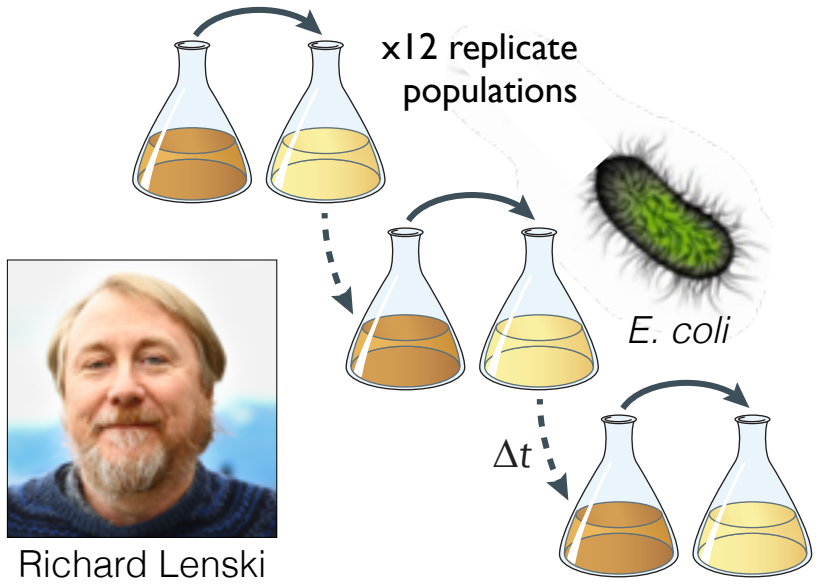

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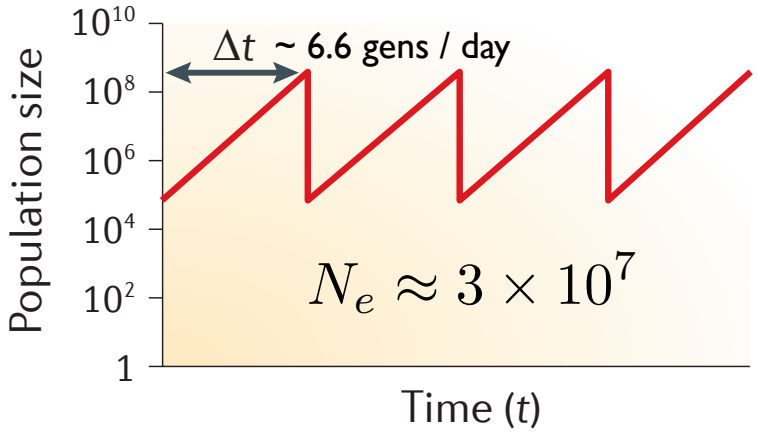

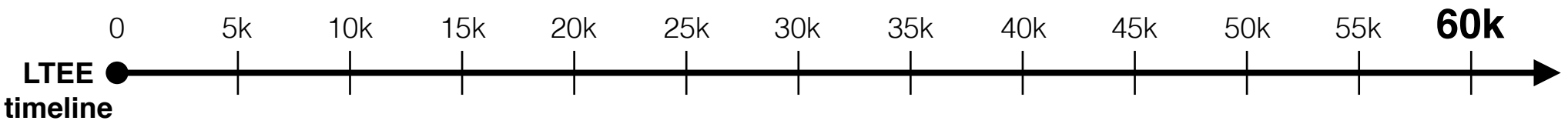

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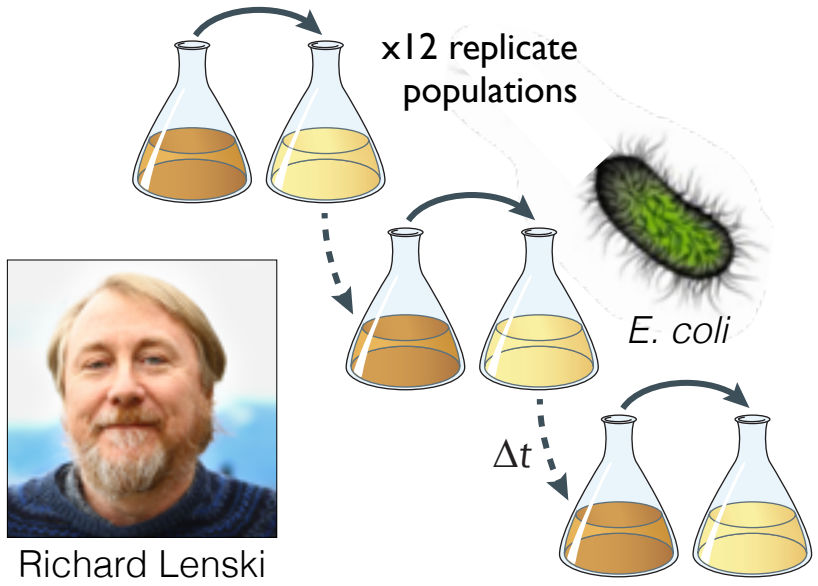

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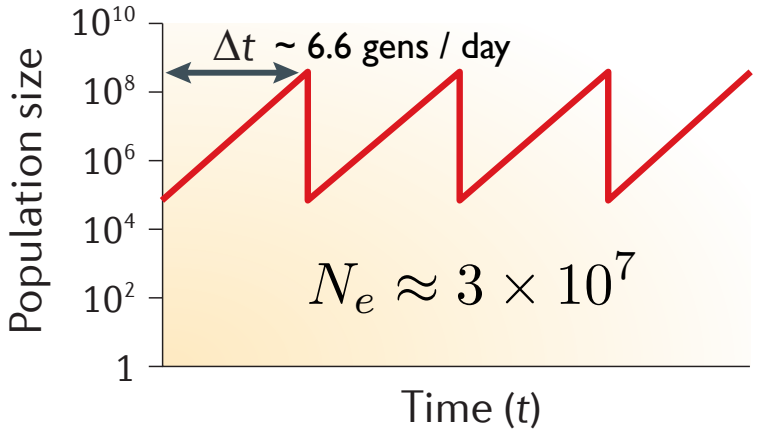

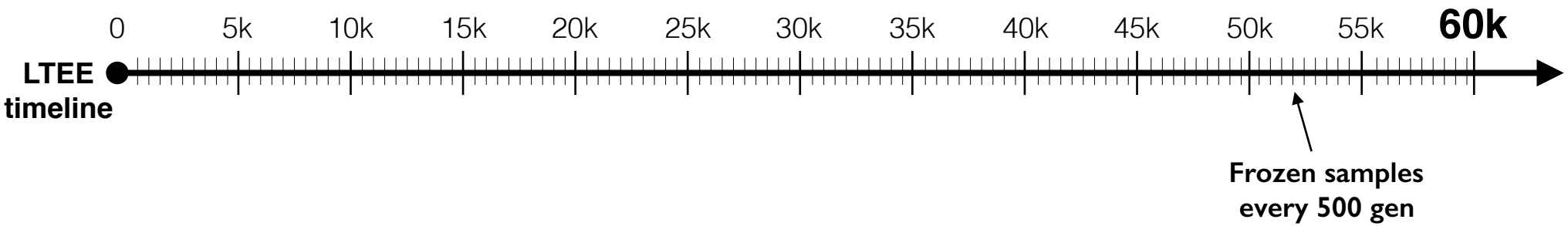

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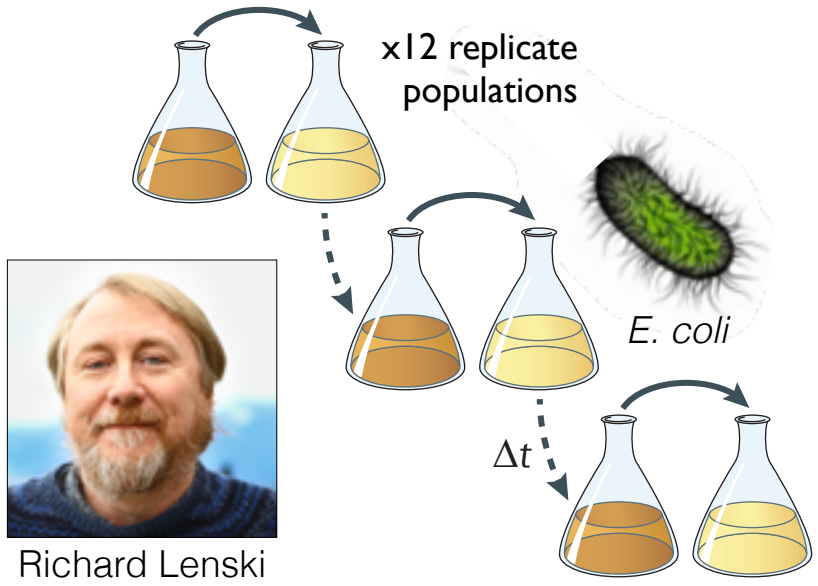

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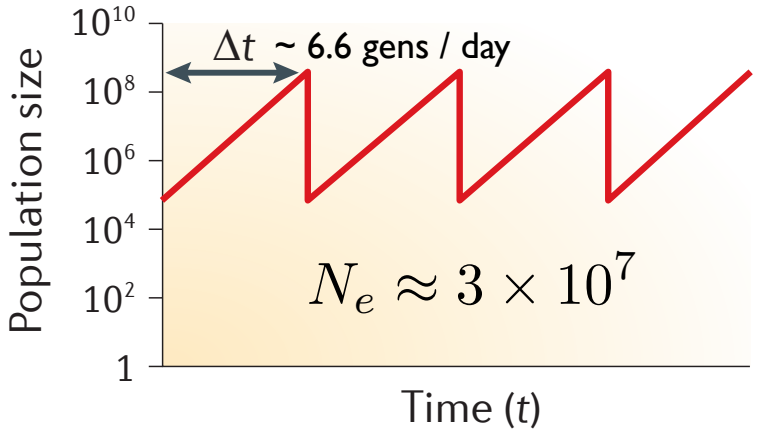

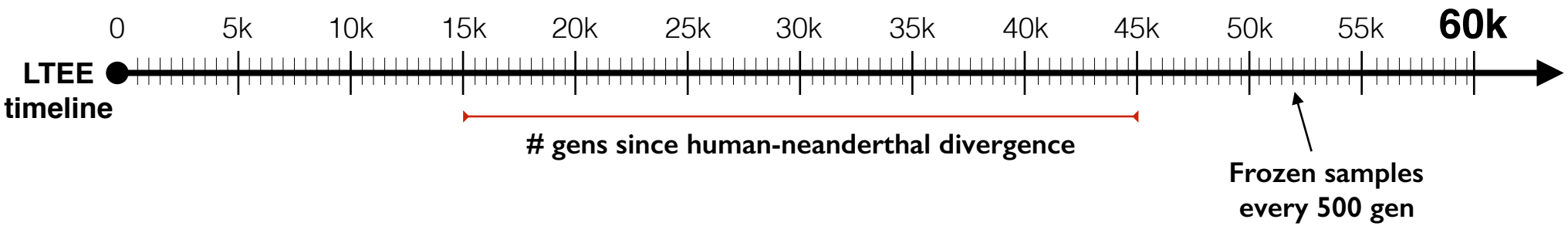

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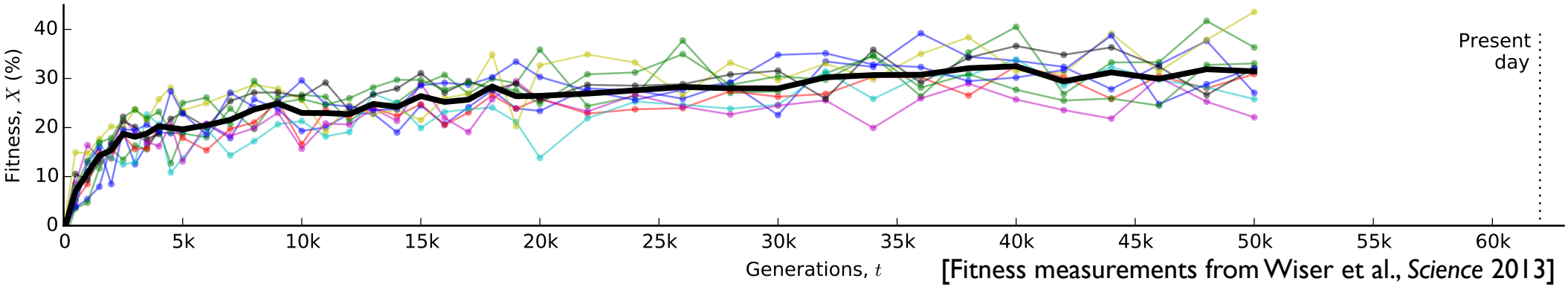

[Fitness measurements from Wiser et al., *Science* 2013]

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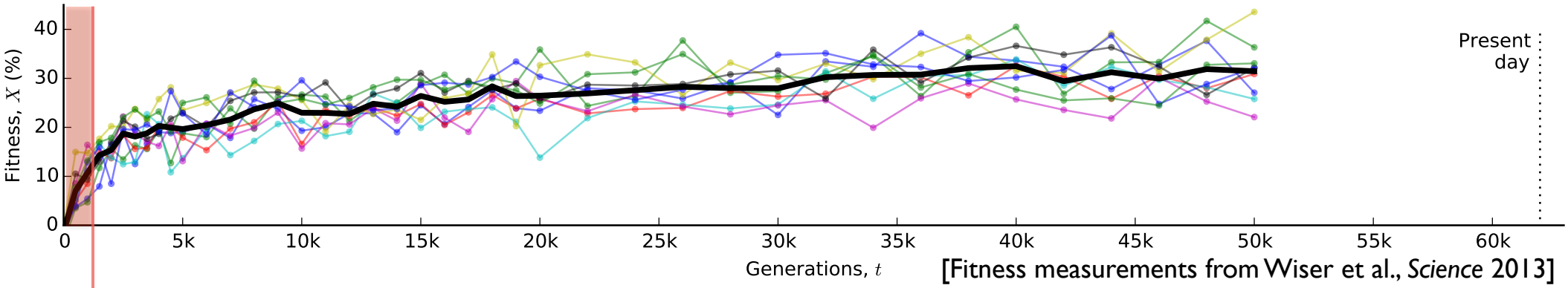

- Lang *et al* (2013), *S. cerevisiae*
- Traverse *et al* (2013), *B. cenocepacia*
- Herron *et al* (2013), *E. coli*
- Barroso-Batista *et al* (2014), *E. coli* in mouse gut
- Kvitek and Sherlock (2013), *S. cerevisiae*

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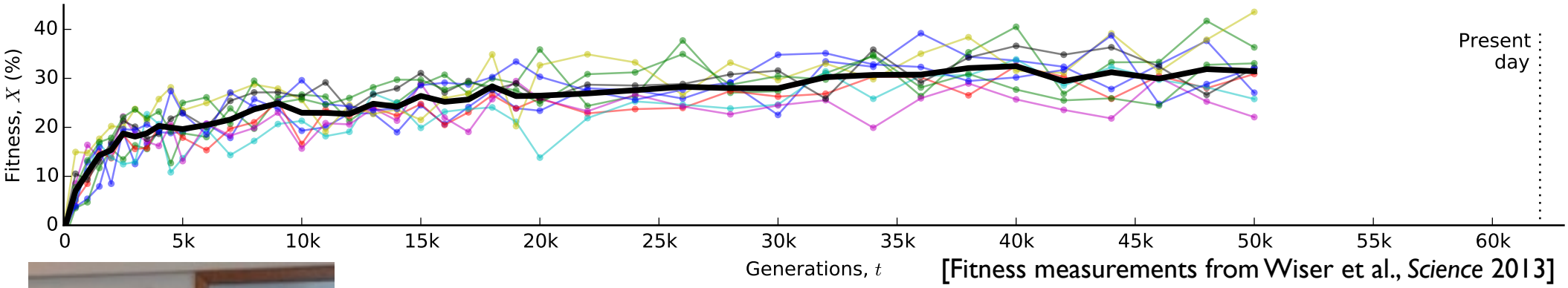

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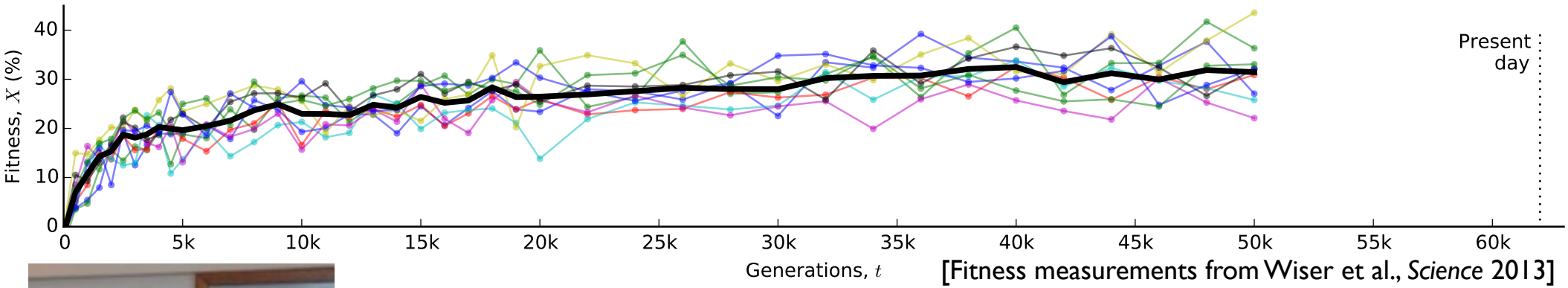

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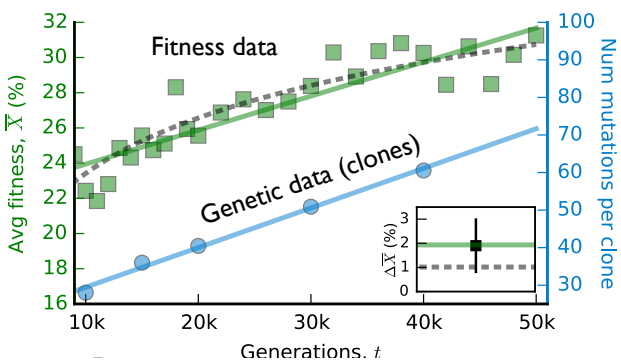
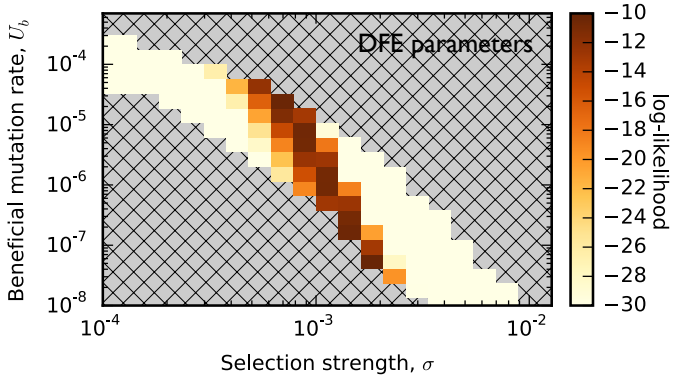
Inference w/ approximate likelihood framework





[Good and Desai, *Genetics* 2015]

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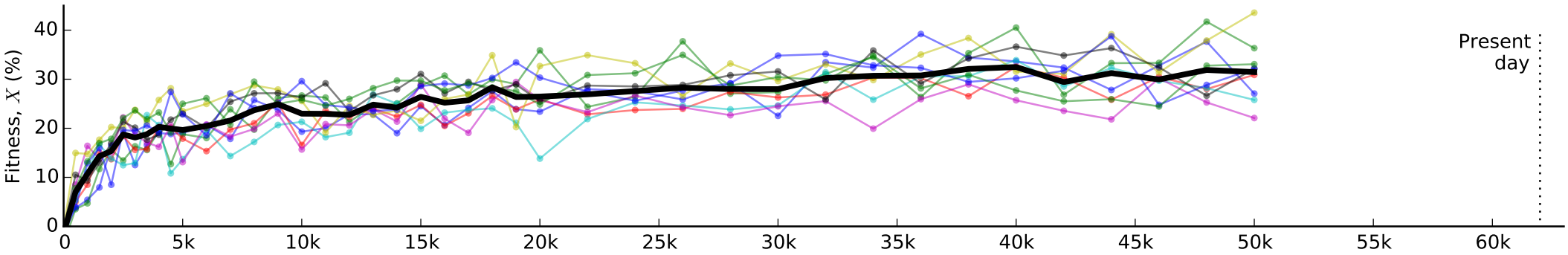

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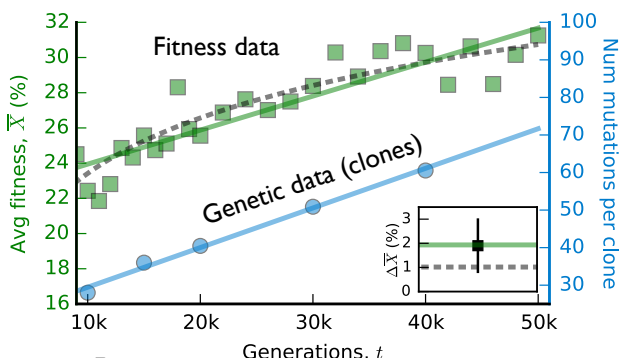
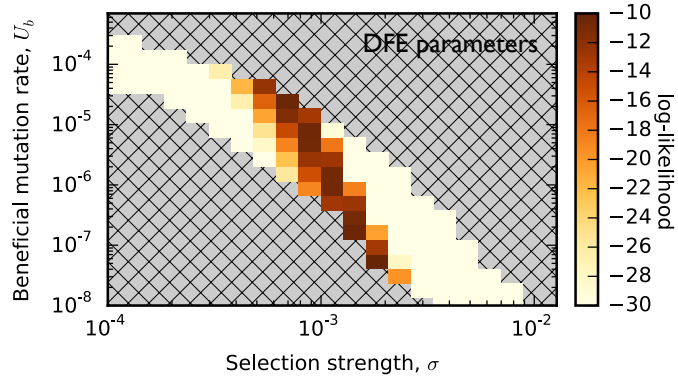
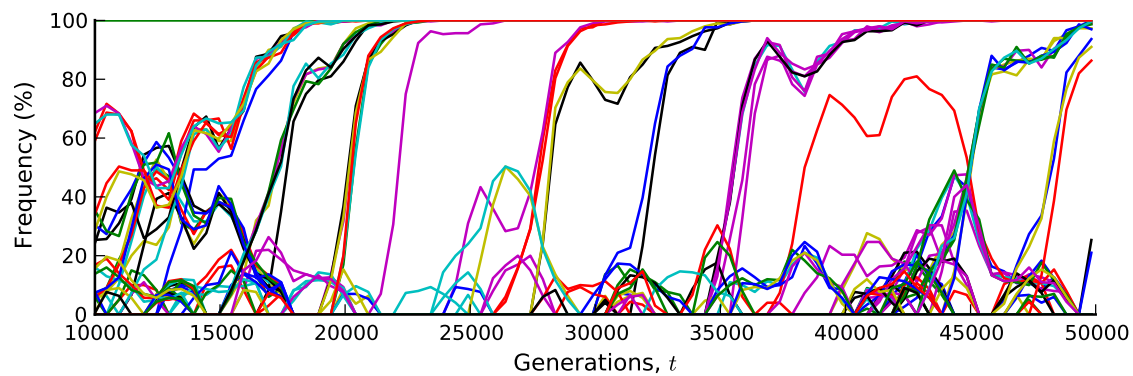




Simulated sequence data



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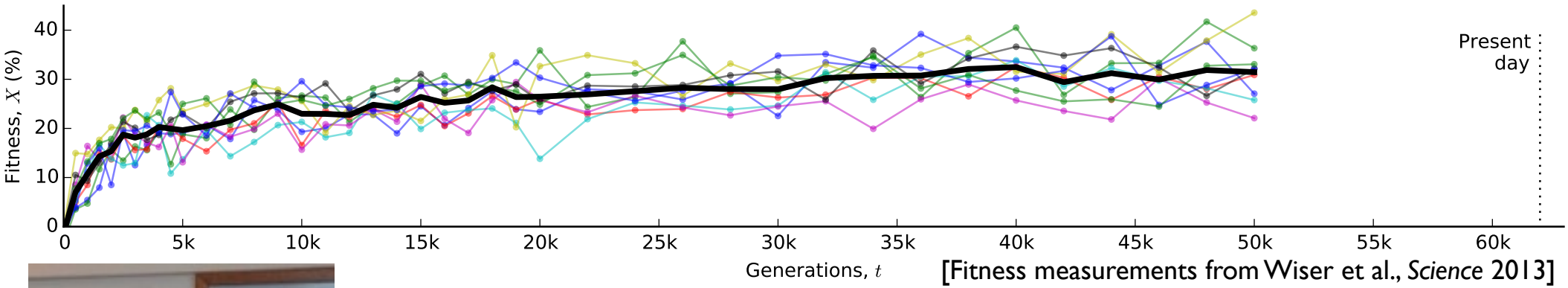

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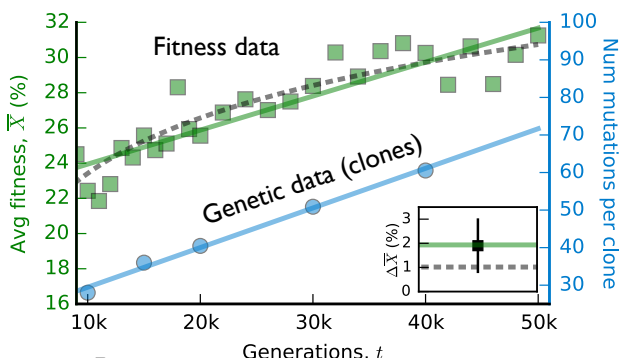

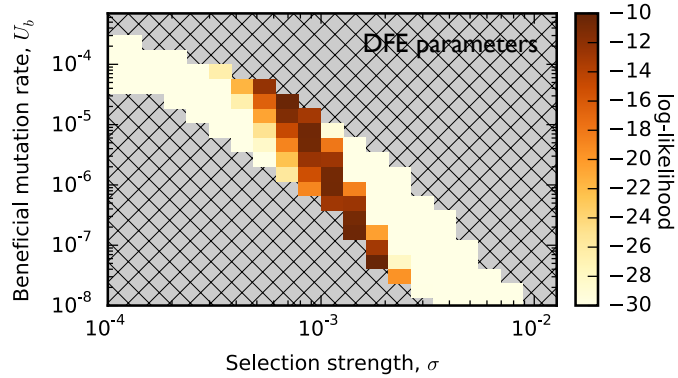

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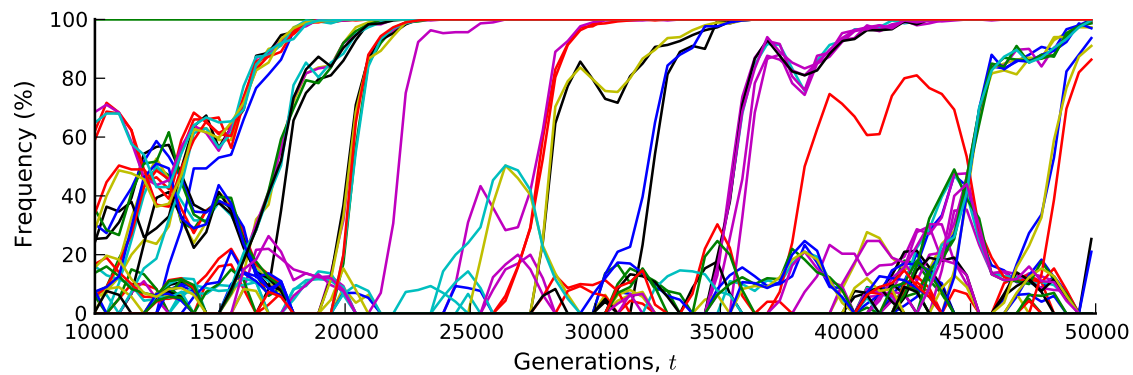

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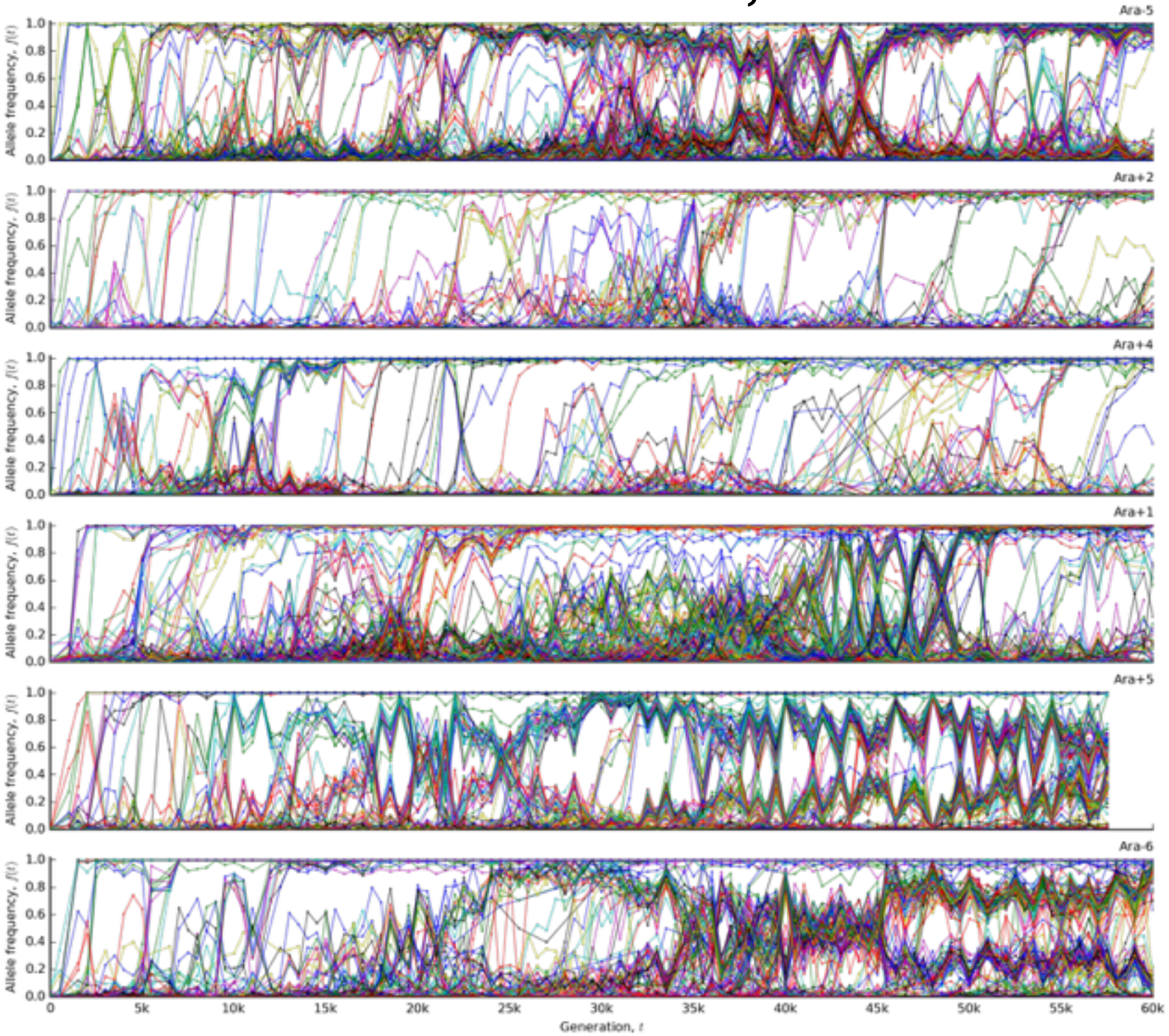
Molecular Evolution Over 60,000 Generations



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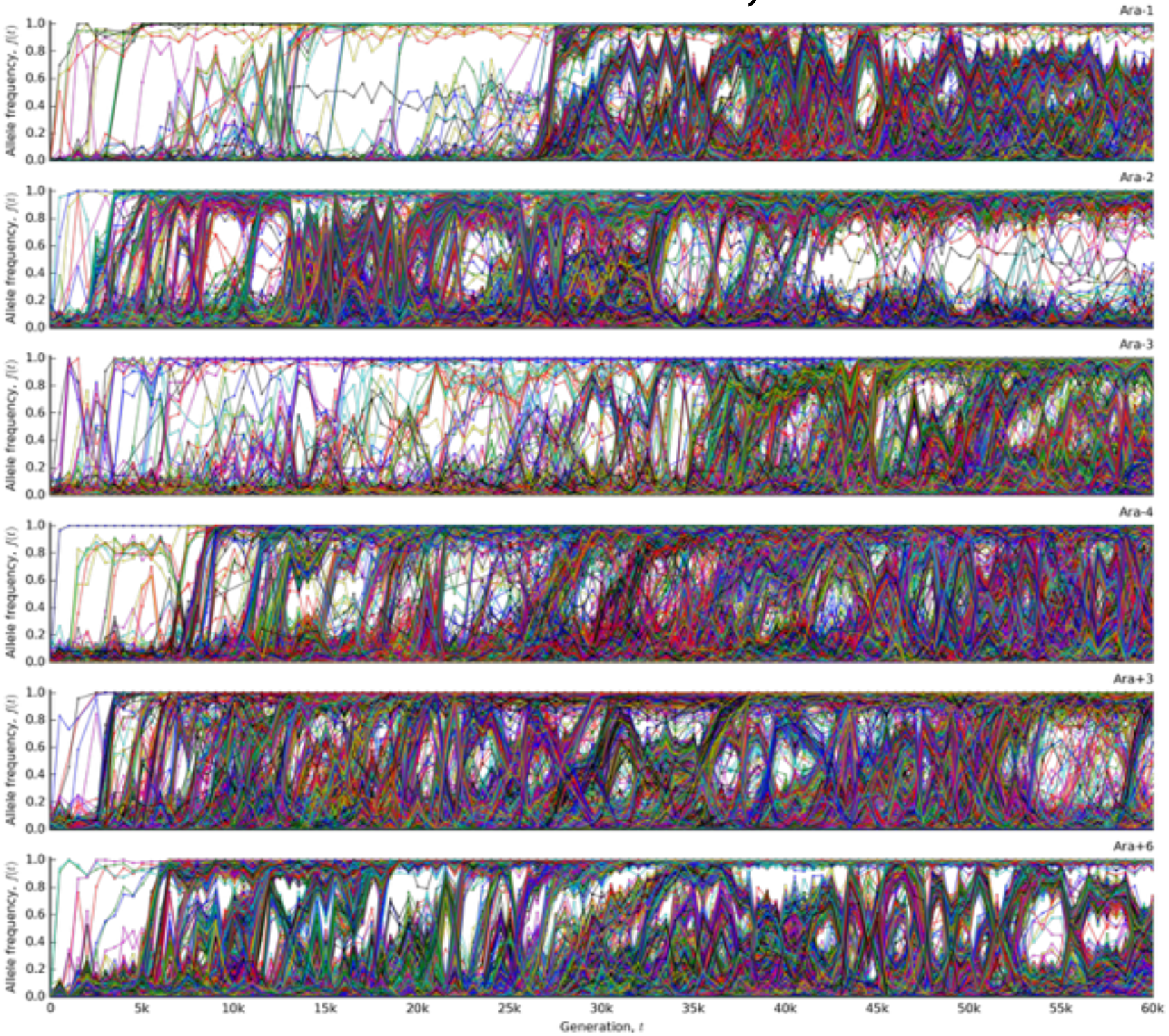
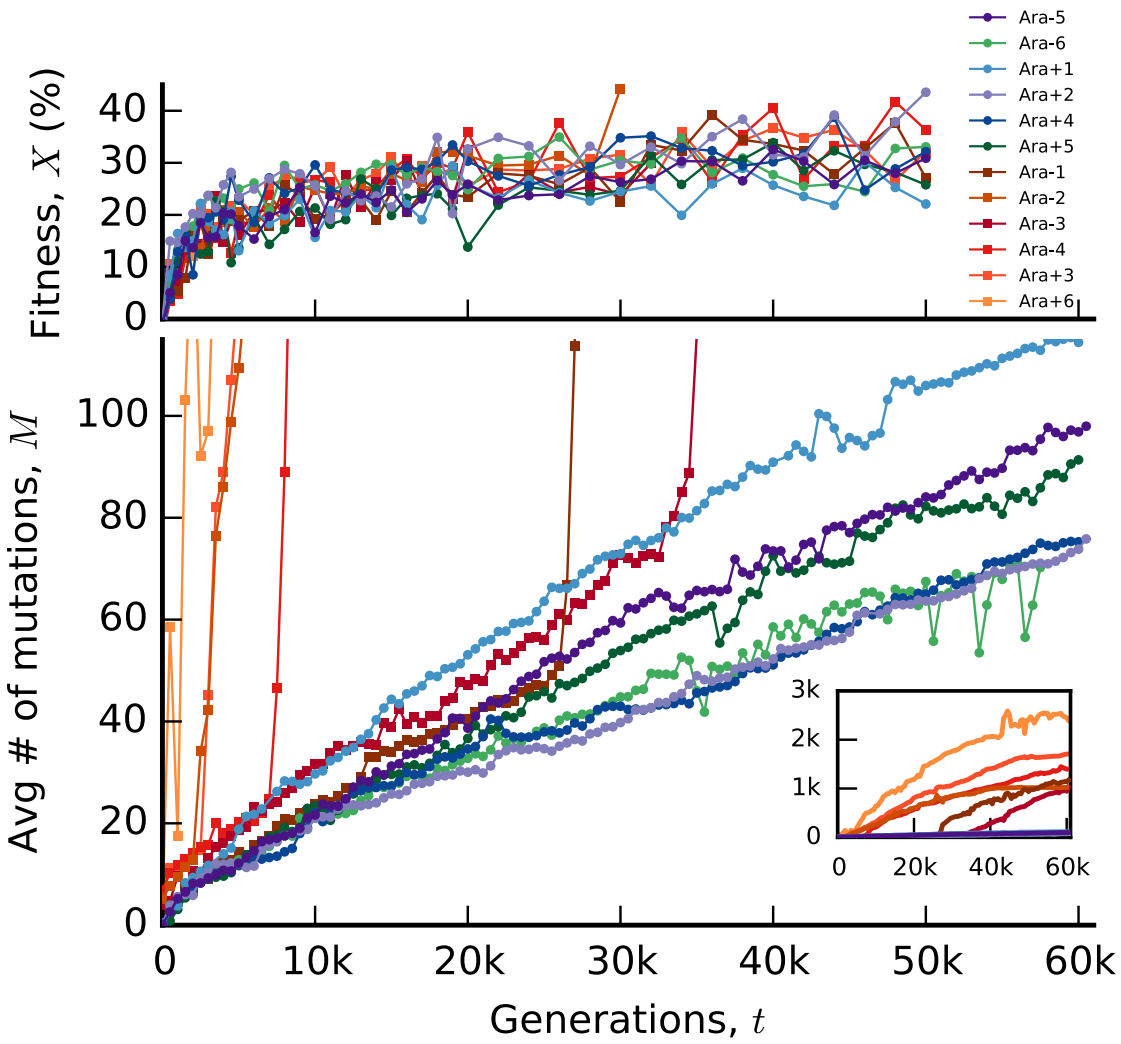


Molecular Evolution is *Rapid* and *Steady*



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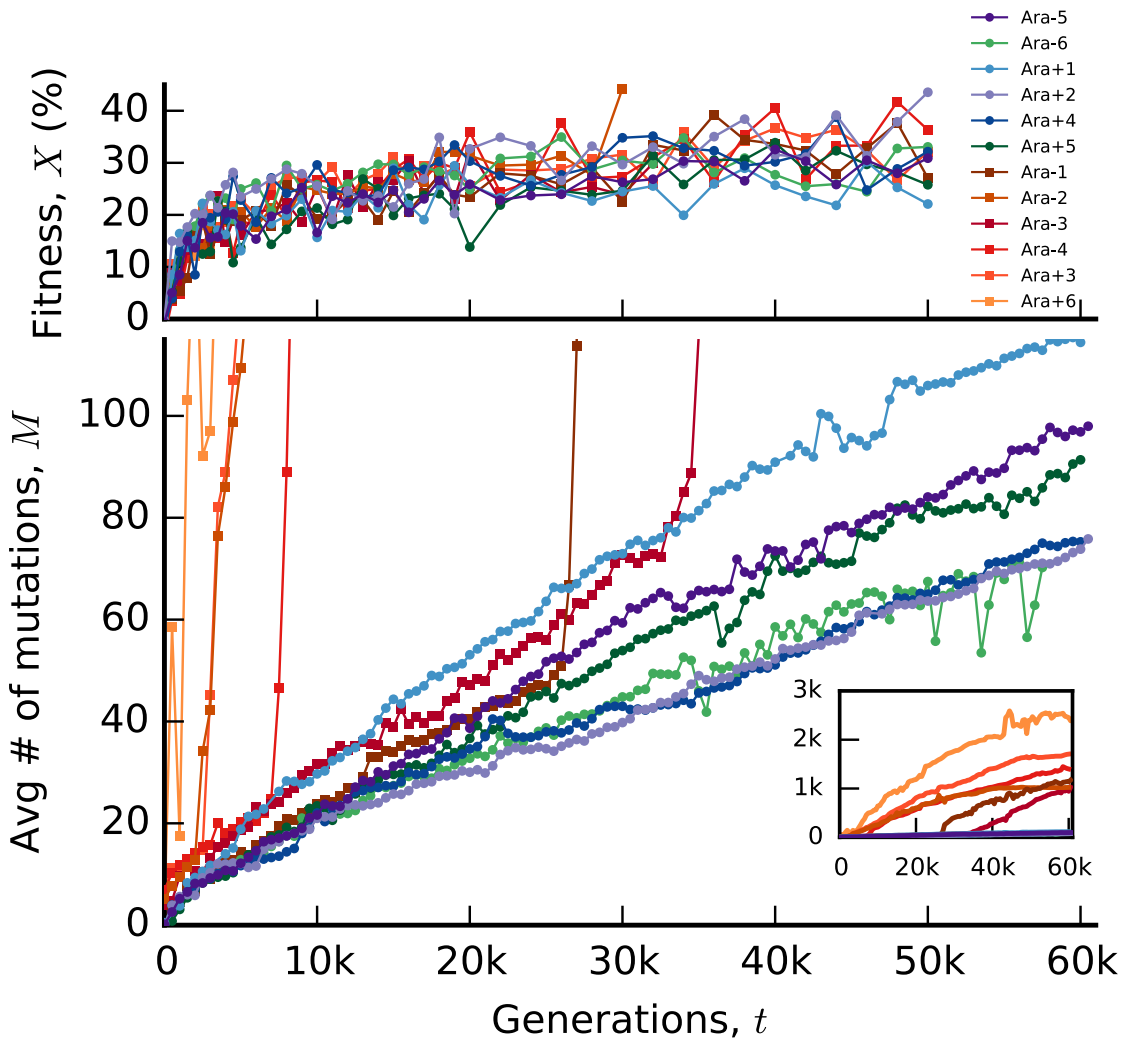
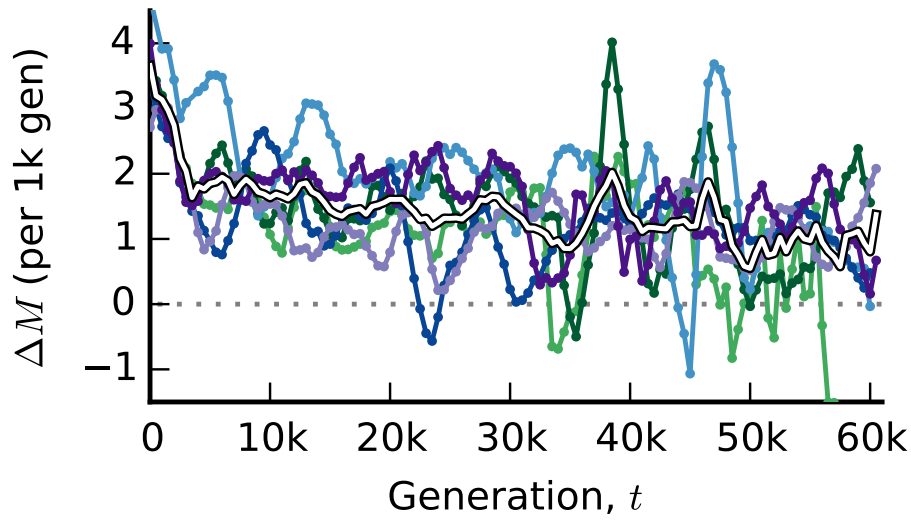
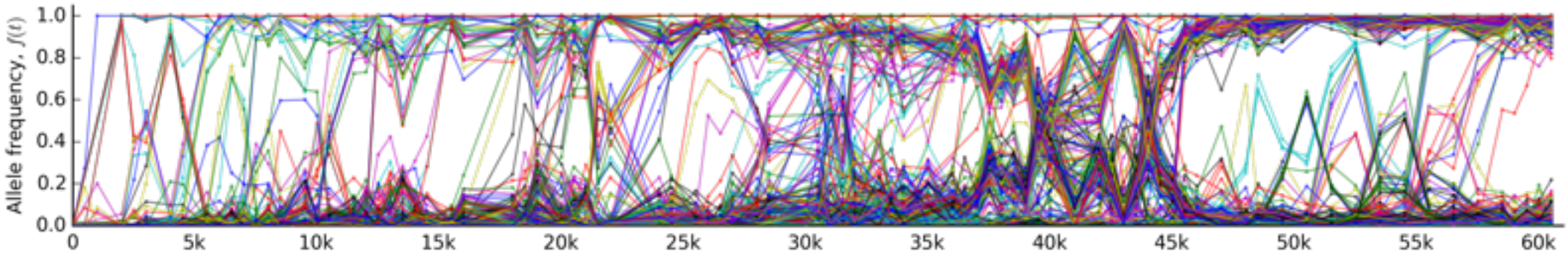




Clonal interference is widespread



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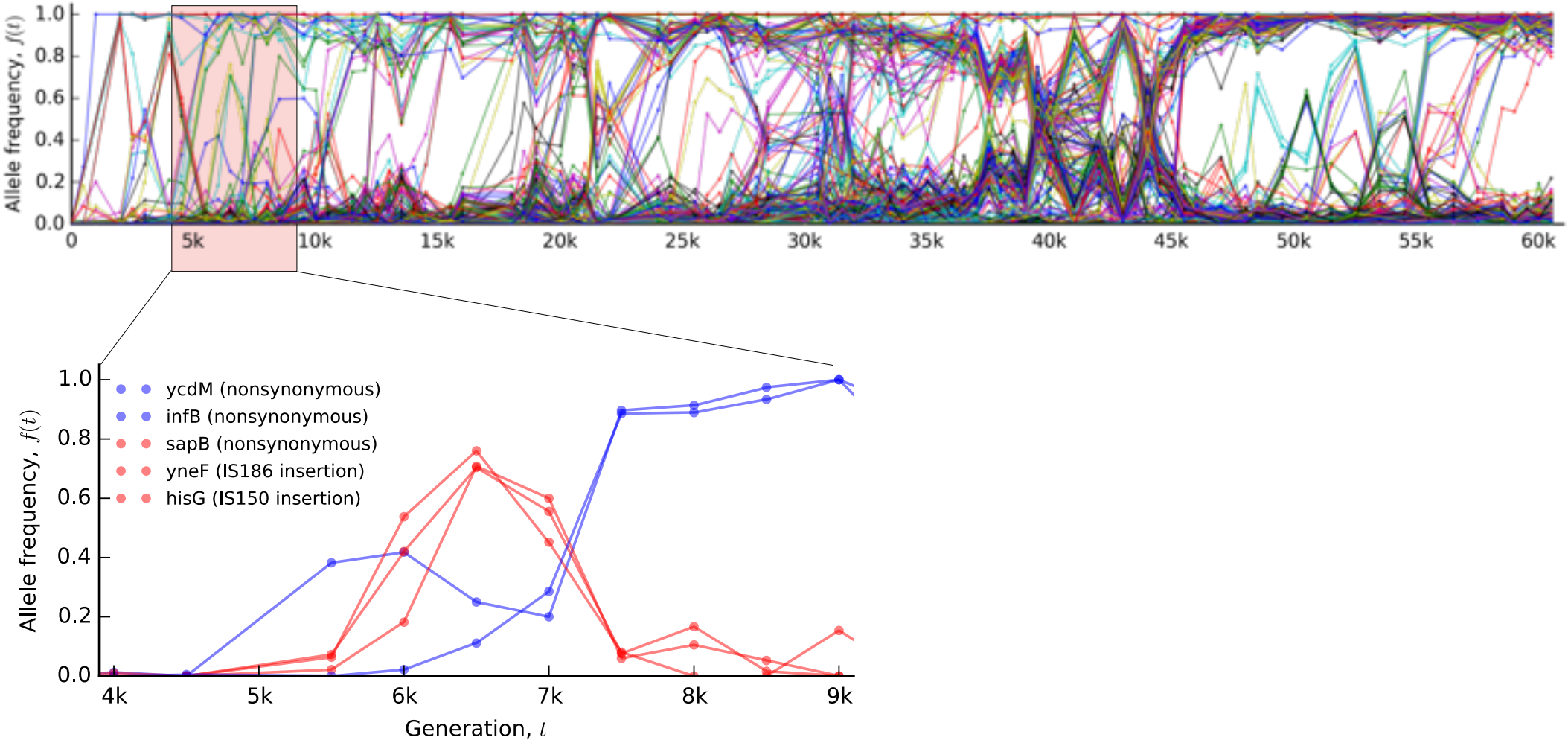

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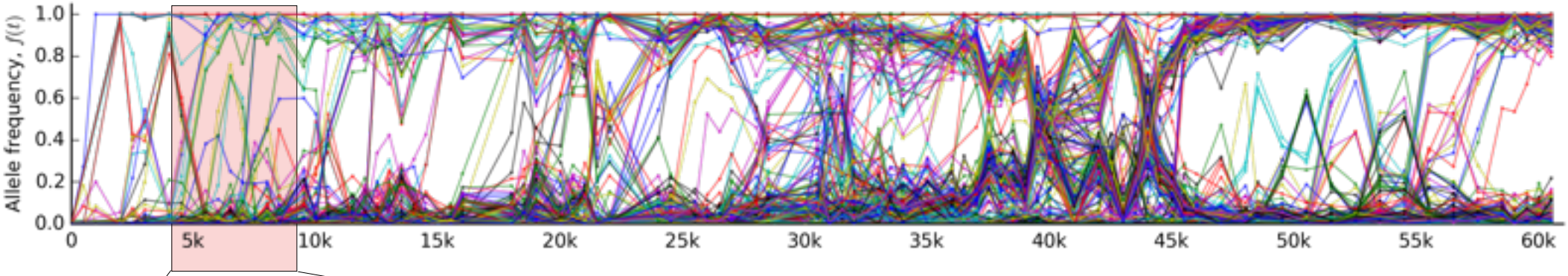

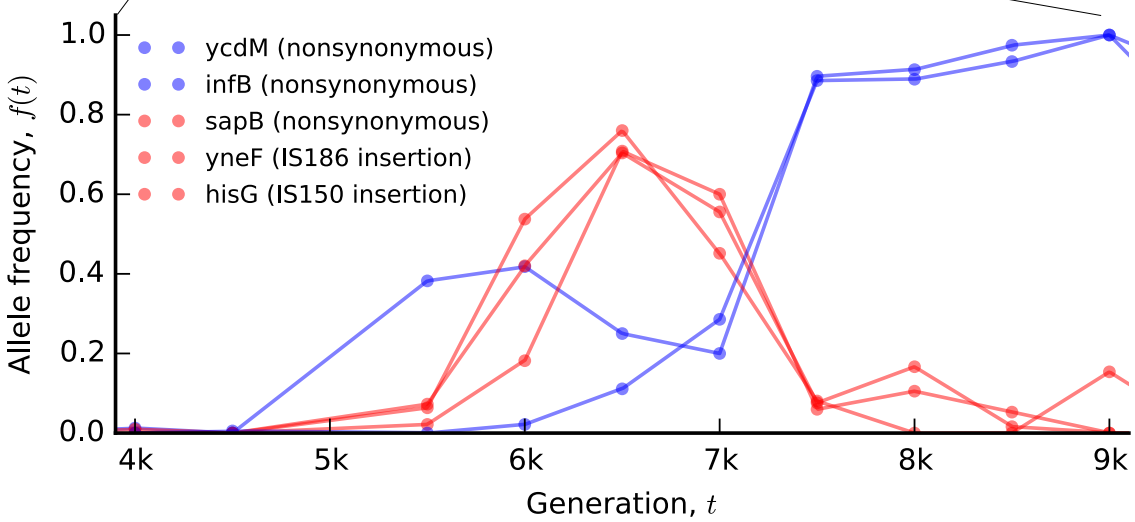

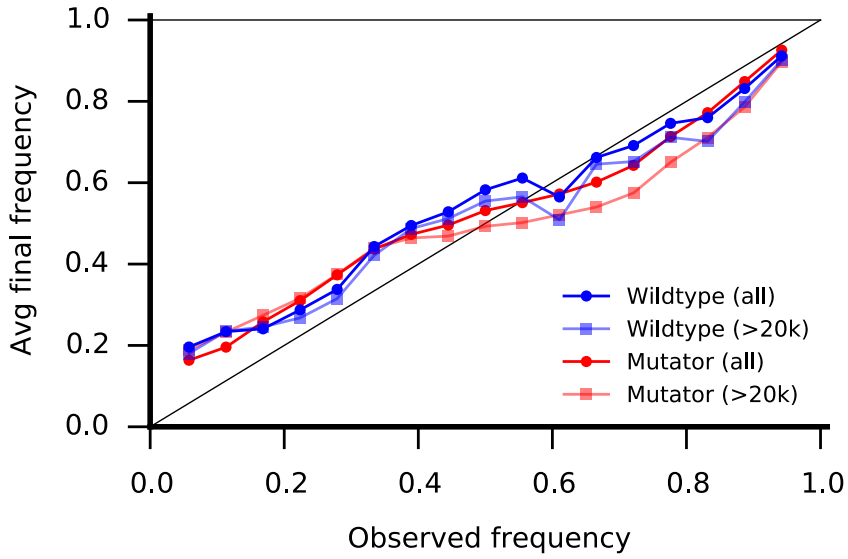

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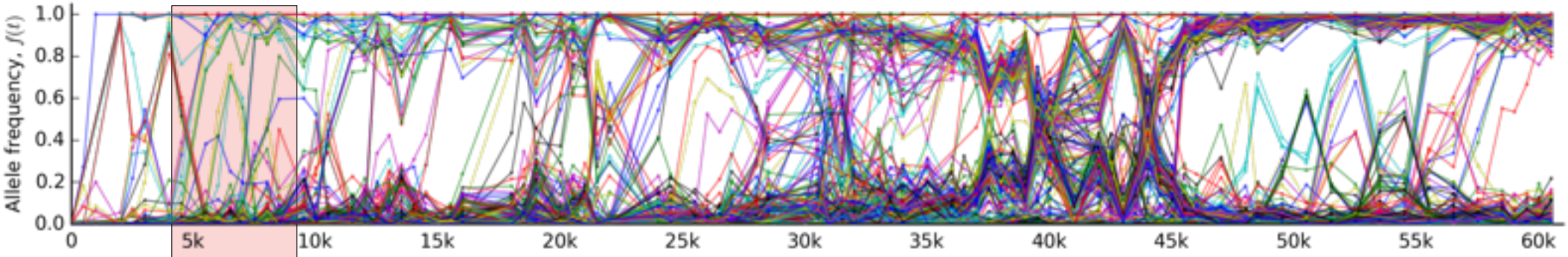

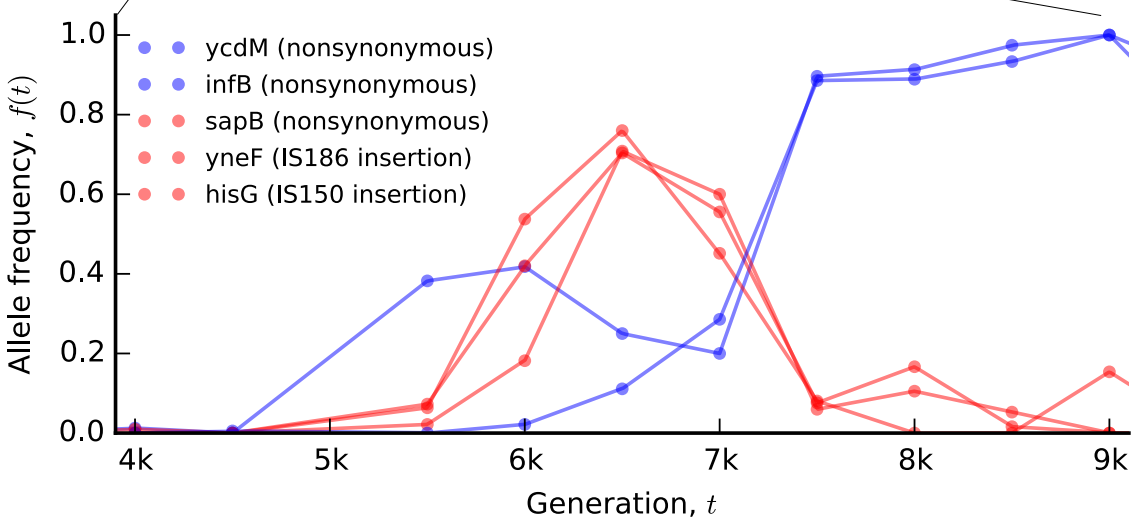

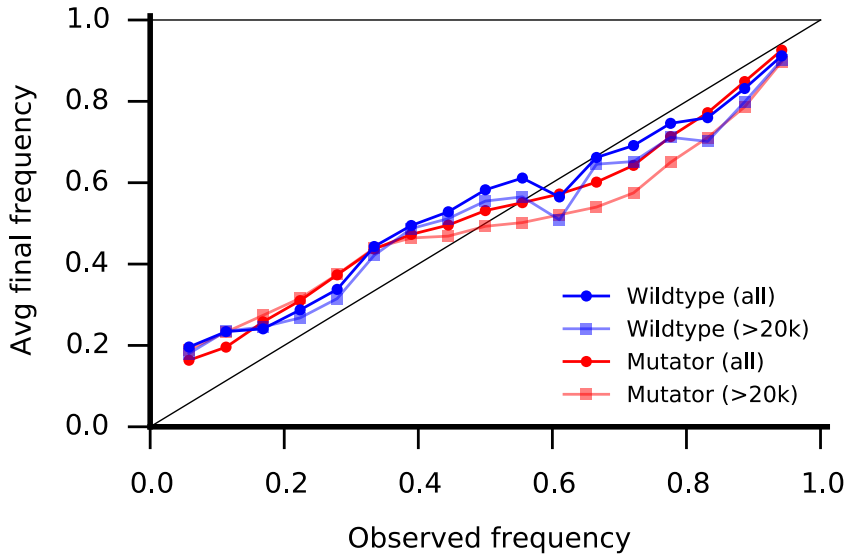

Adaptive evolution:

$$\Delta f_{\text{drift}} \sim t/N < 1\%$$

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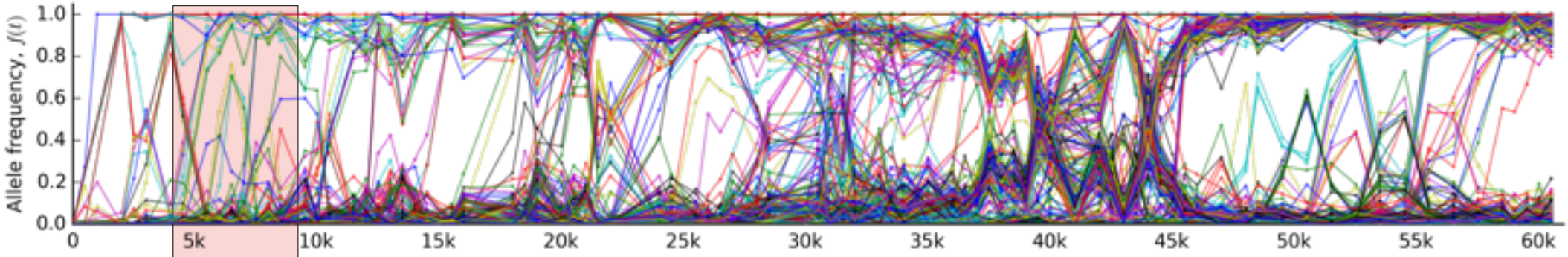

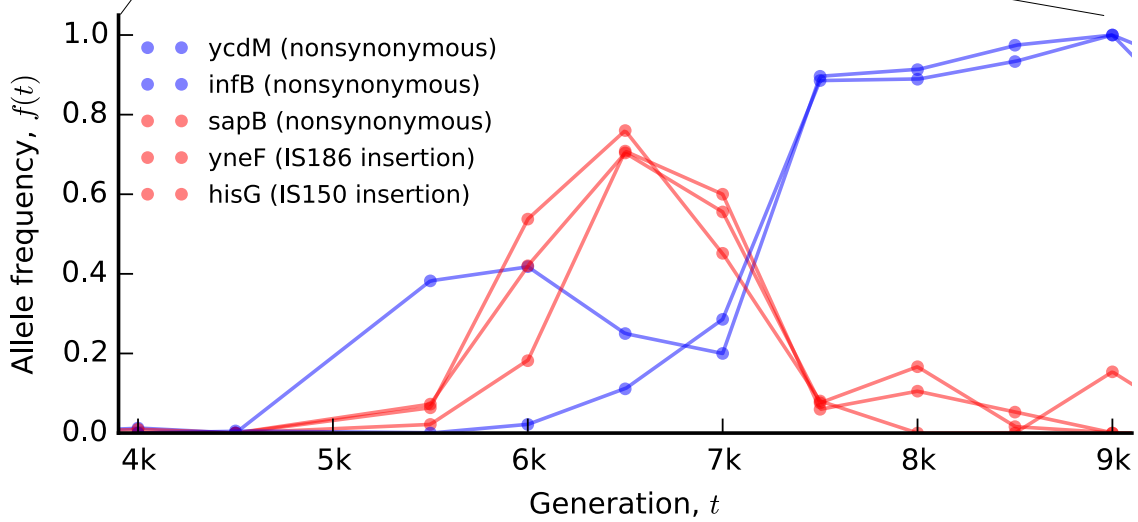

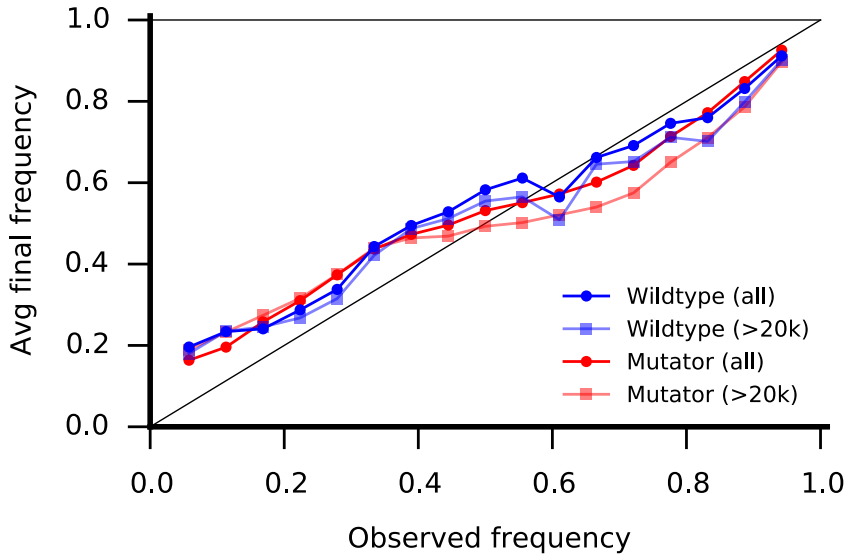

Adaptive evolution:

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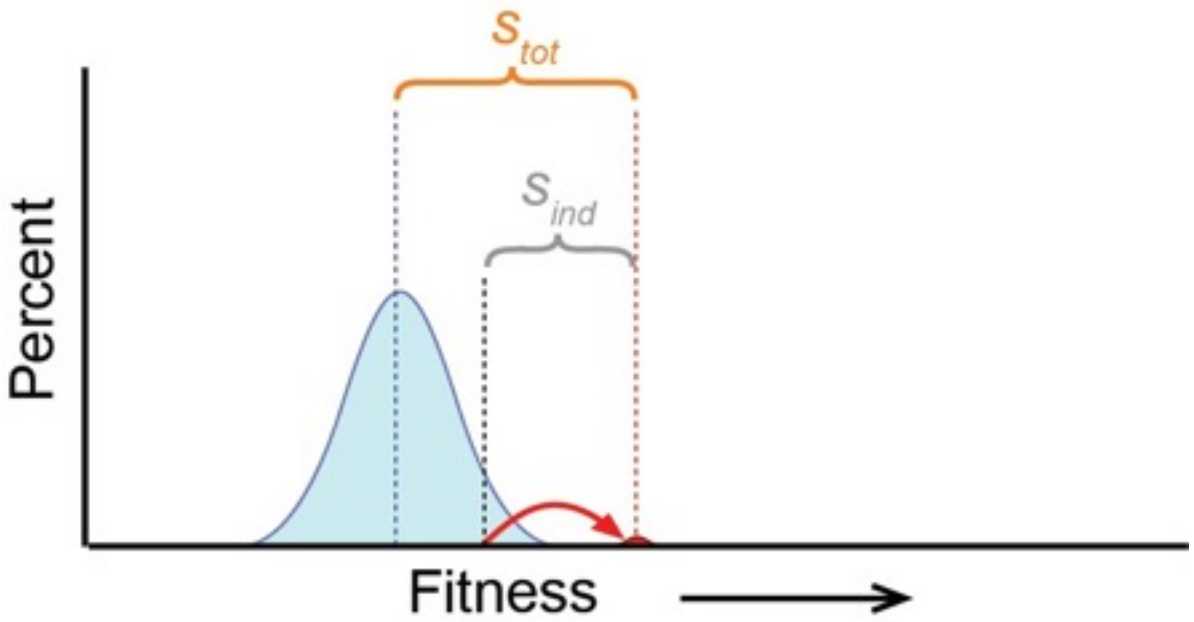
But: The *dynamics* of the evolutionary process can be as important as biology in determining the fate of a mutation

The interaction between each mutation and all other variation



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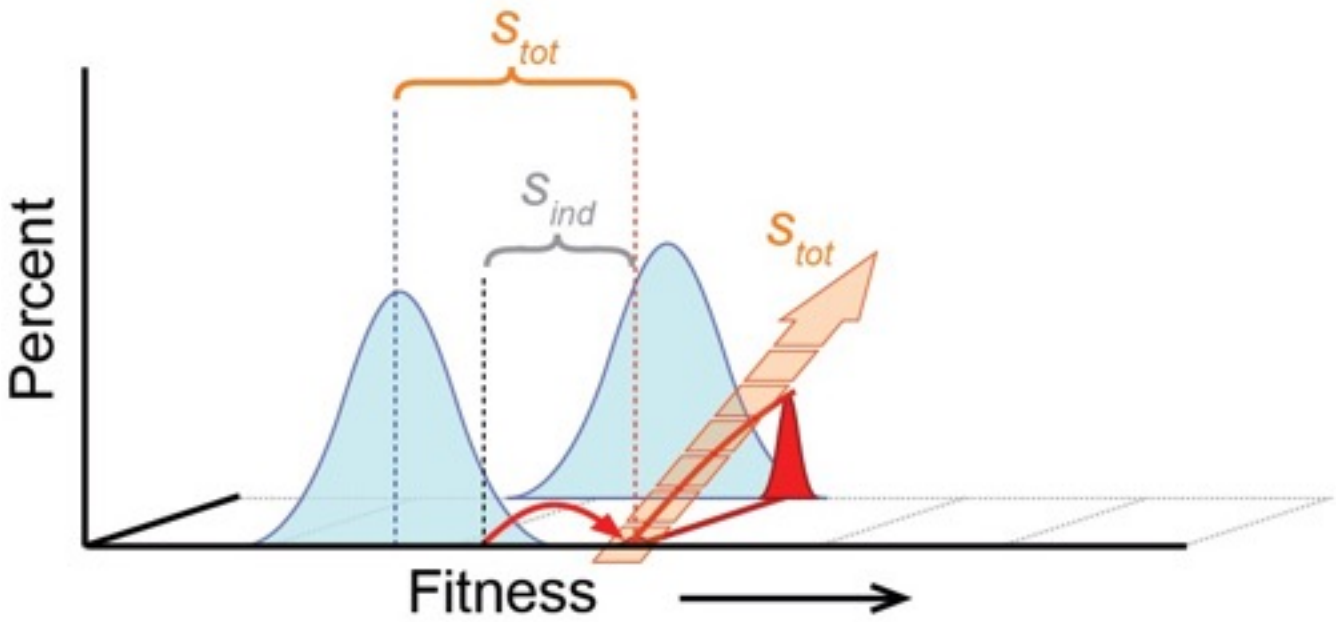
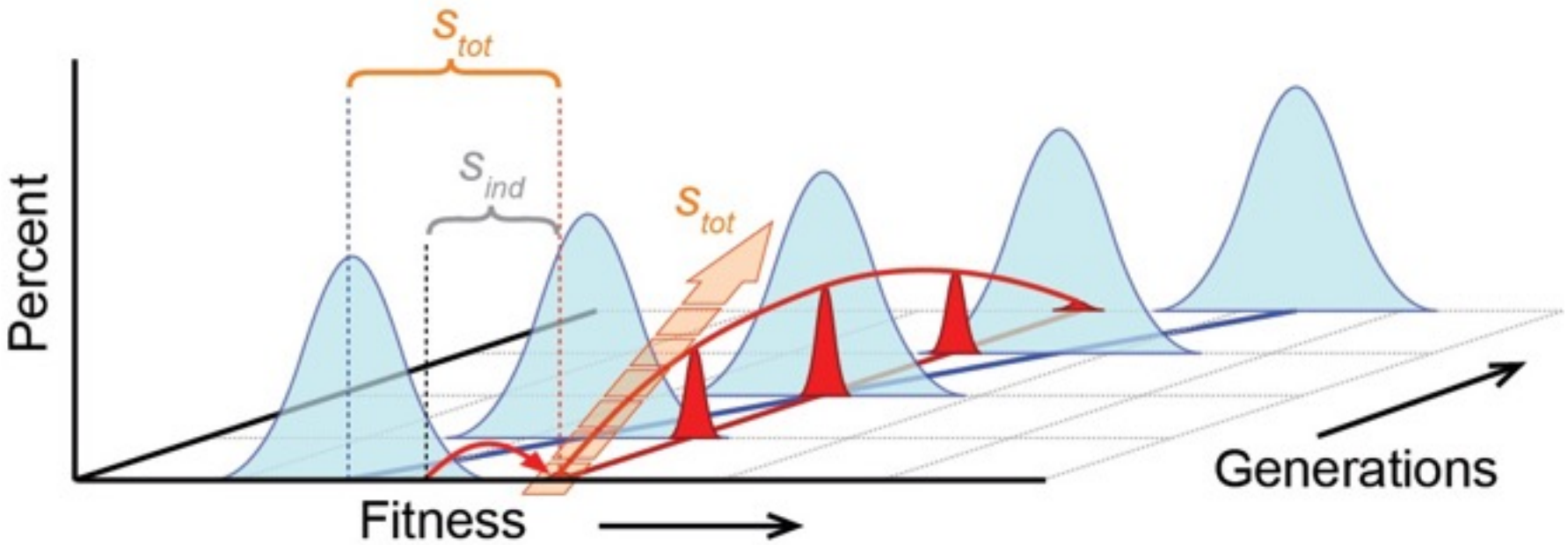


The interaction between each mutation and all other variation



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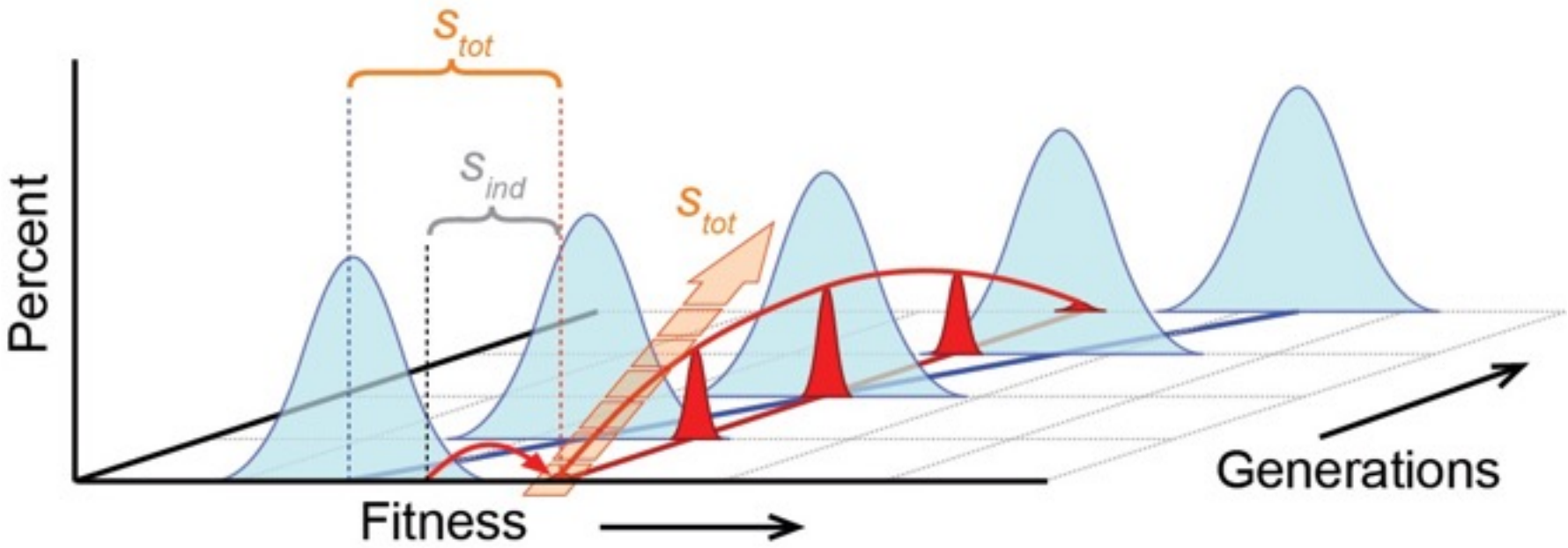
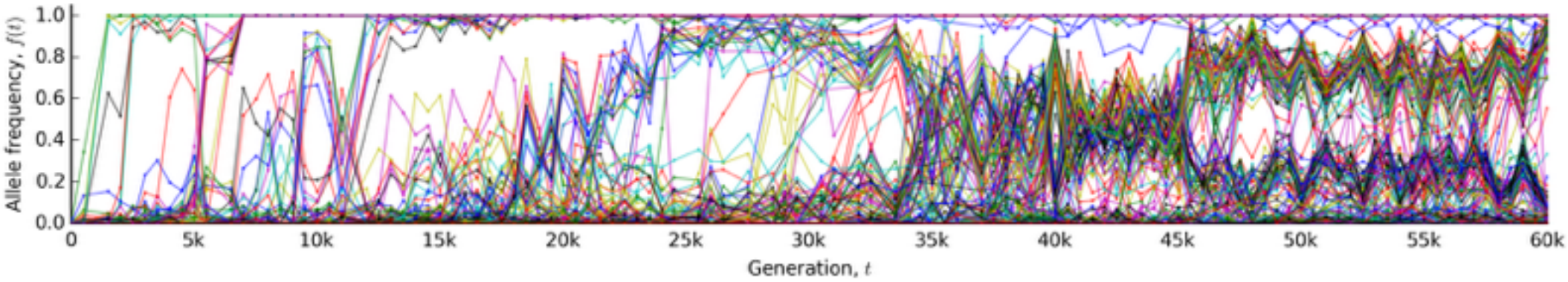


Rare large-effect mutations that can fix in many genetic backgrounds versus common neutral or deleterious mutations that fix when they occur in exceptionally lucky backgrounds

Emergence of Quasi-Stable Ecology



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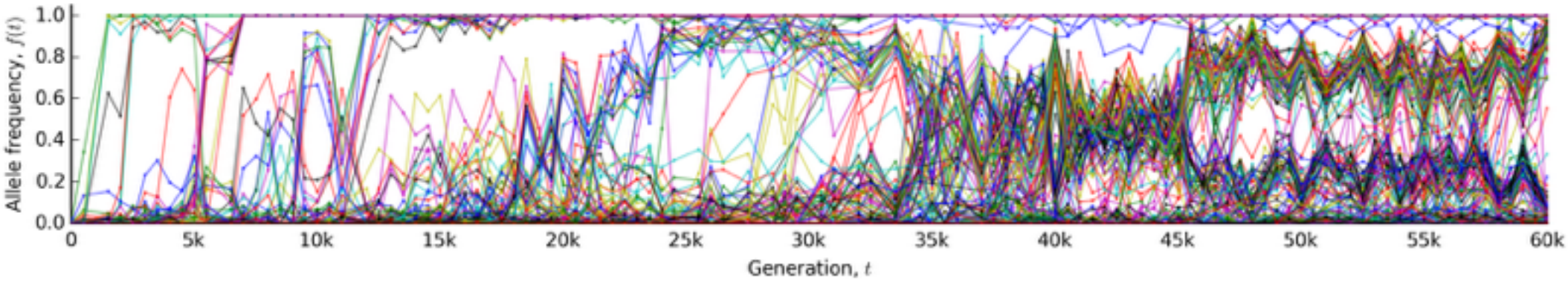

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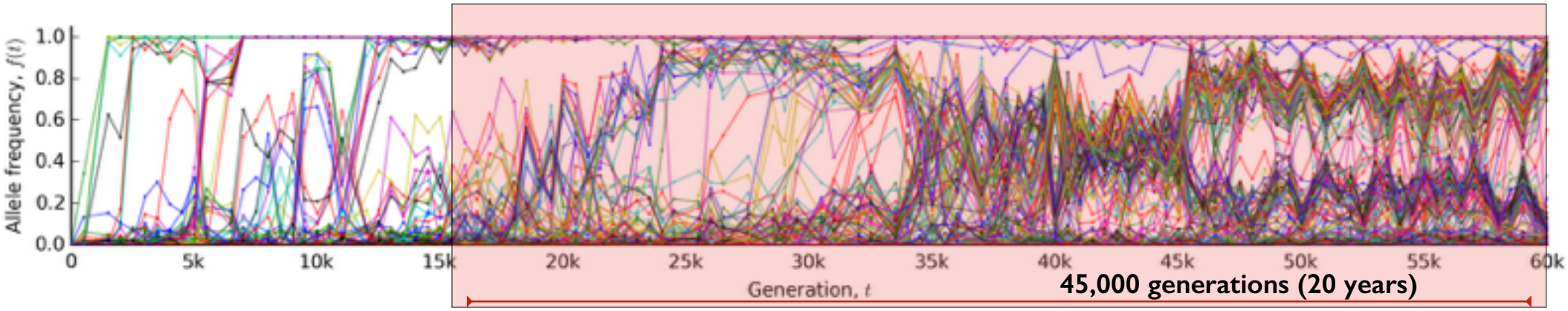

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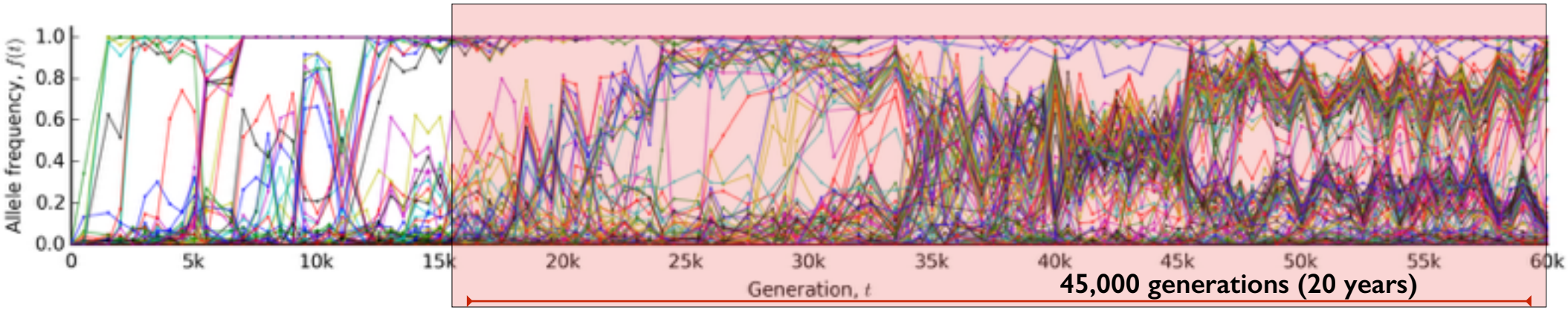

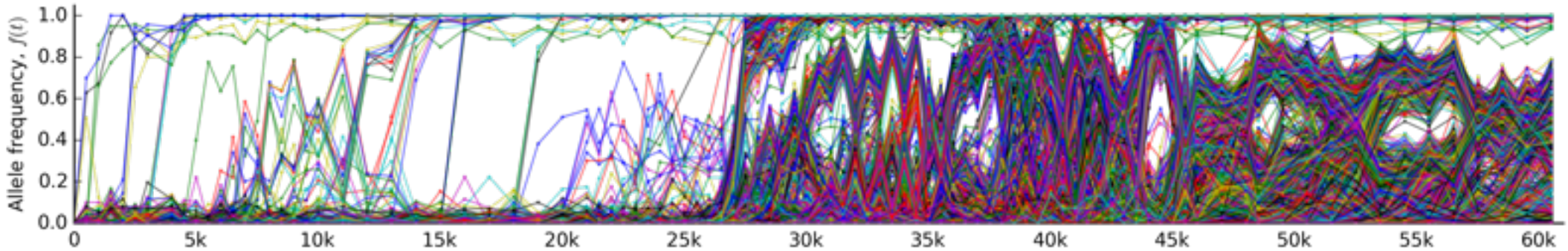

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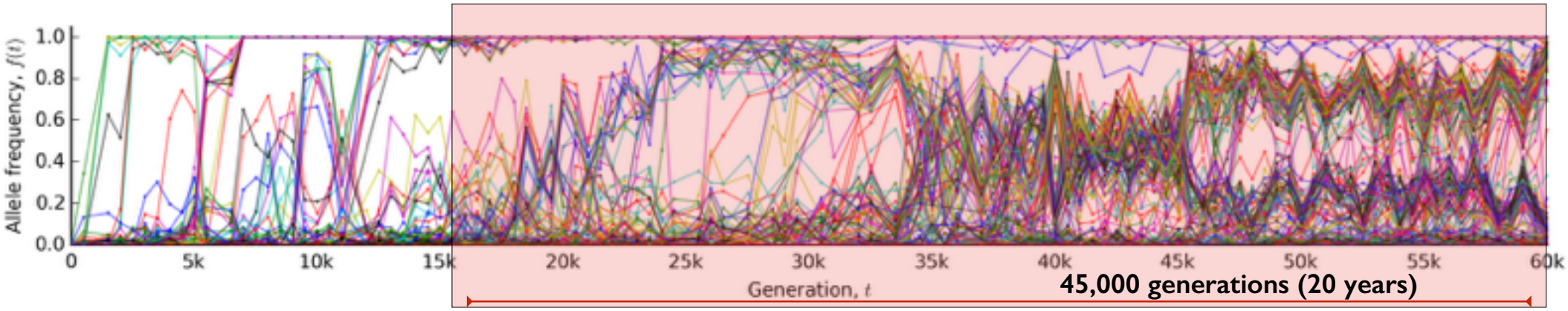

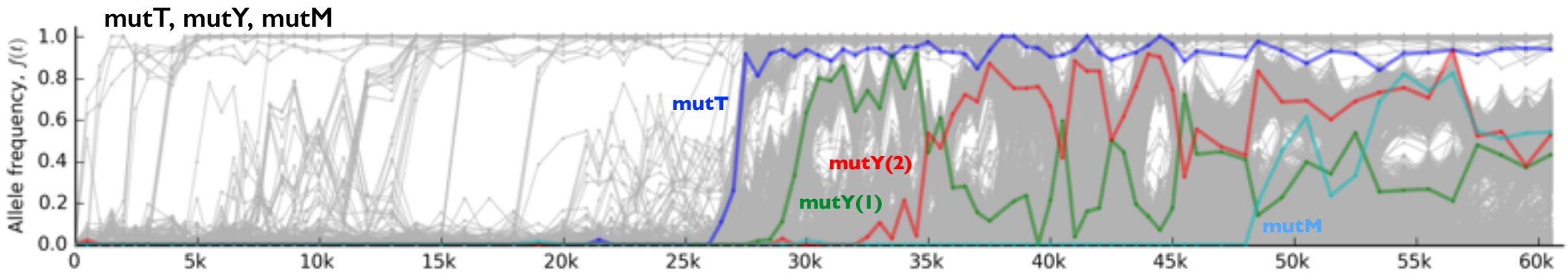

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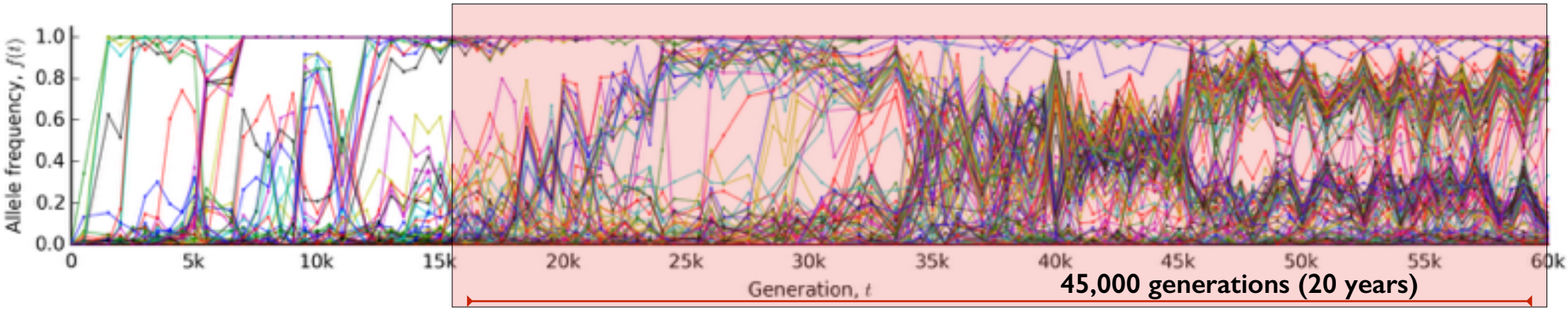
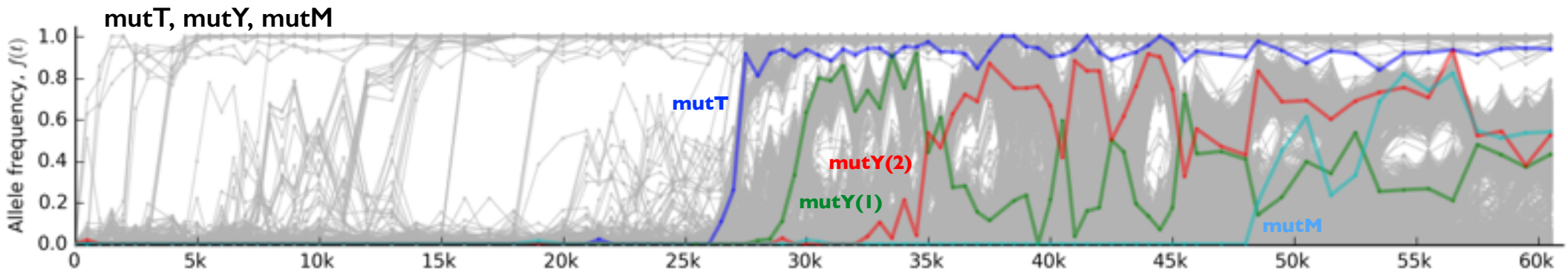
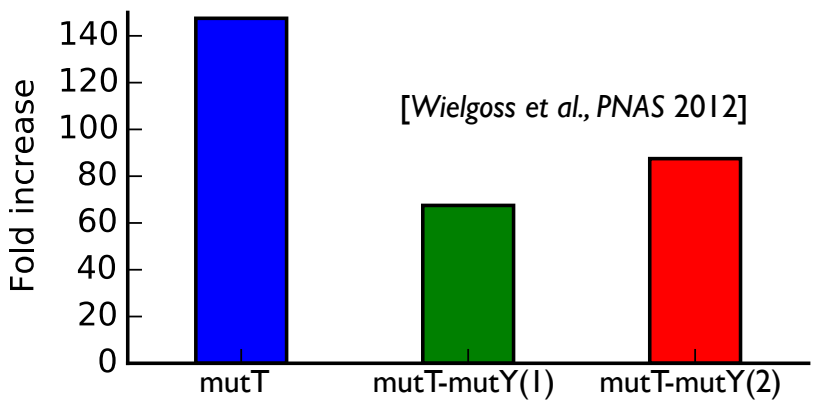






[*Wielgoss et al., PNAS* 2012]

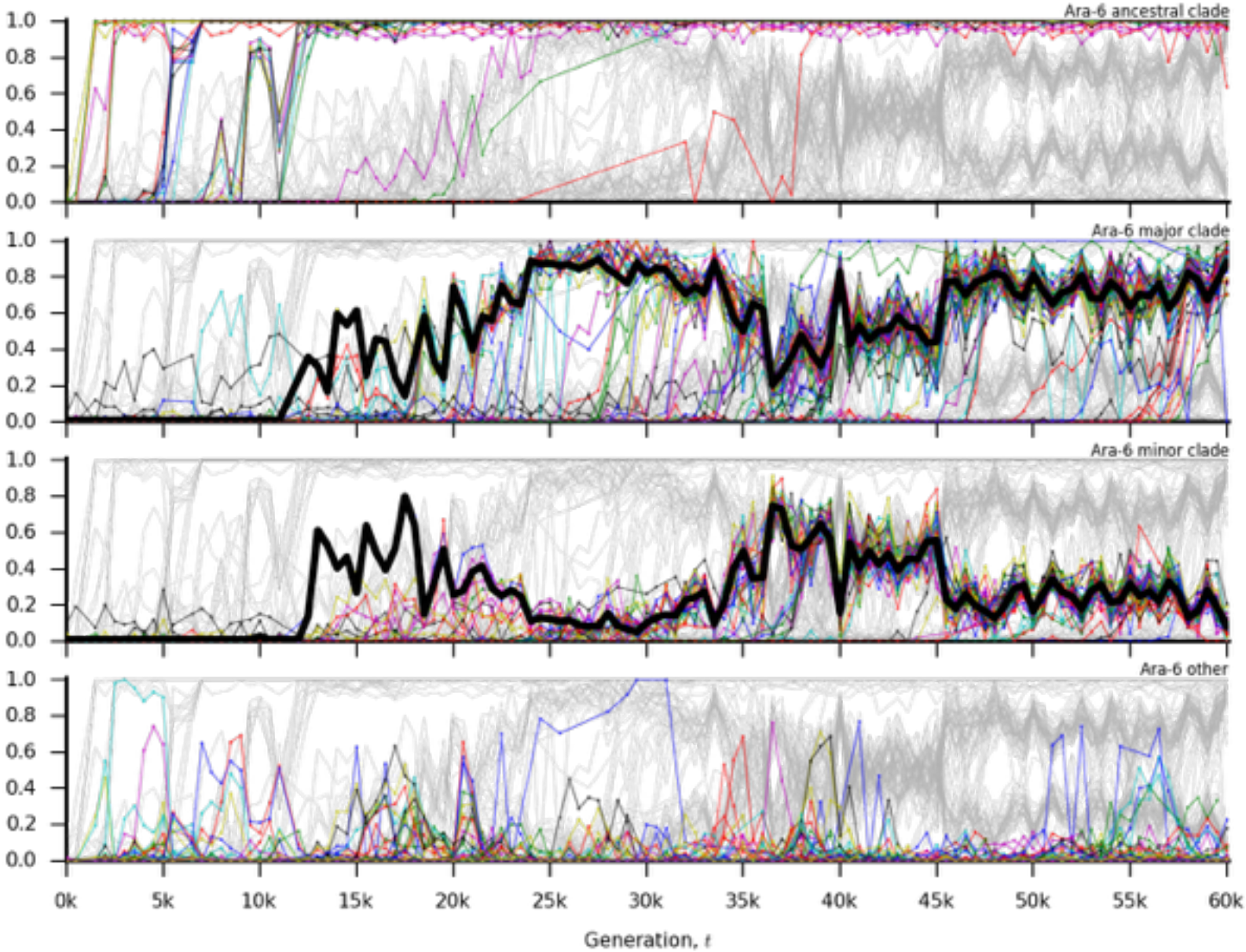
Why do antimutators succeed right after mutators?

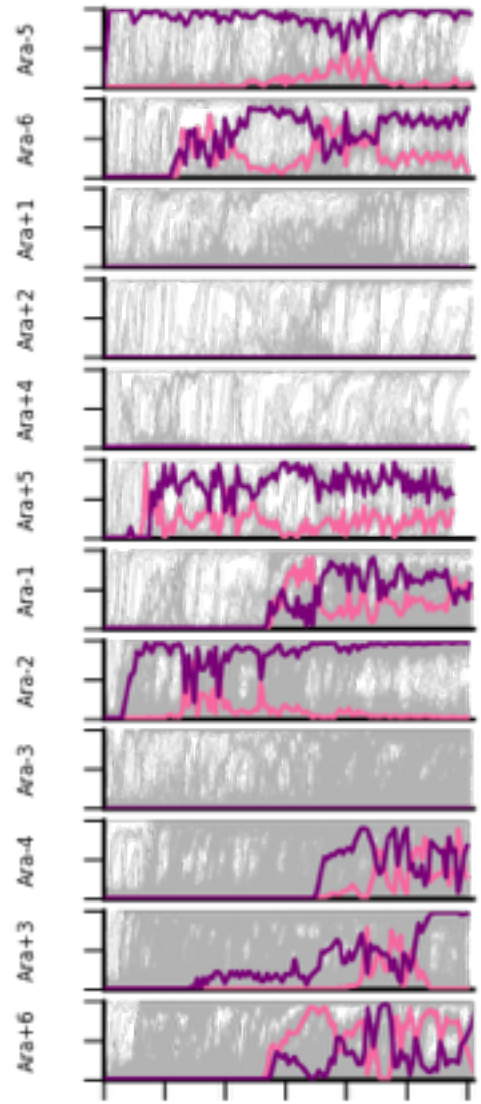
Why don't mutators change the rate of adaptation?

Why do mutators fix in half the lines?

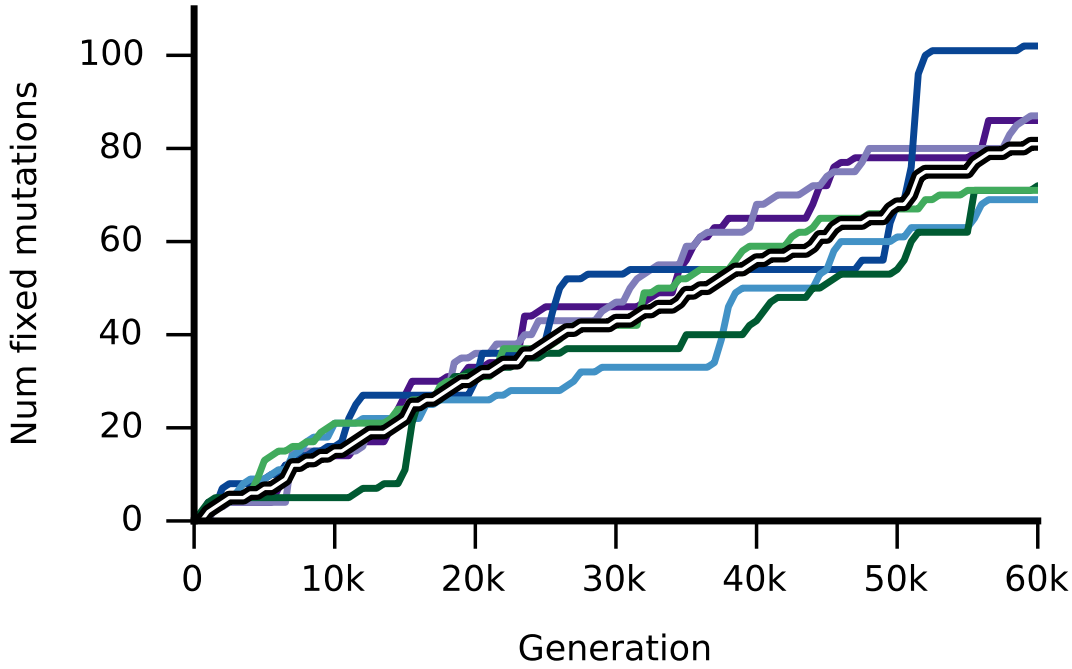
[Good and Desai, *Genetics* 2016]

Semi-Stable Coexistence is Widespread





Within-Clade Evolution Doesn’t “Slow Down”



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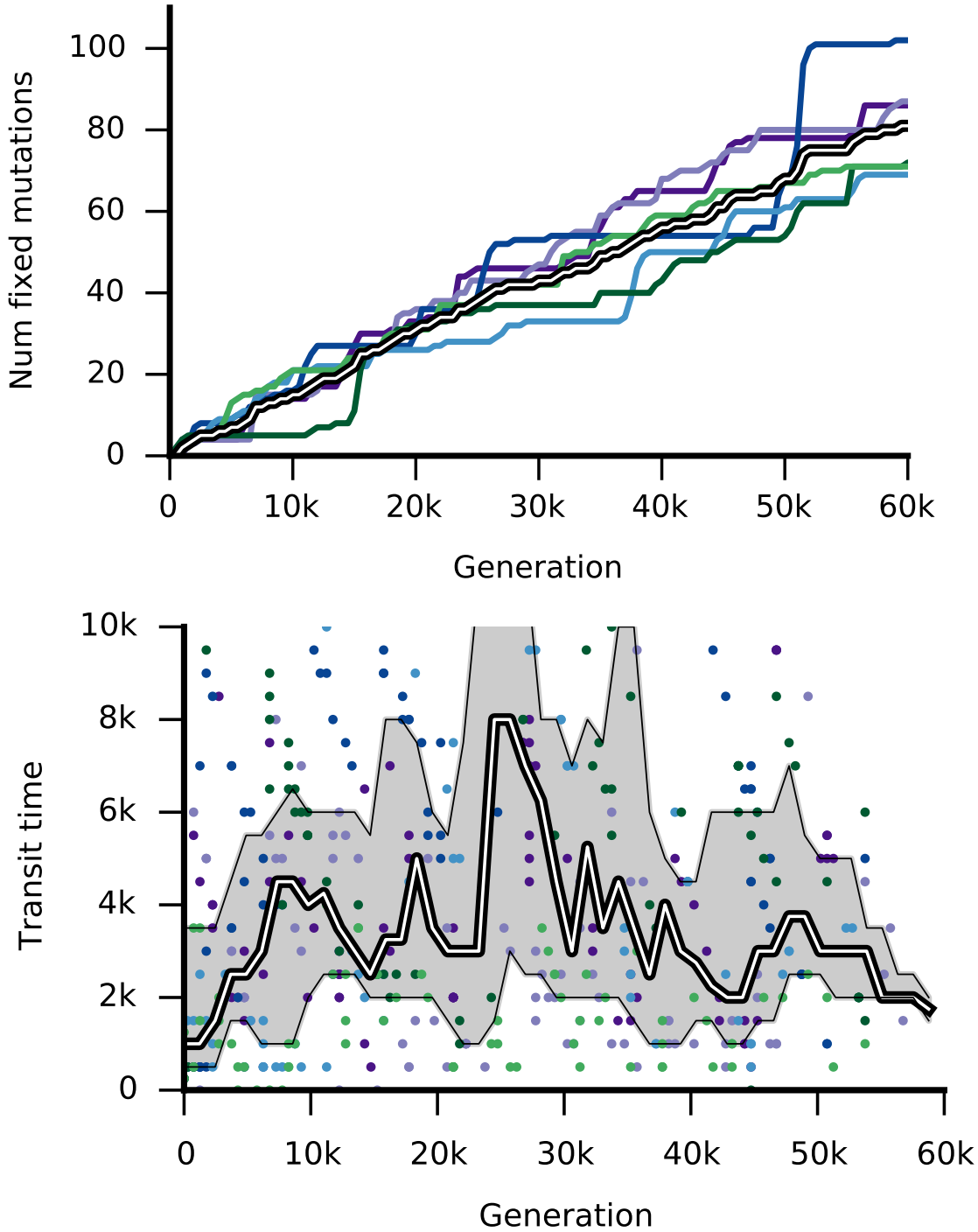
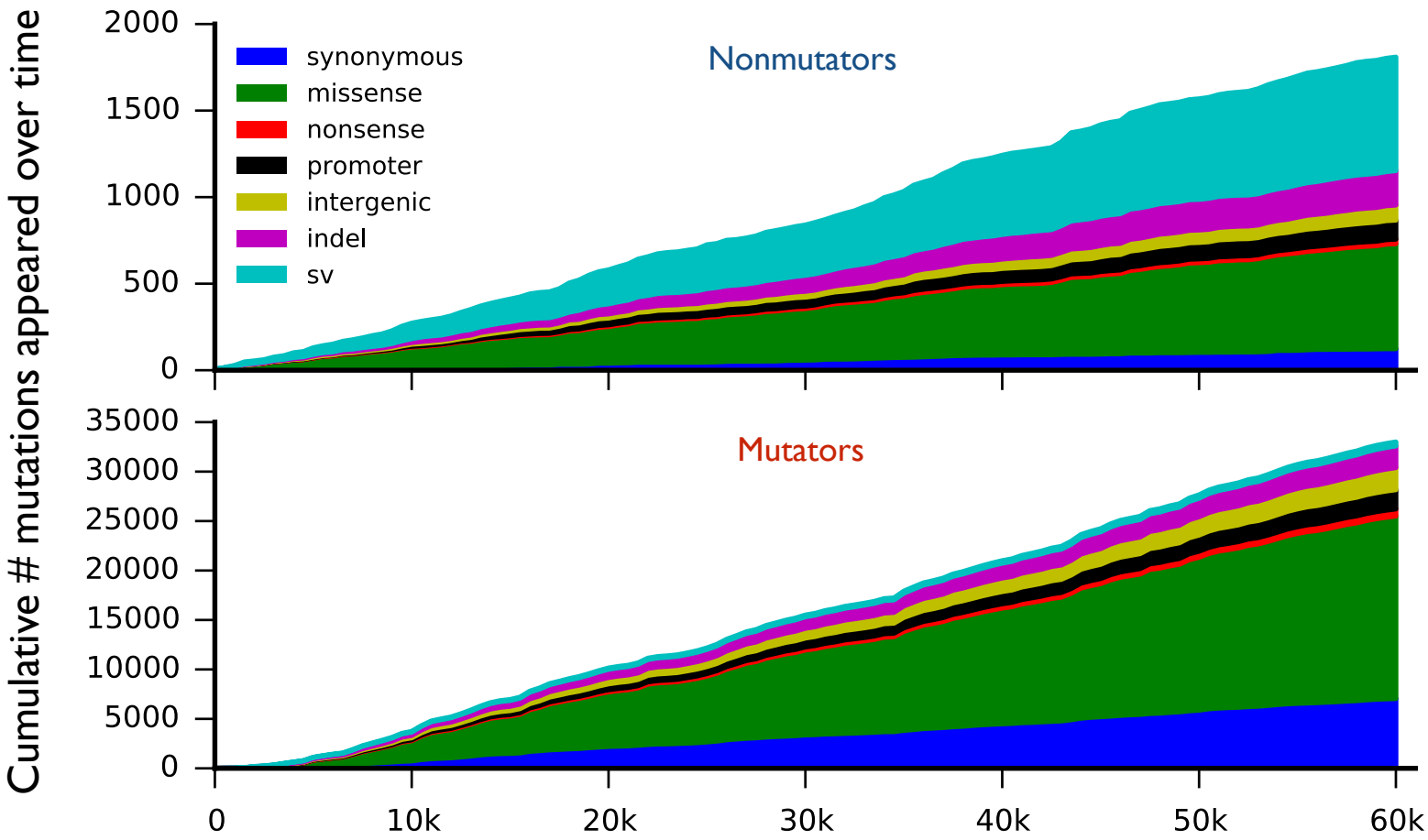


What Types of Mutations Accumulate Over Time?



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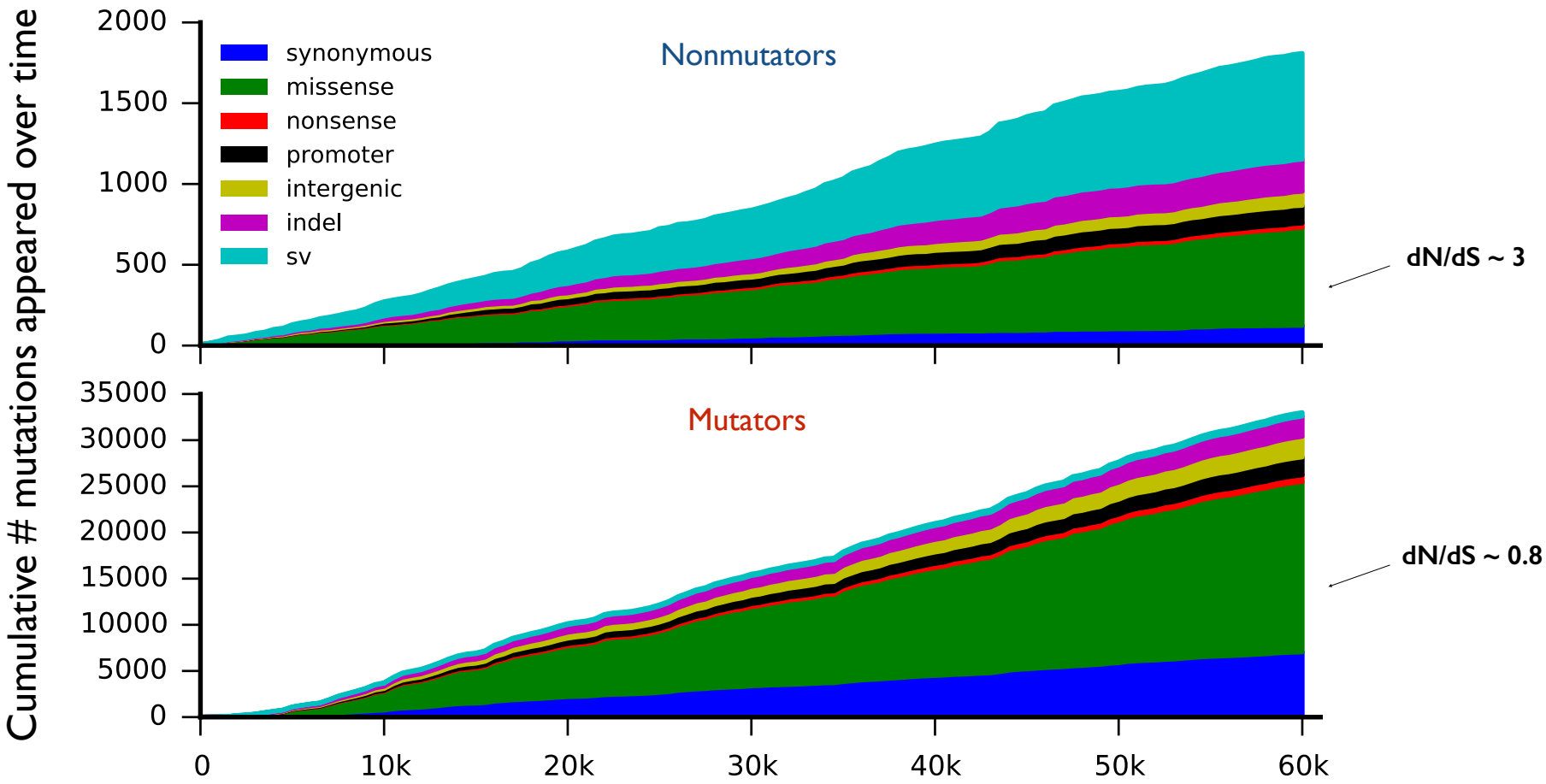

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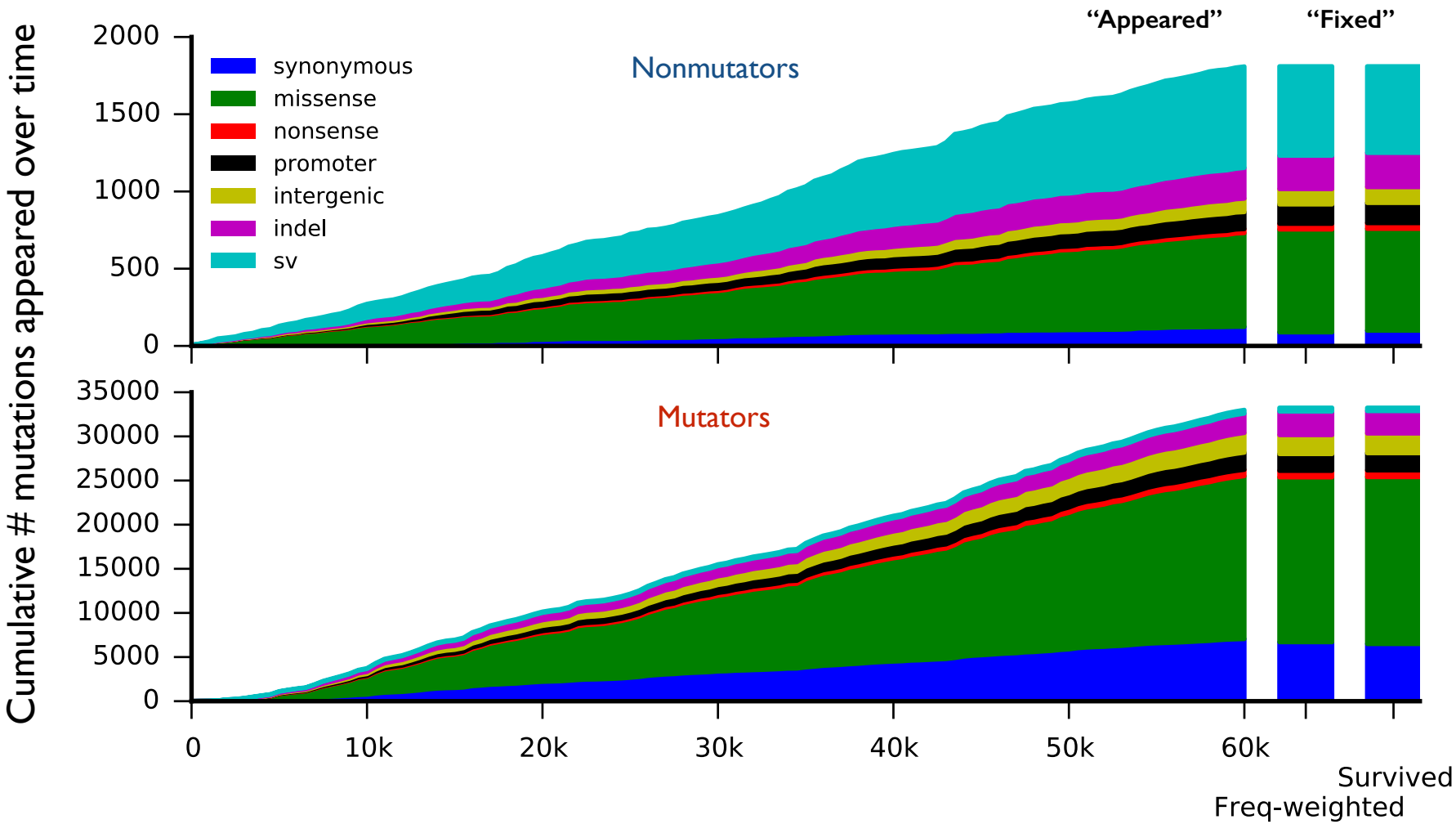
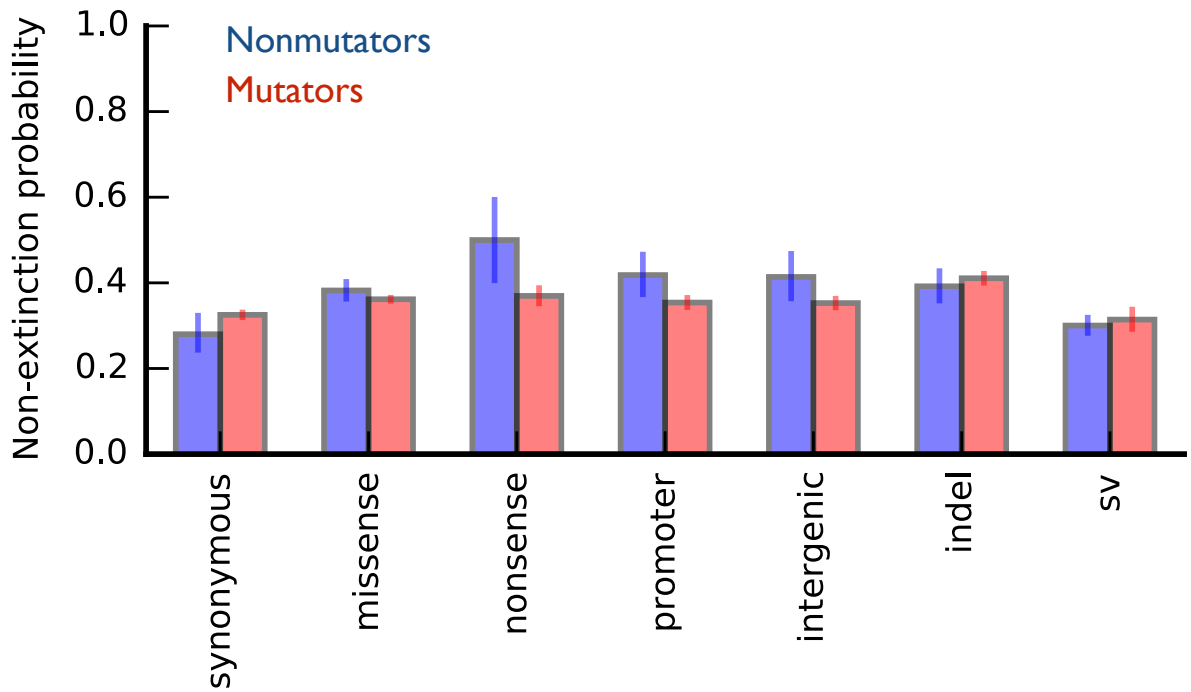


Effects of Selection and Draft



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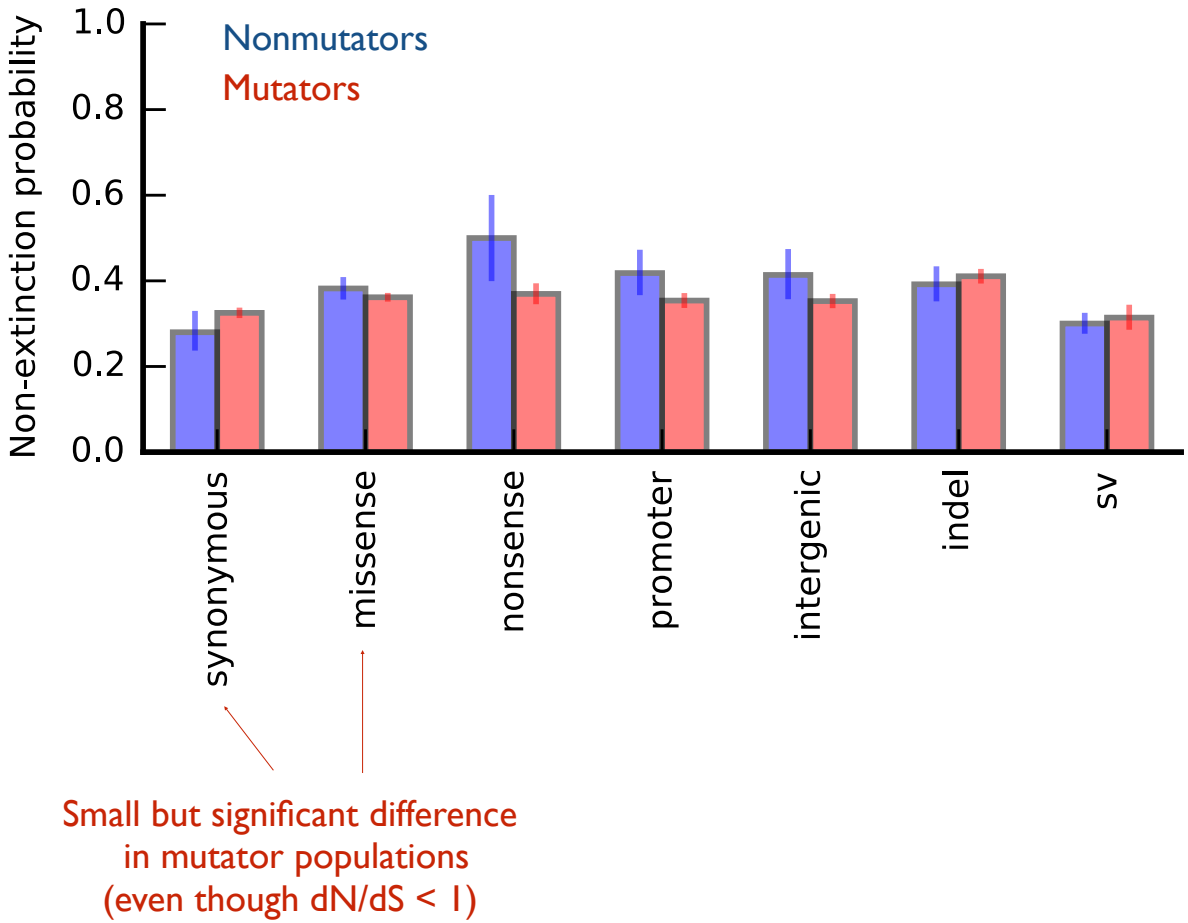

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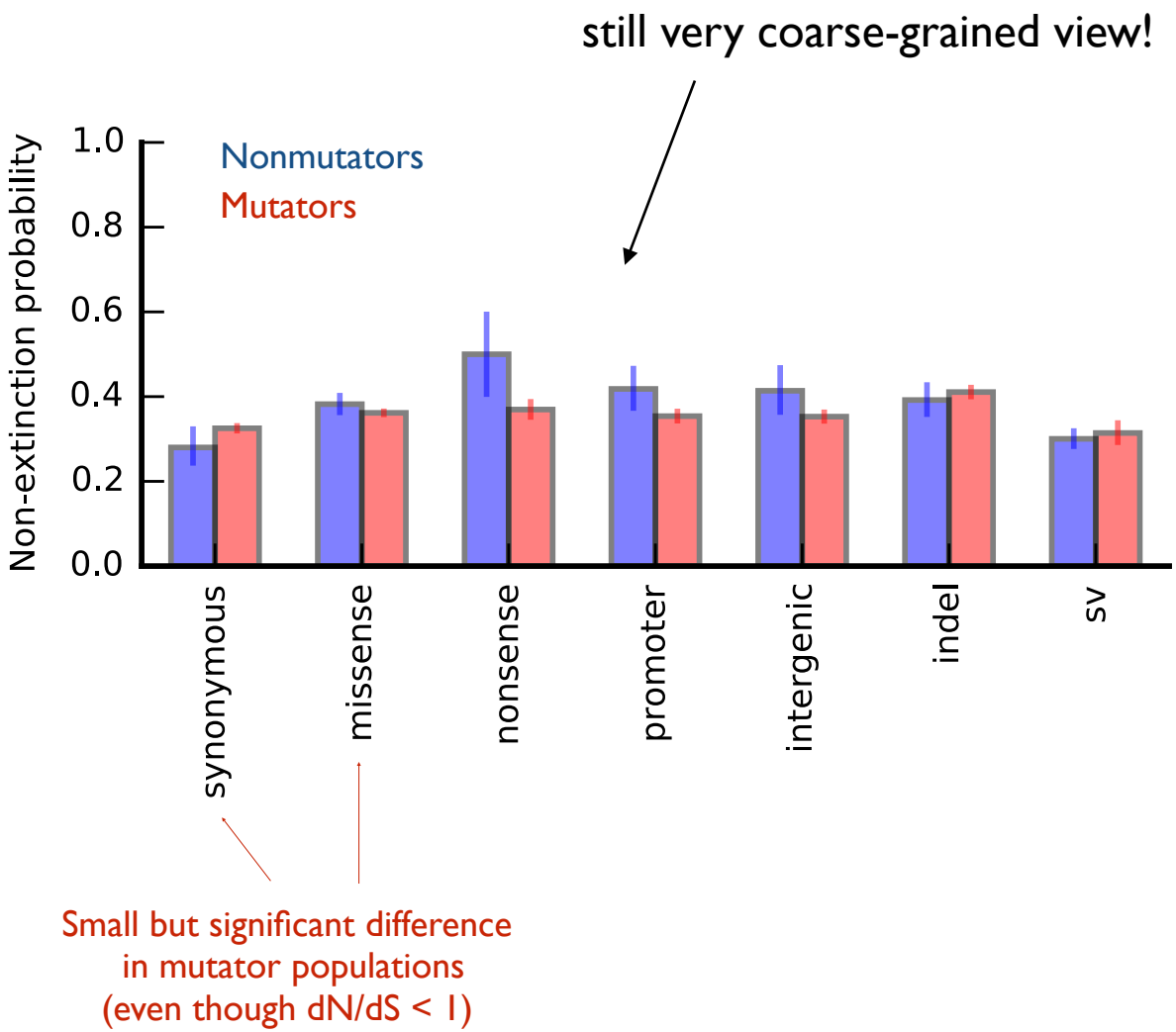
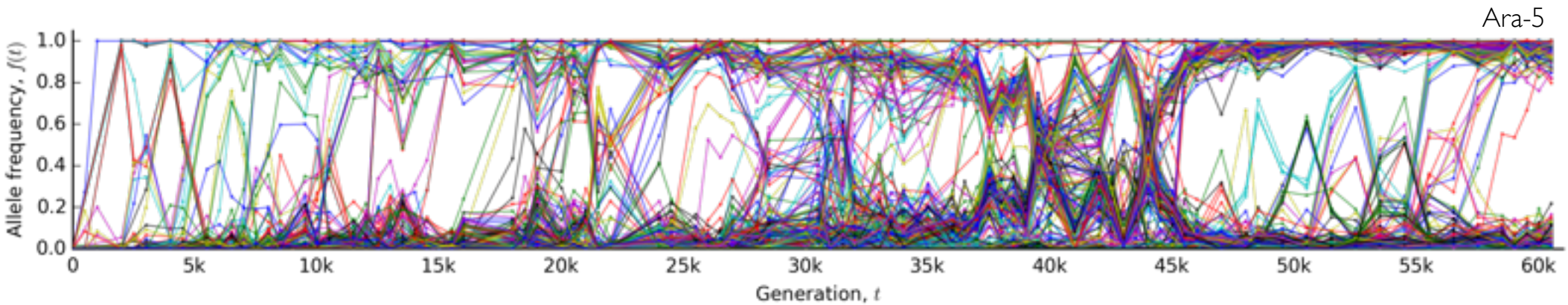


Parallelism at the Gene Level



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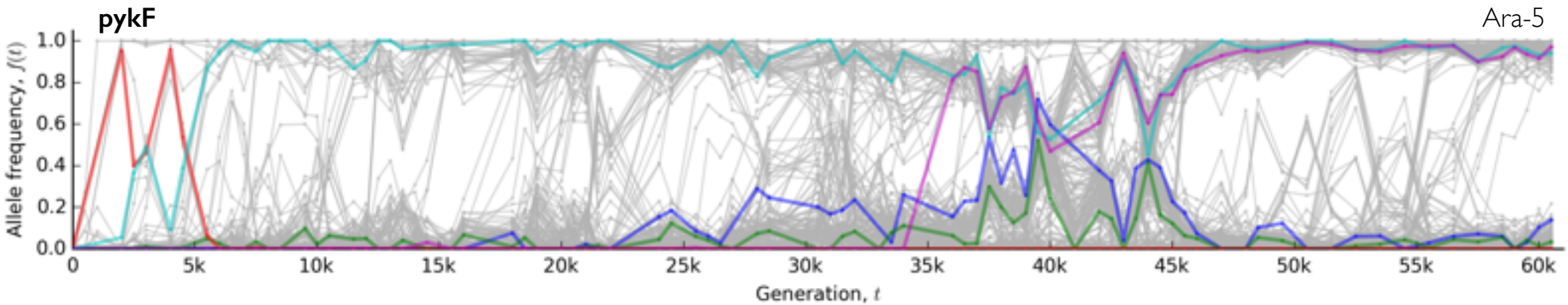

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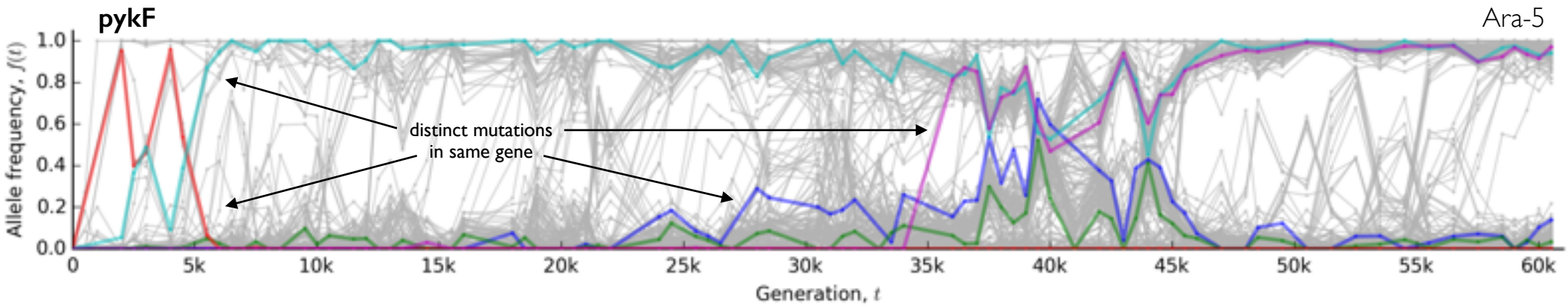

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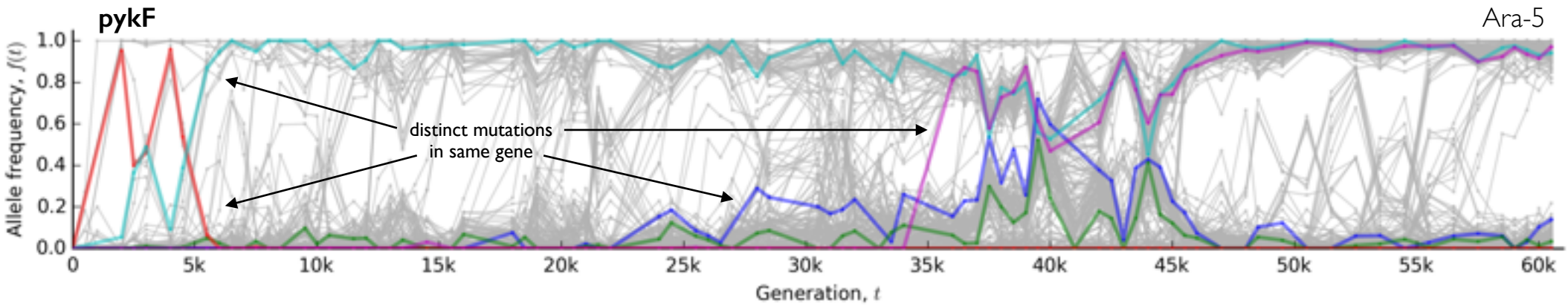

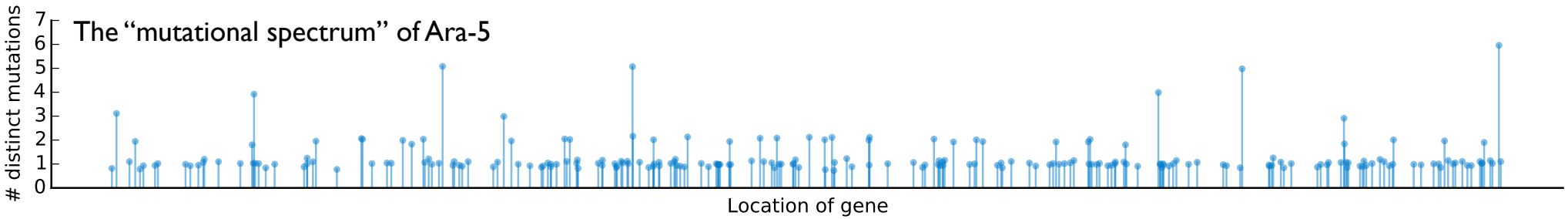

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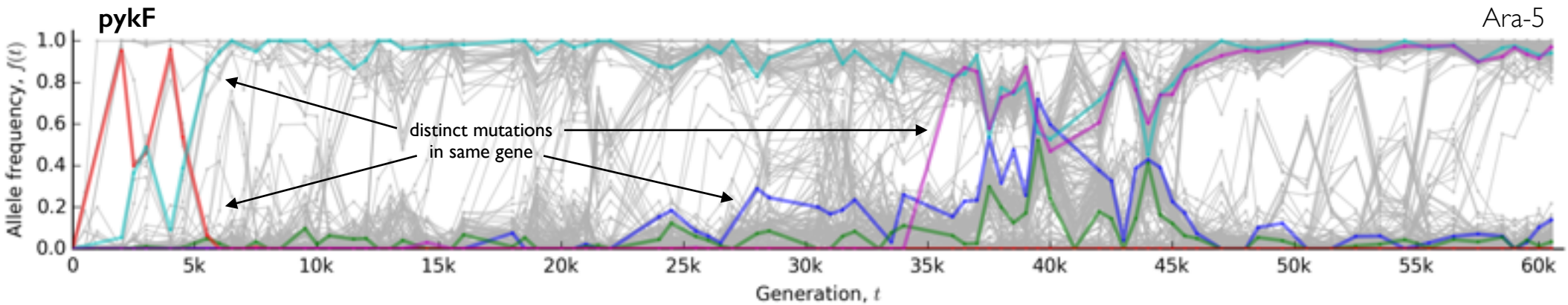

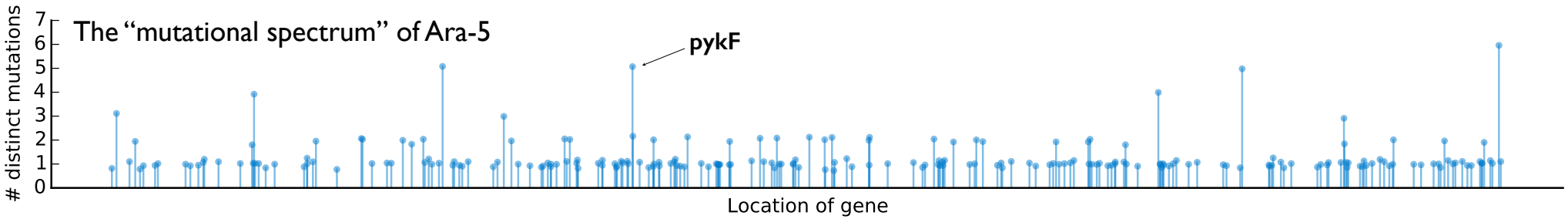

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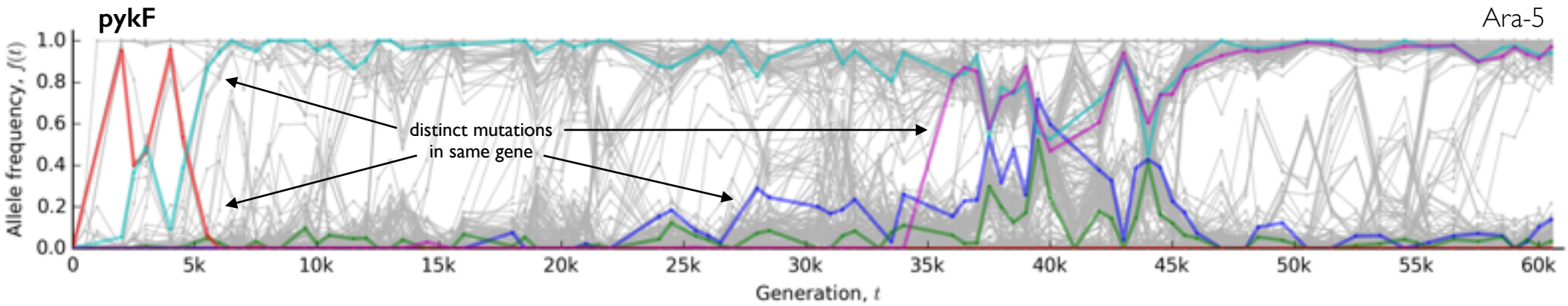
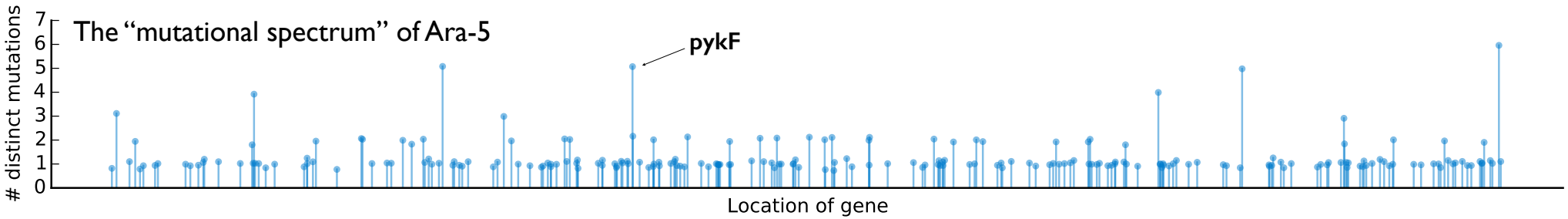
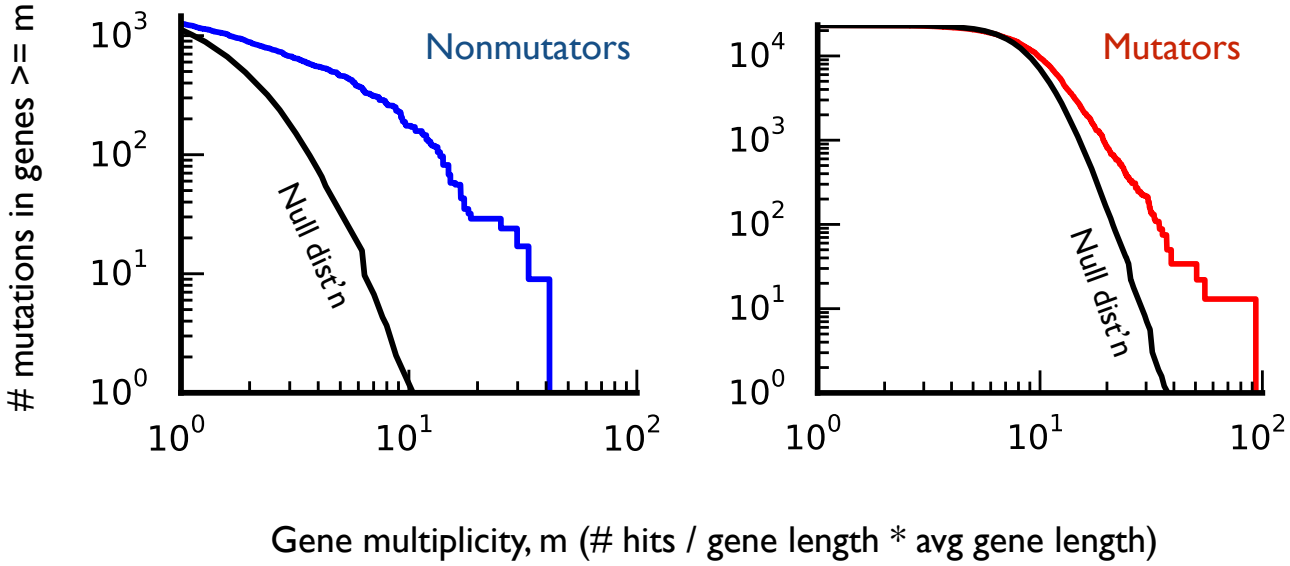




+

other 11 populations…

Parallelism at the Gene Level



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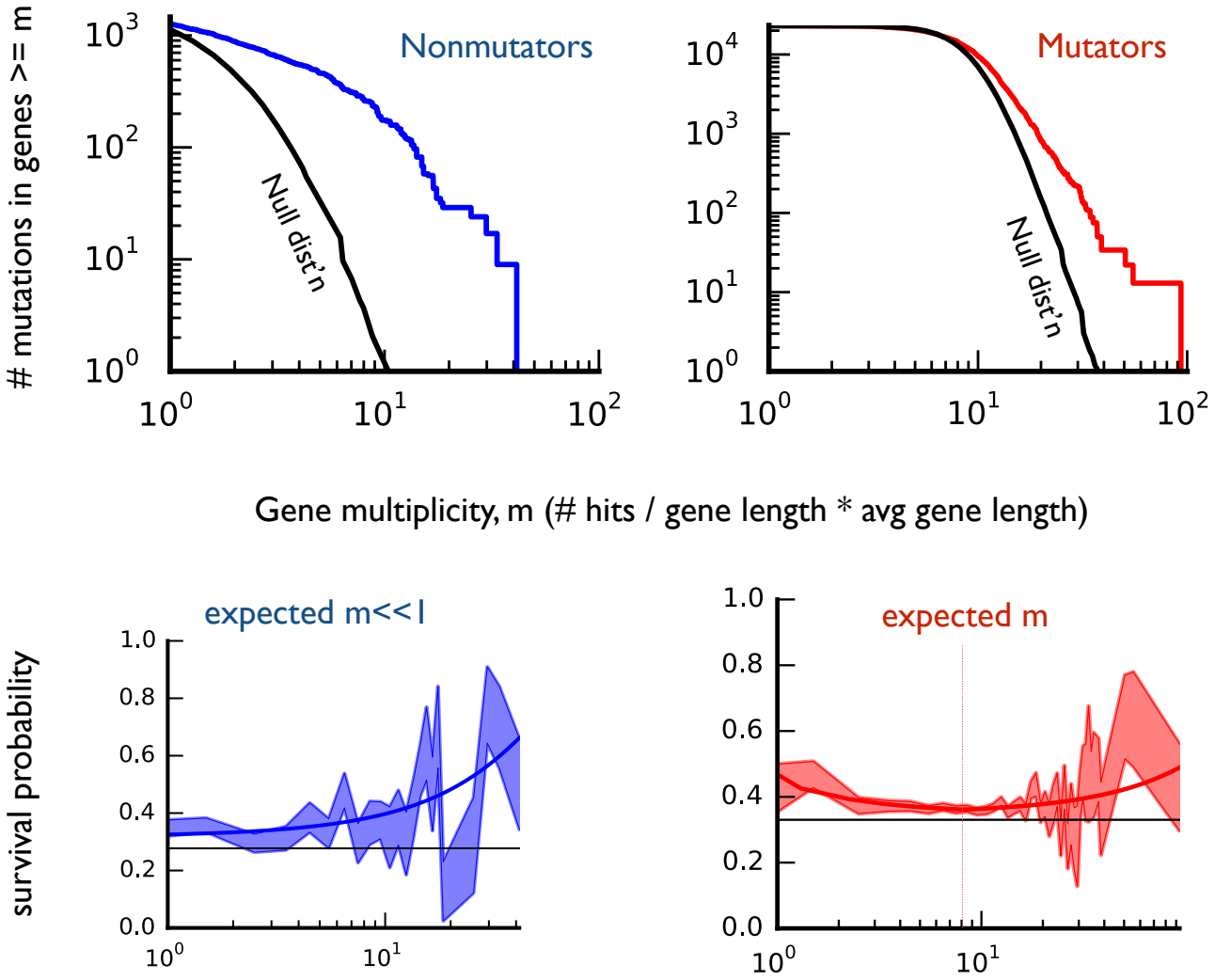

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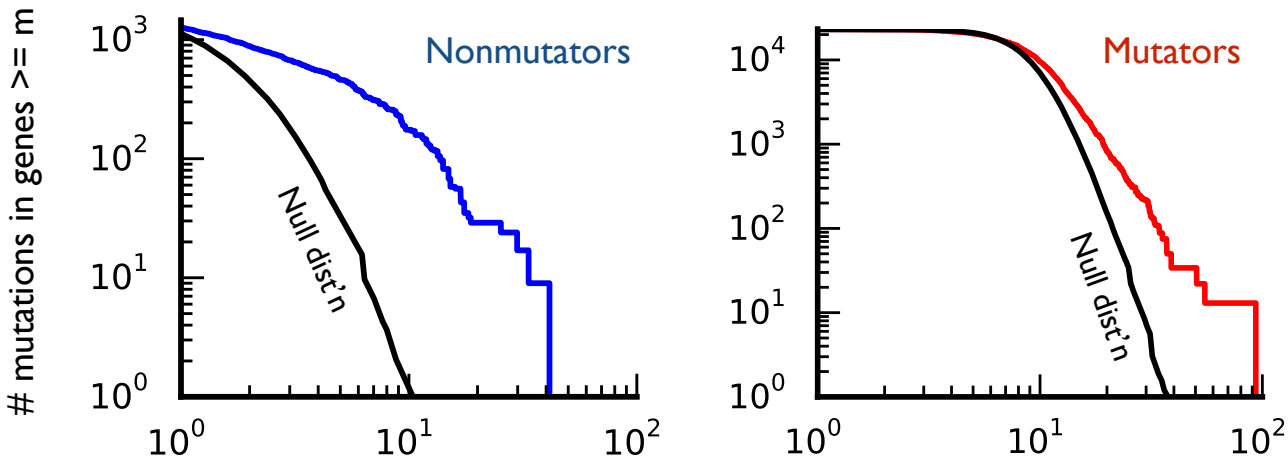
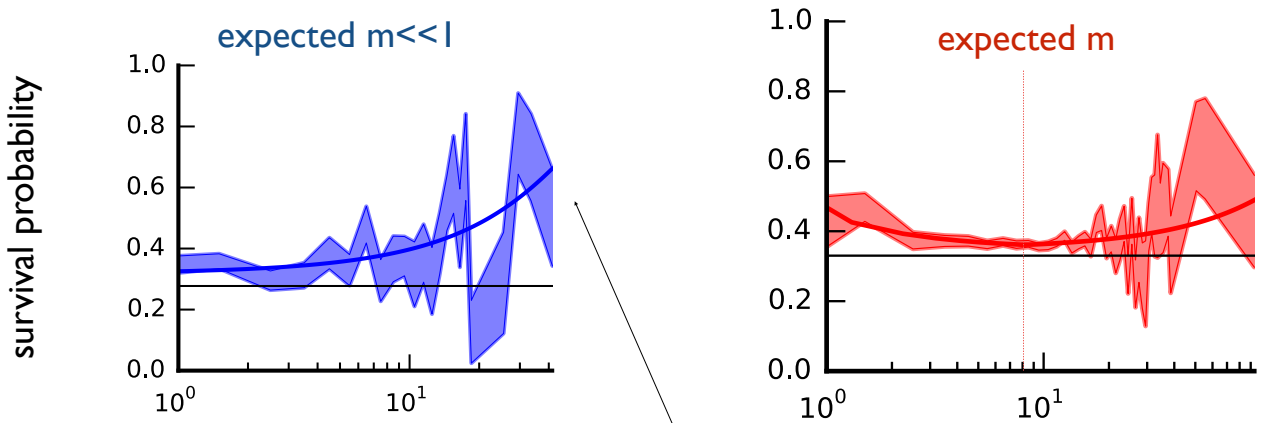
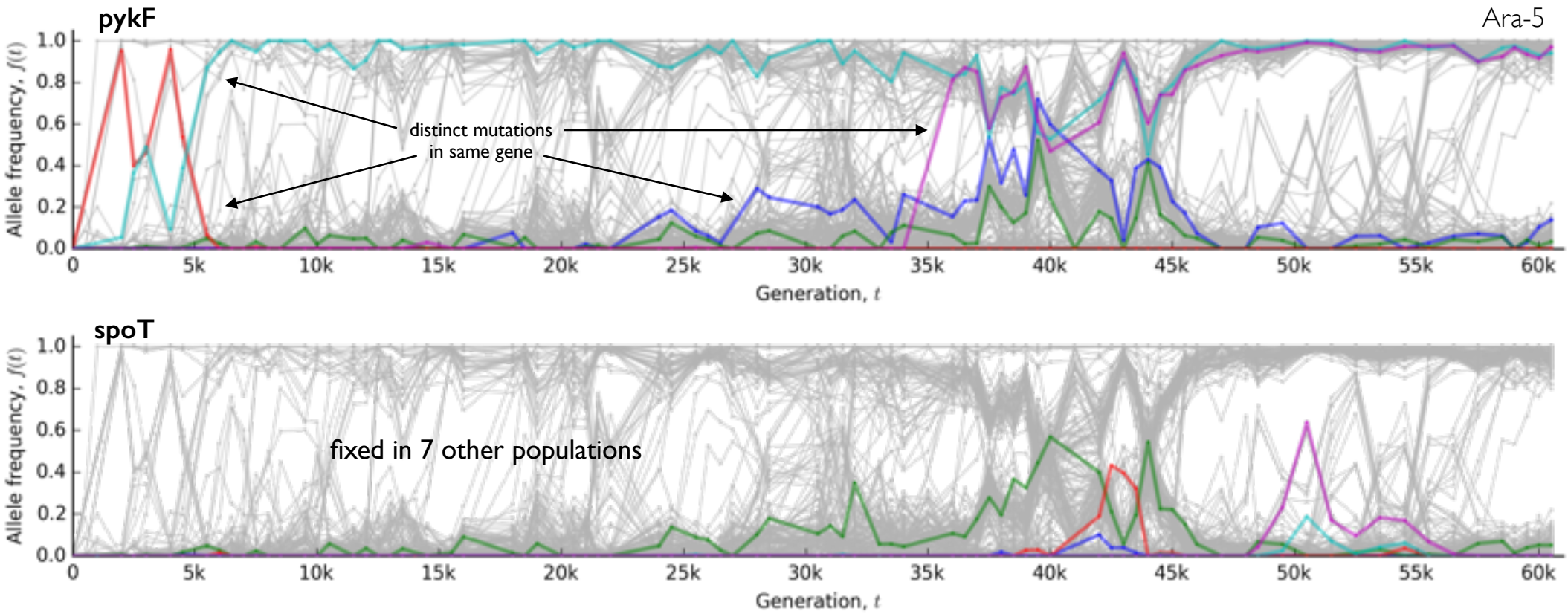




genetic draft still important for determining fate

Parallelism at the Gene Level



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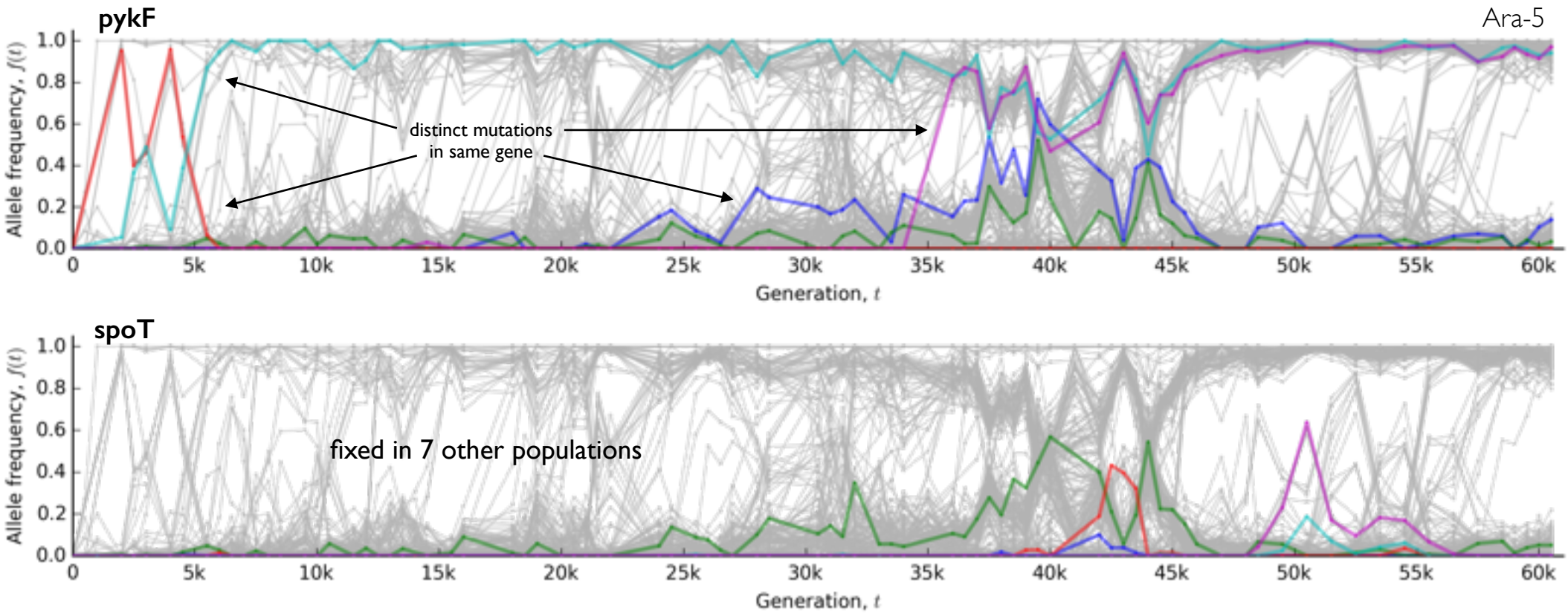

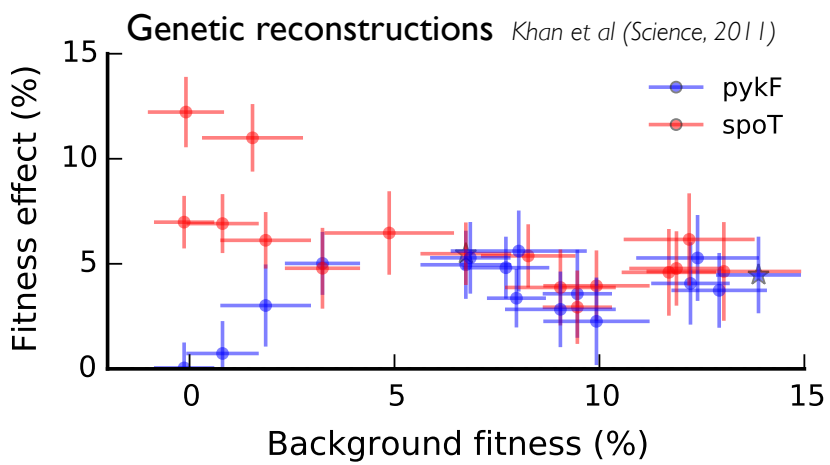

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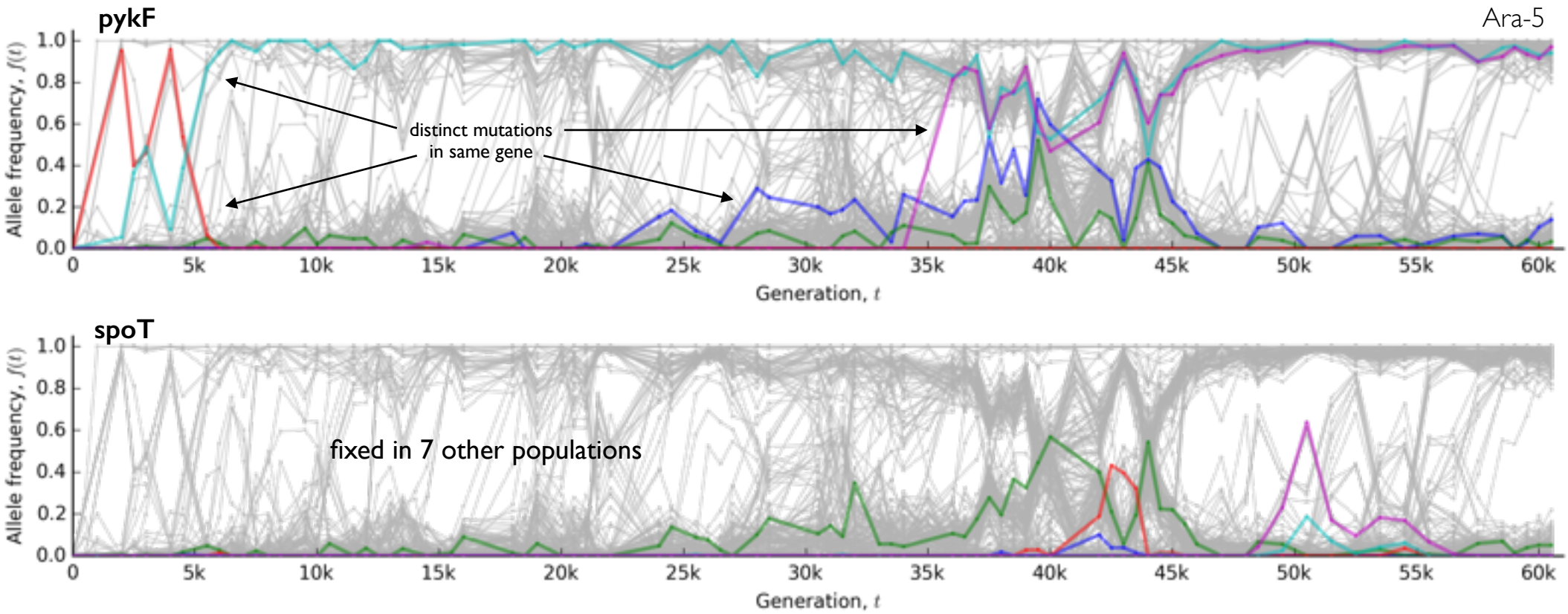
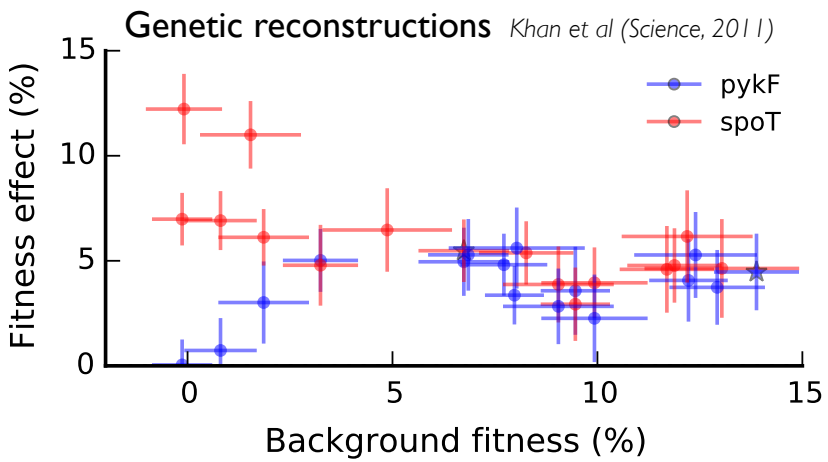
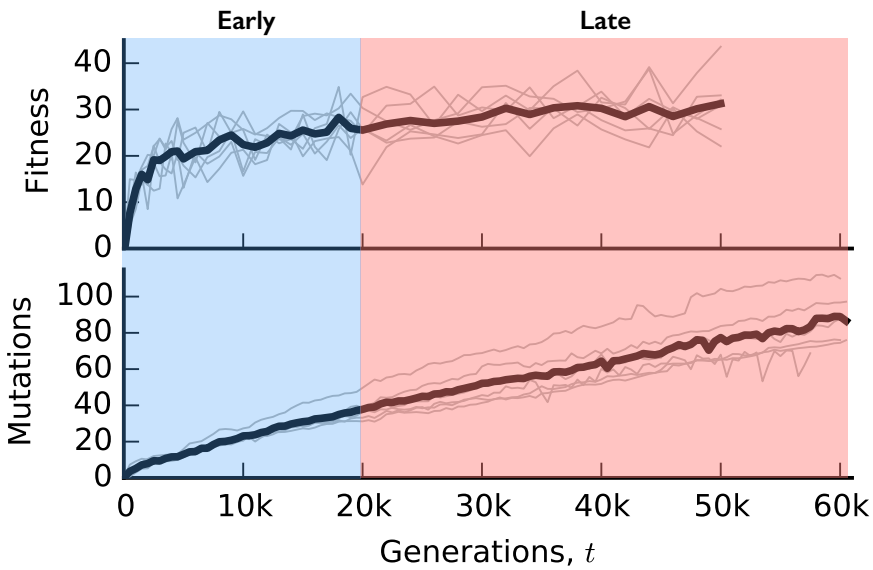




The ***dynamics*** of the evolutionary process can be as important as biology for determining the fate of a mutation

Targets of Selection Over Time



Are different mutations targeted in different parts of the experiment?

(1) do strongly beneficial mutations "run out"?

(2) do additional targets arise to compensate?

Targets of Selection Over Time

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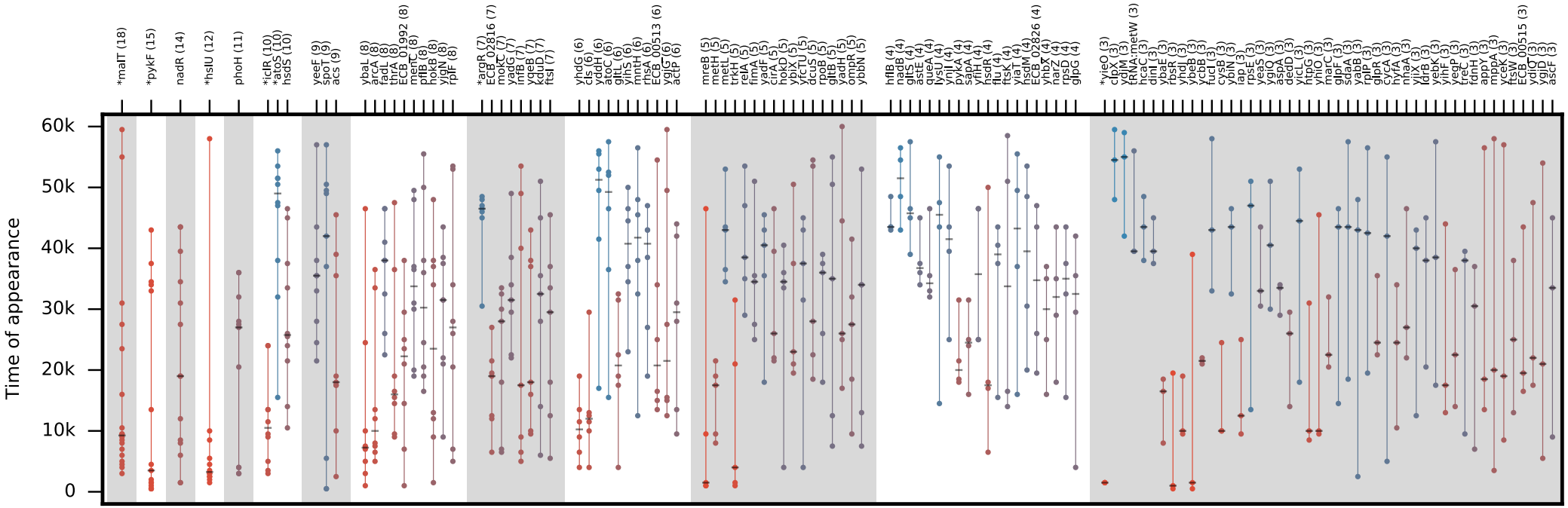

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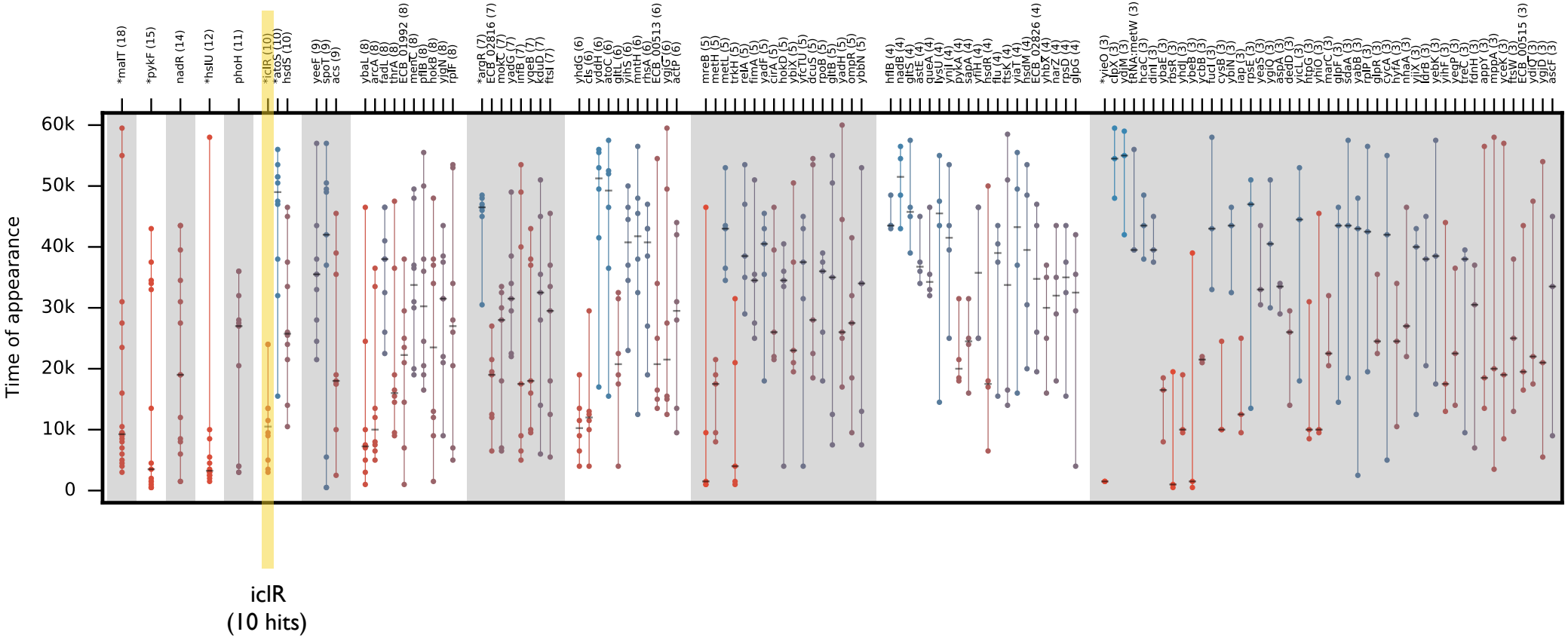
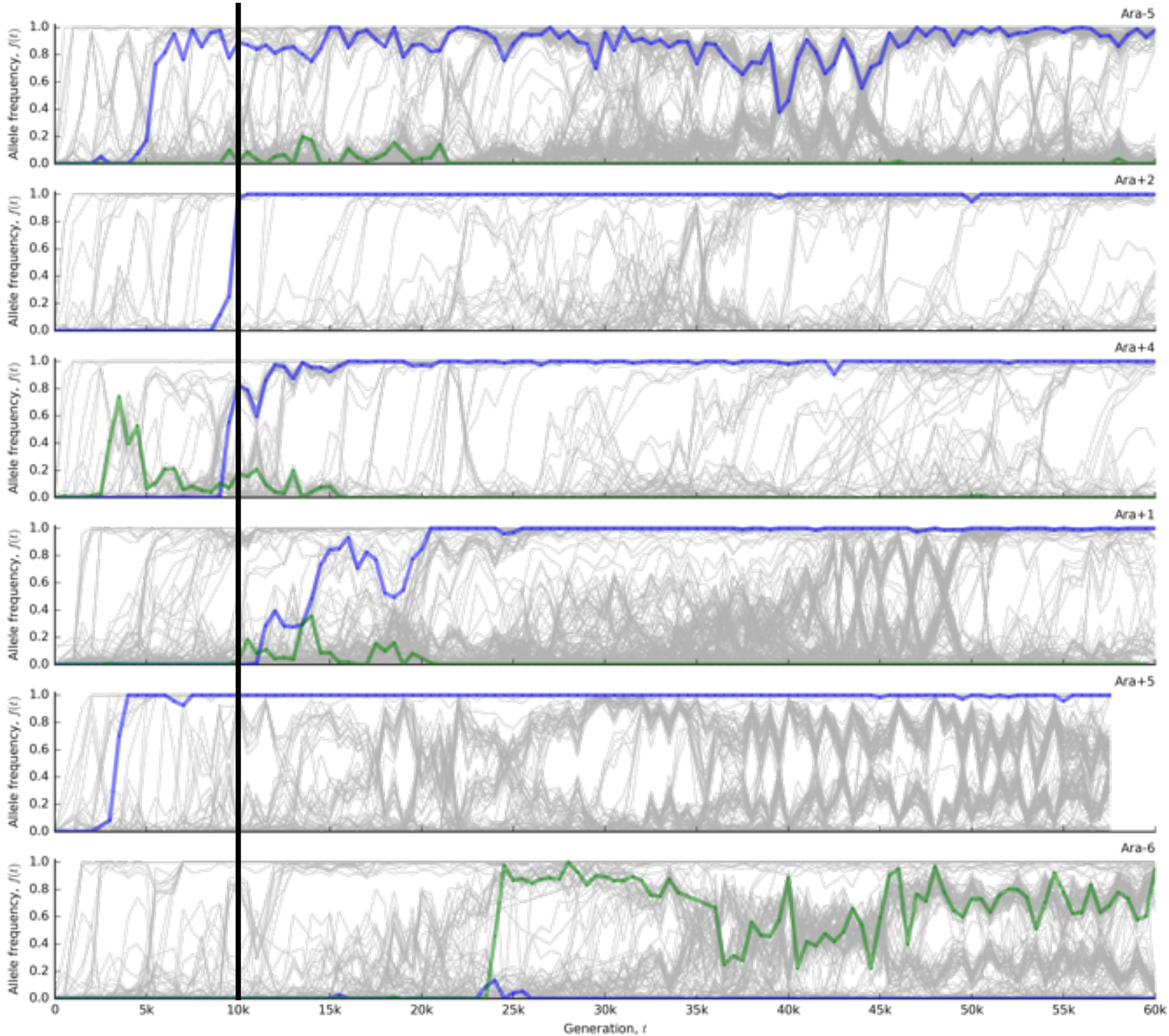


mutations in iclR



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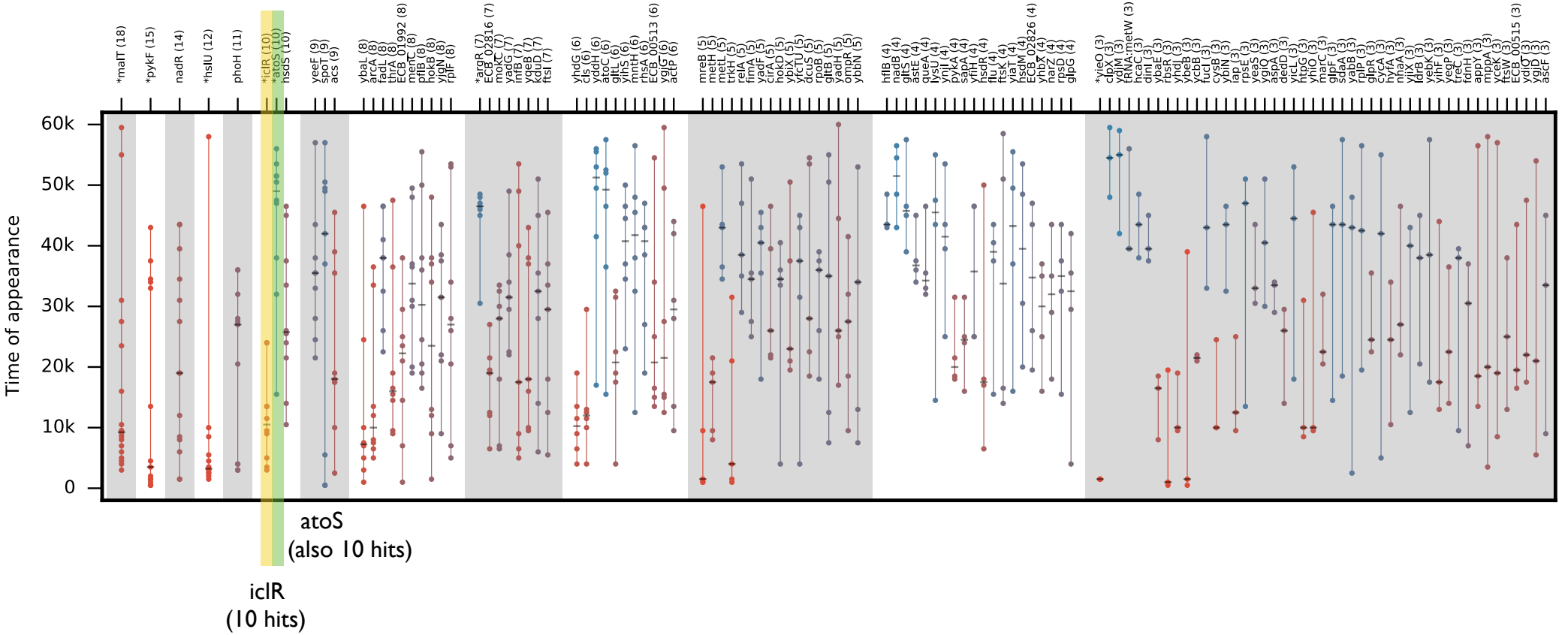
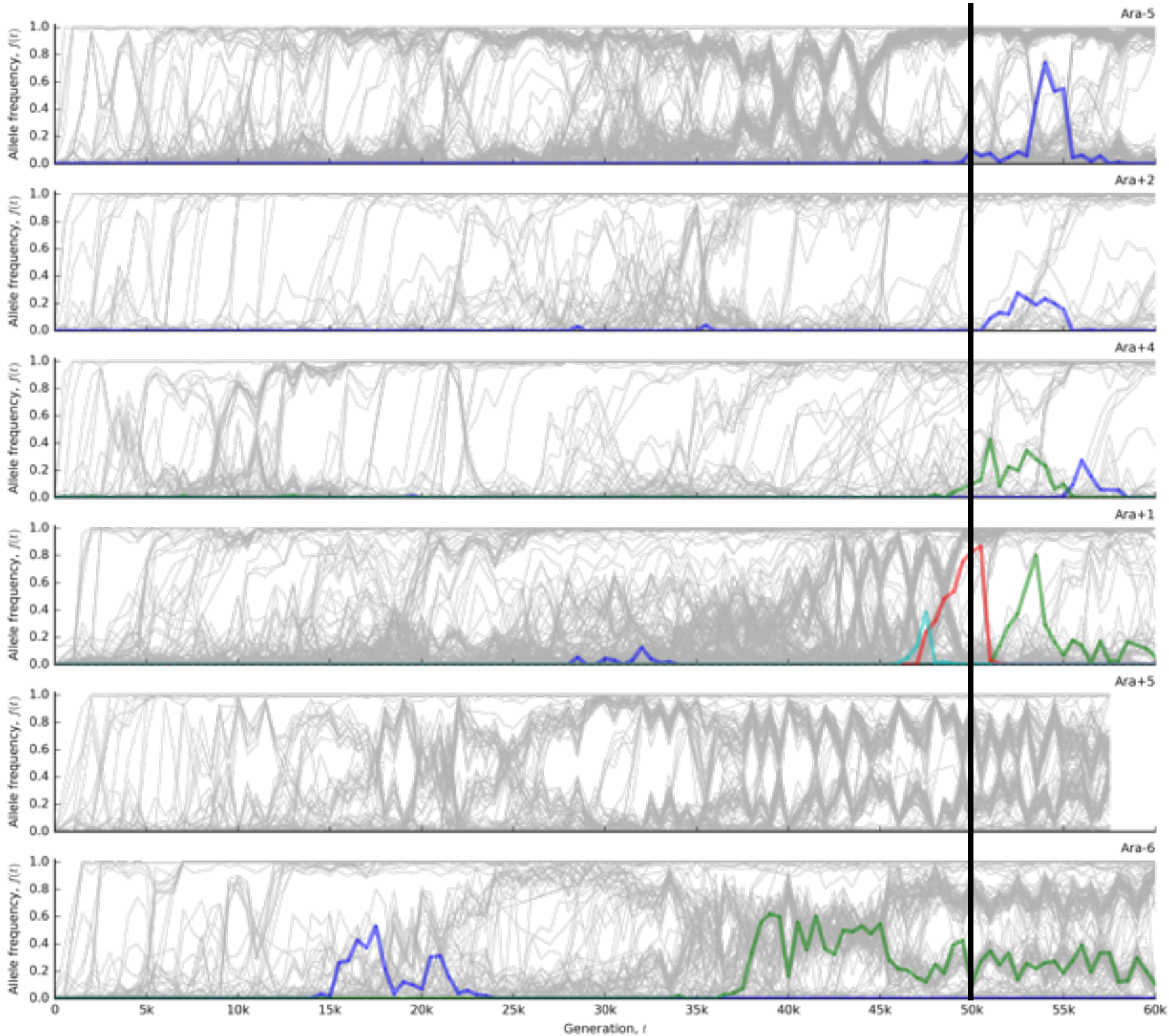


mutations in atoS



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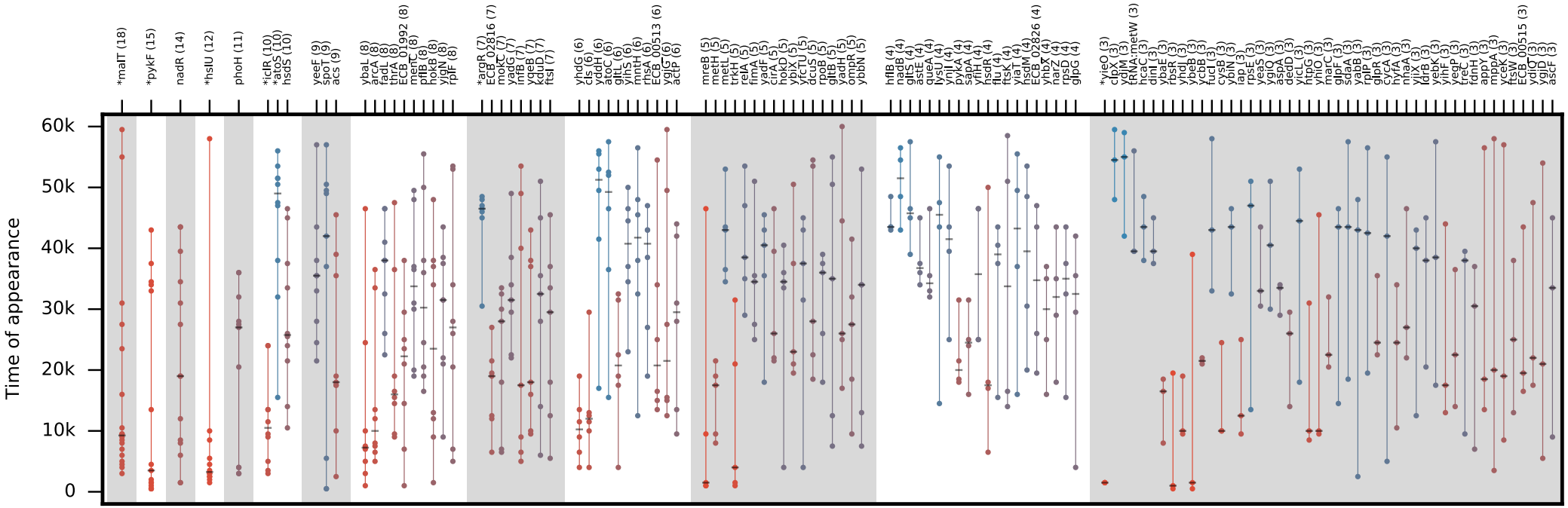

After taking out individually significant genes, within-gene times are still statistically ***non-random***

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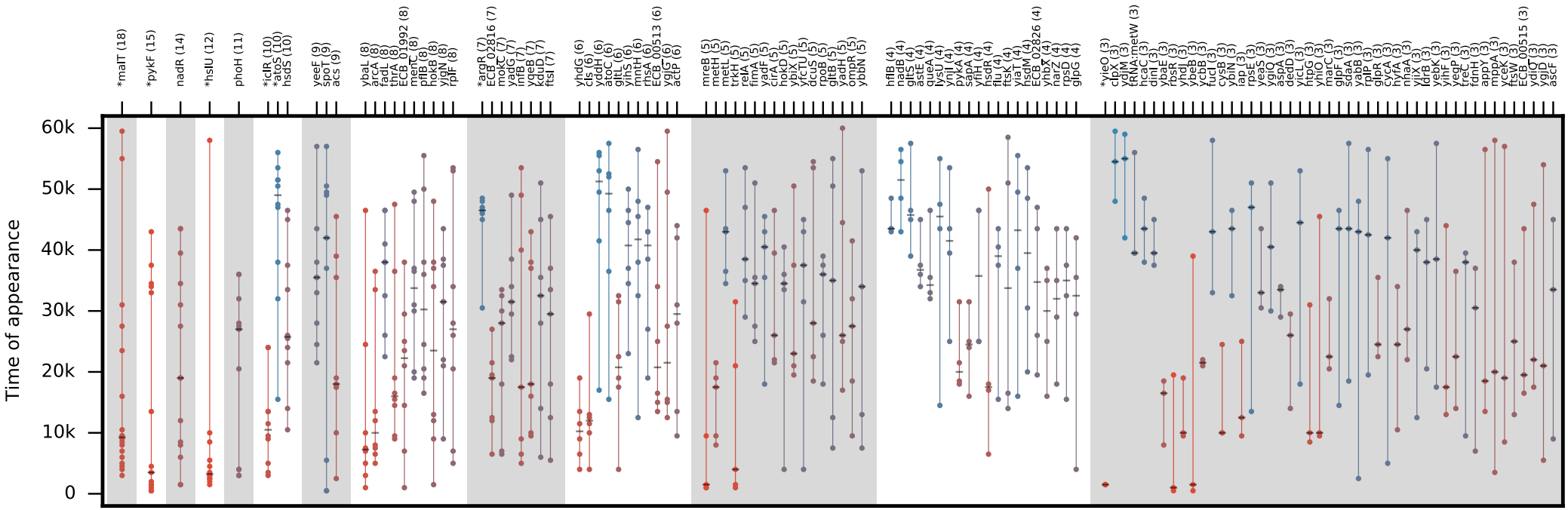

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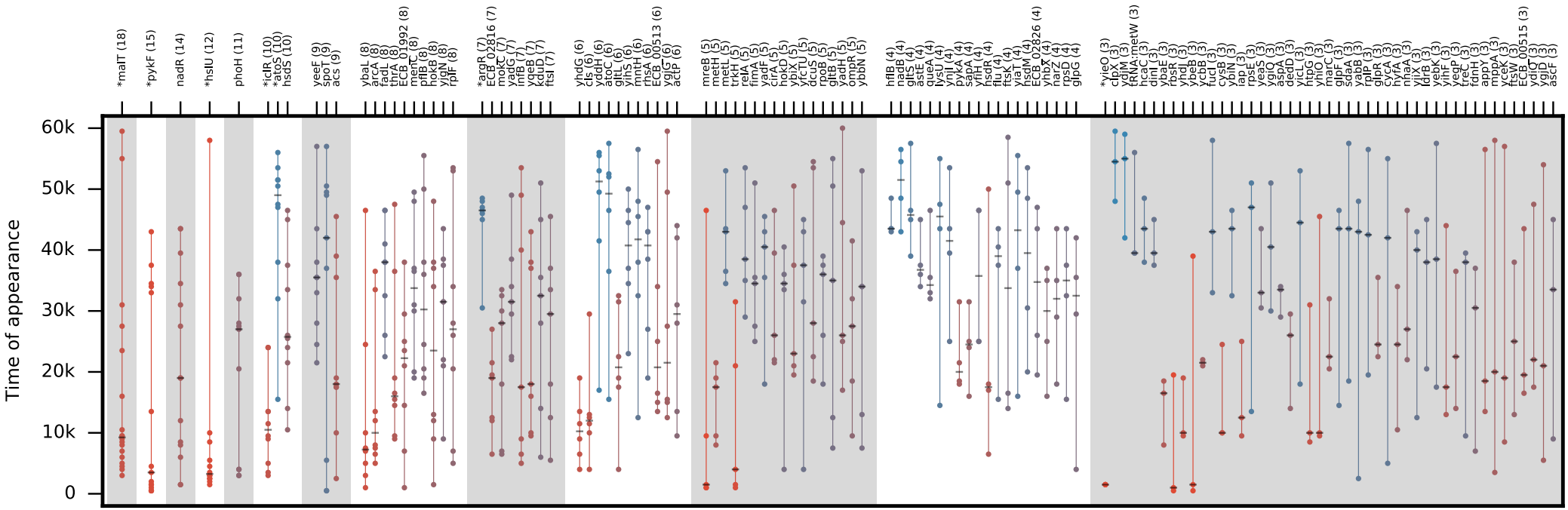
…and mutations in 2-hit genes occur closer to each other than expected by chance

Targets of Selection Over Time



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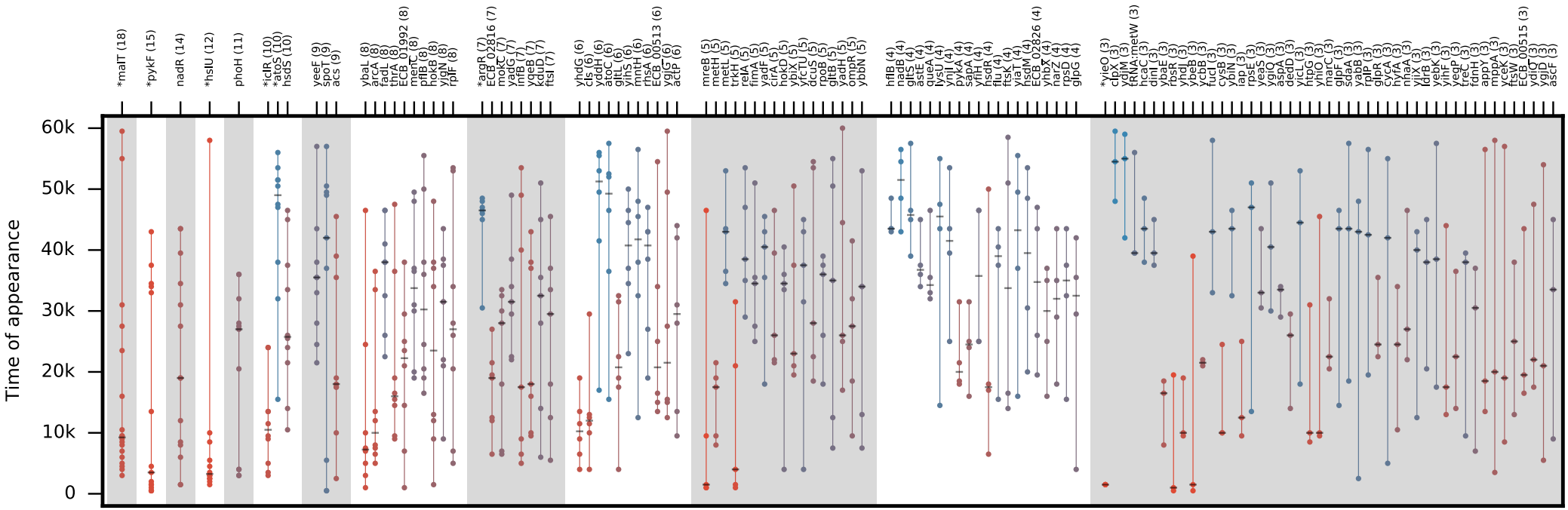
the spectrum of adaptive mutations changes over time

Targets of Selection Over Time



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→ **the spectrum of adaptive mutations changes over time**

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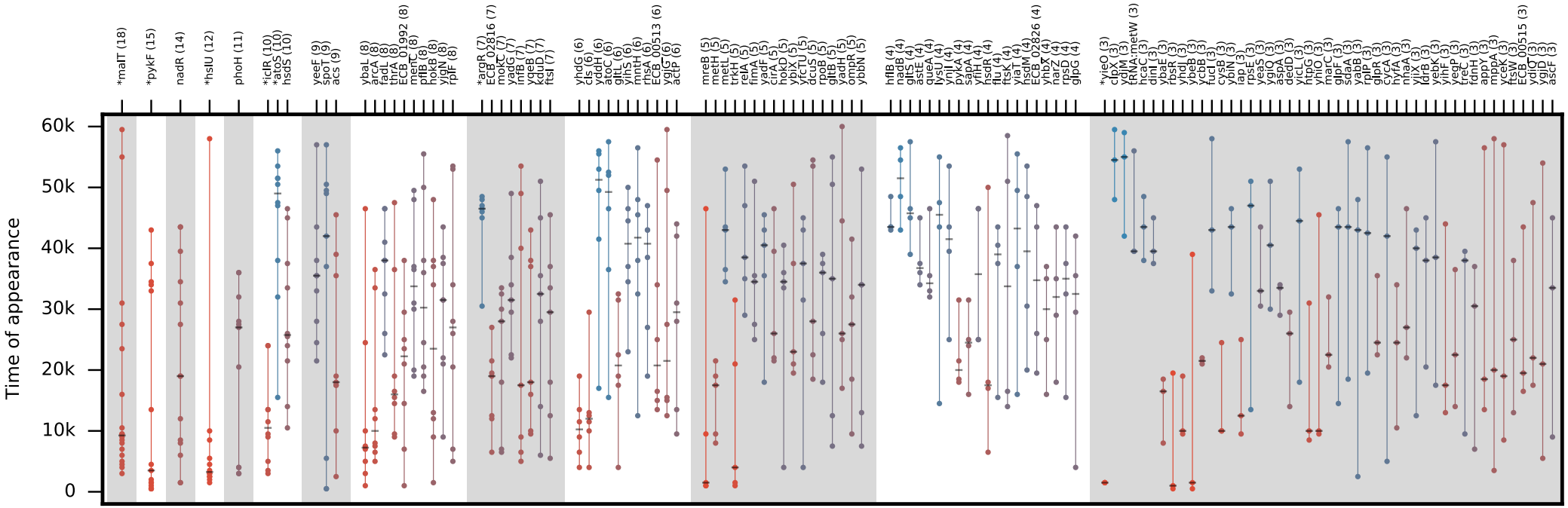
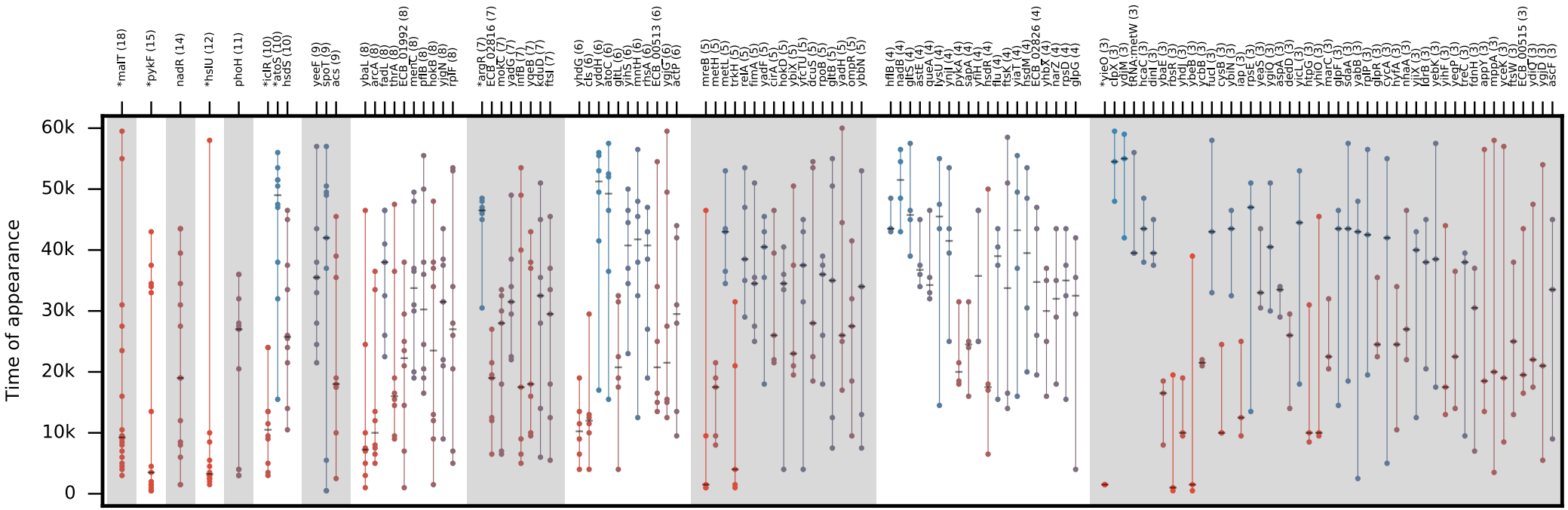


What could cause this?

(1) Running out of mutations / coupon collecting

Targets of Selection Over Time



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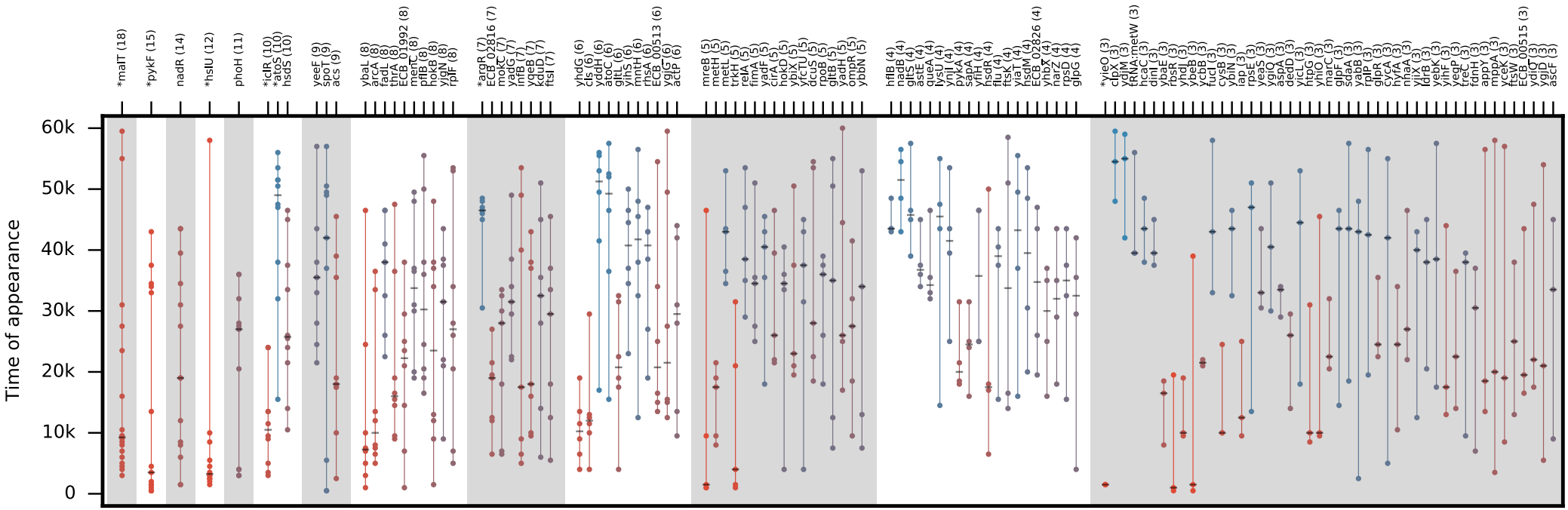
Targets of Selection Over Time



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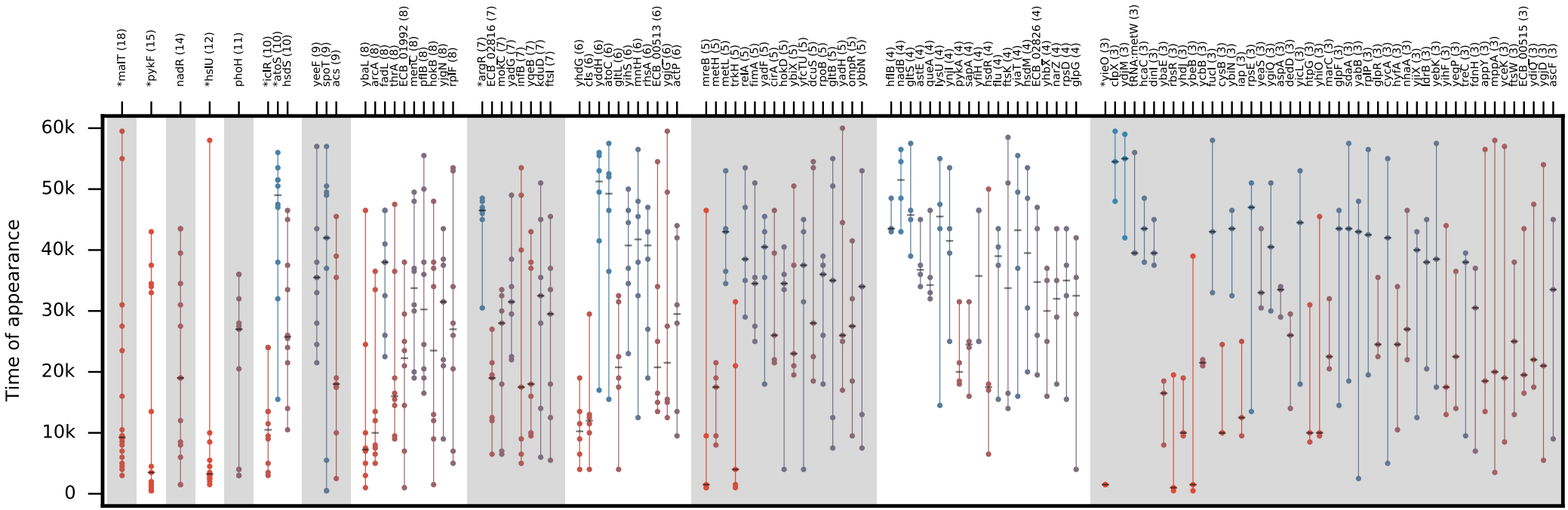

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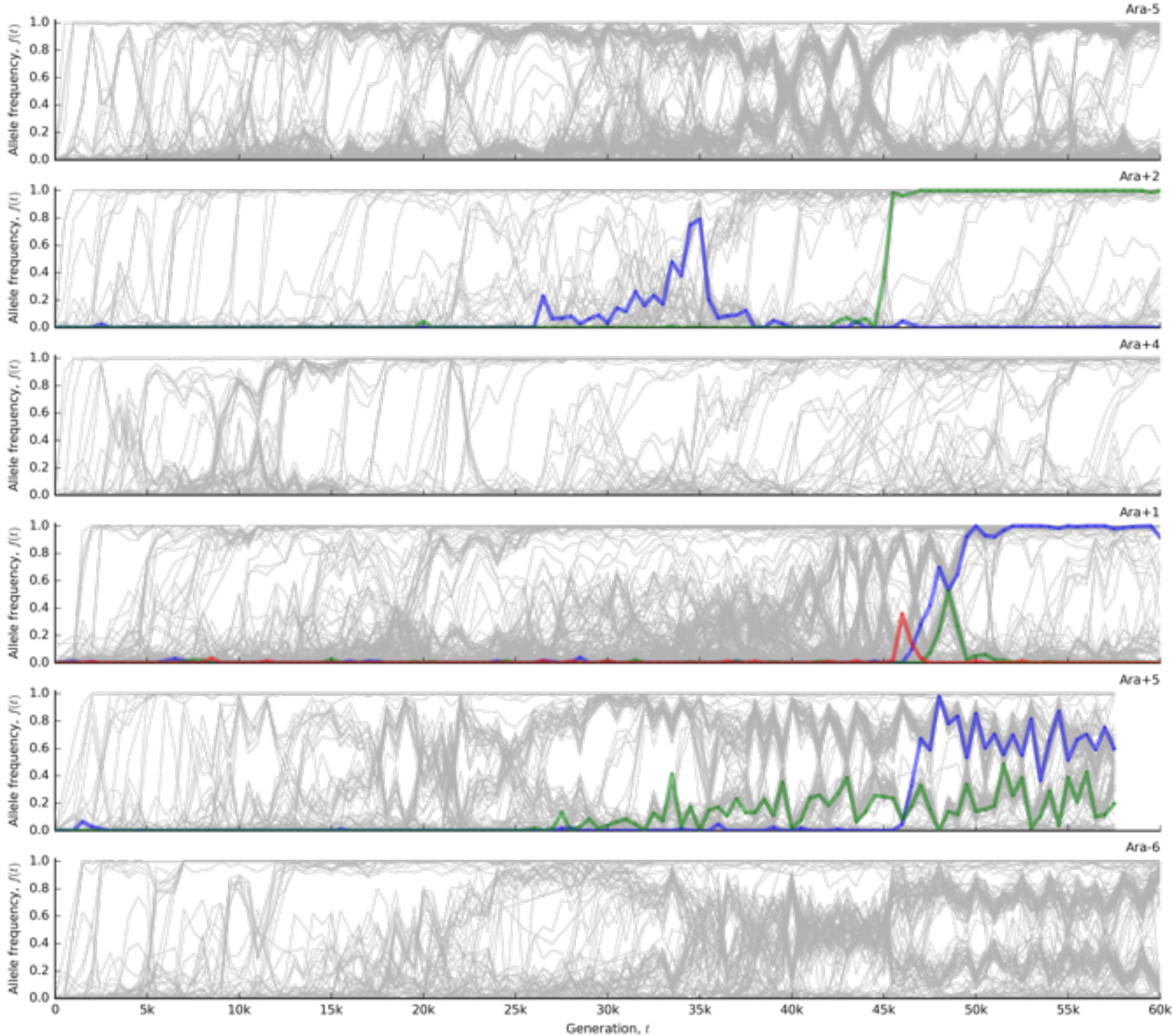
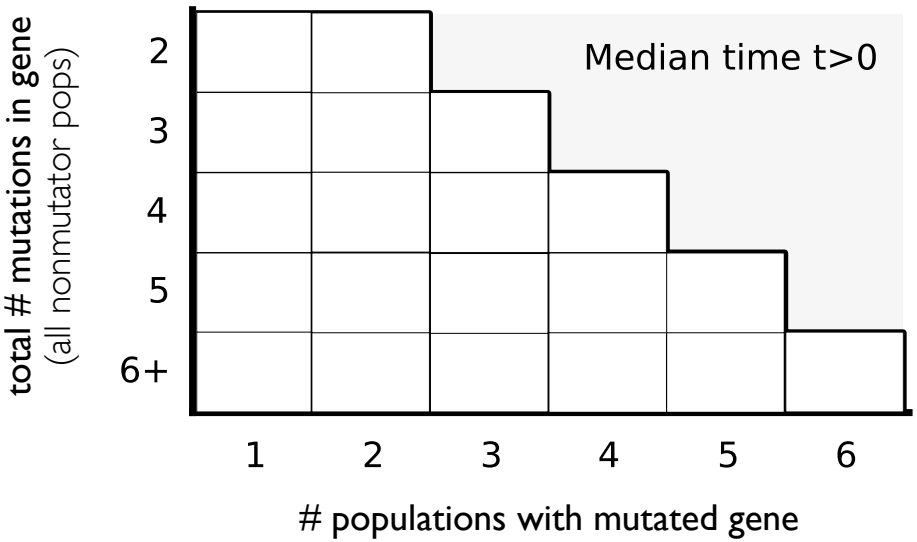
→ expect mutations to be ***clustered*** in certain pops
(i.e., those that got potentiating mutation)

e.g. argR

7 hits
mostly late
3/6 pops



Signatures of Contingency



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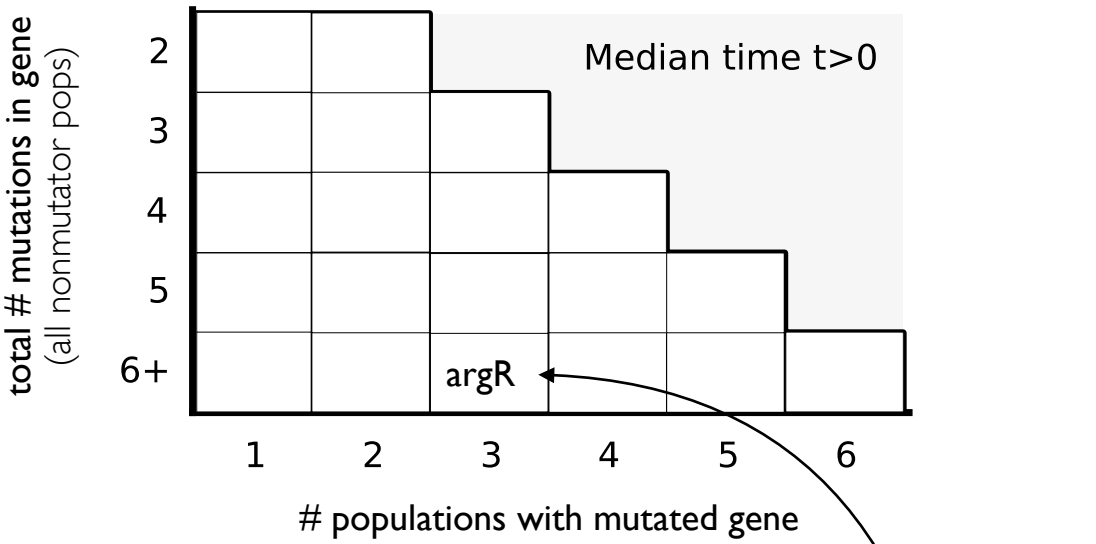
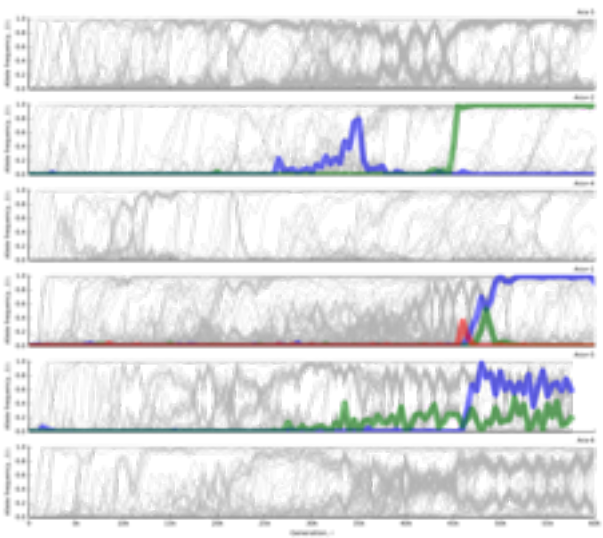
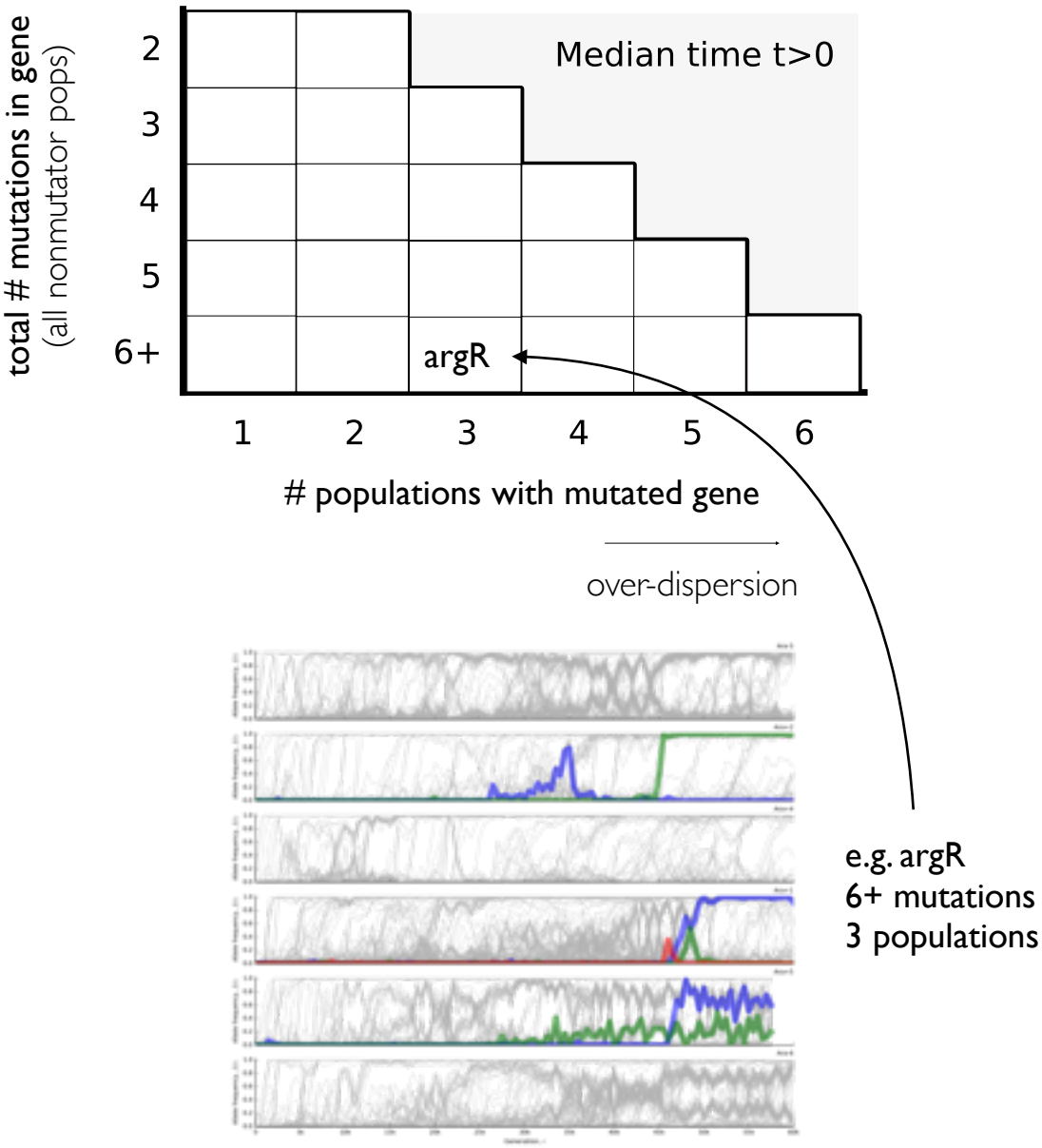




e.g. argR
6+ mutations
3 populations

Signatures of Contingency



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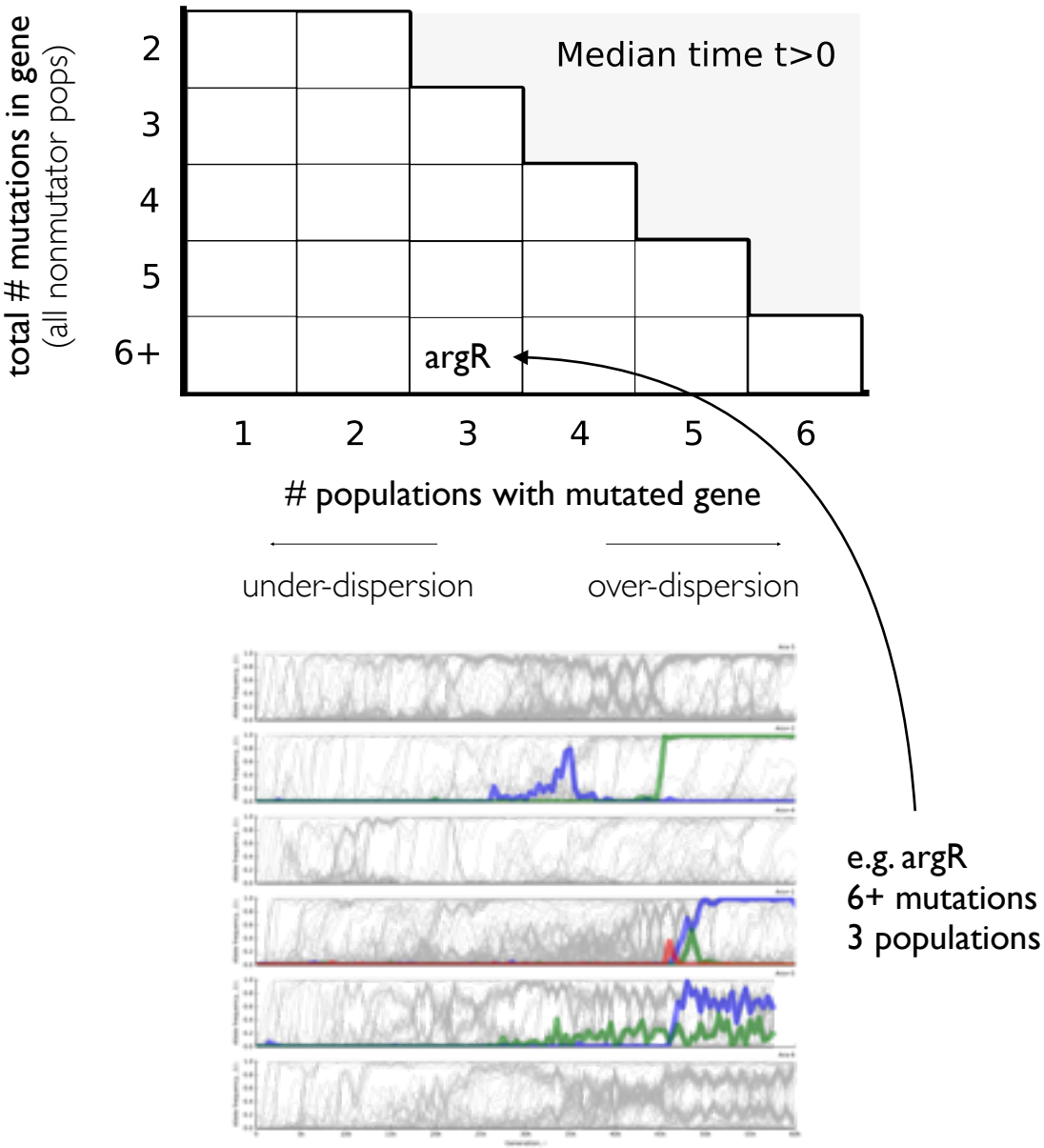

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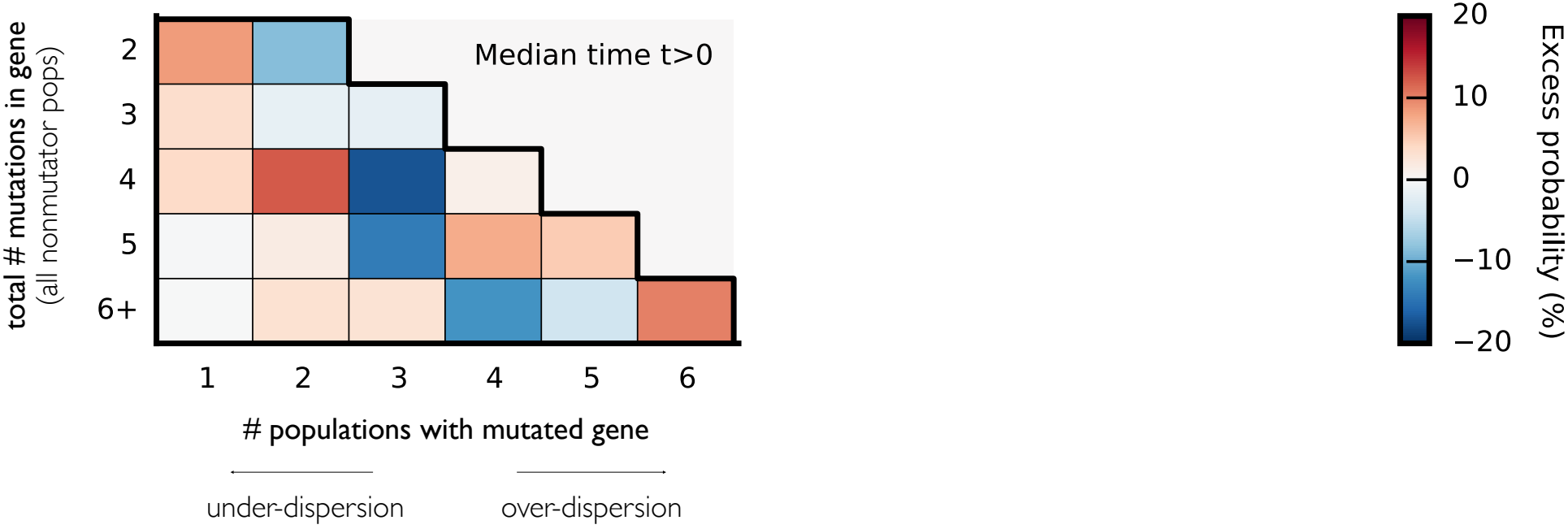

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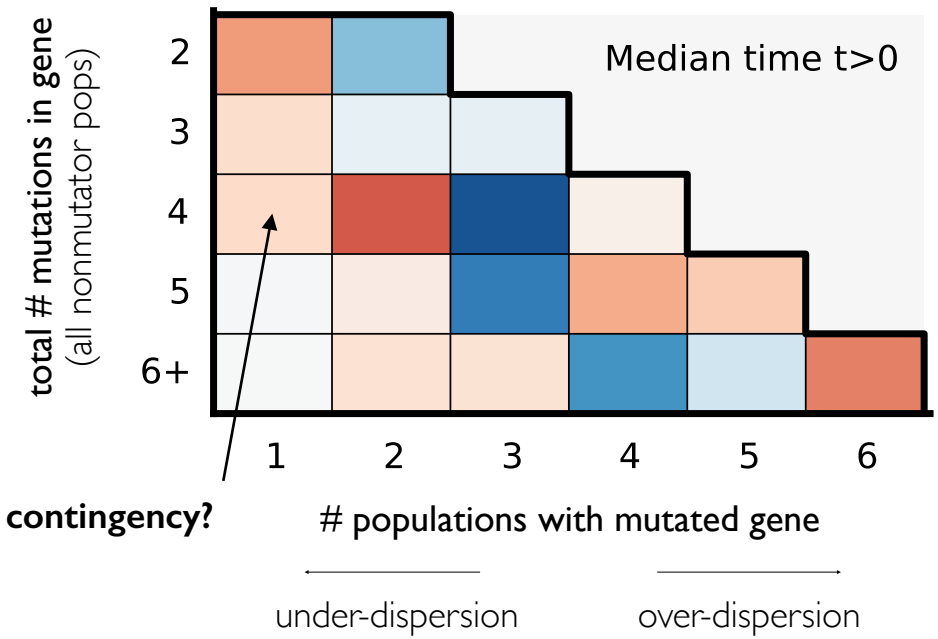

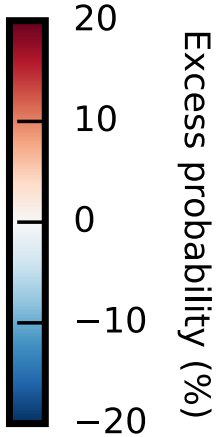

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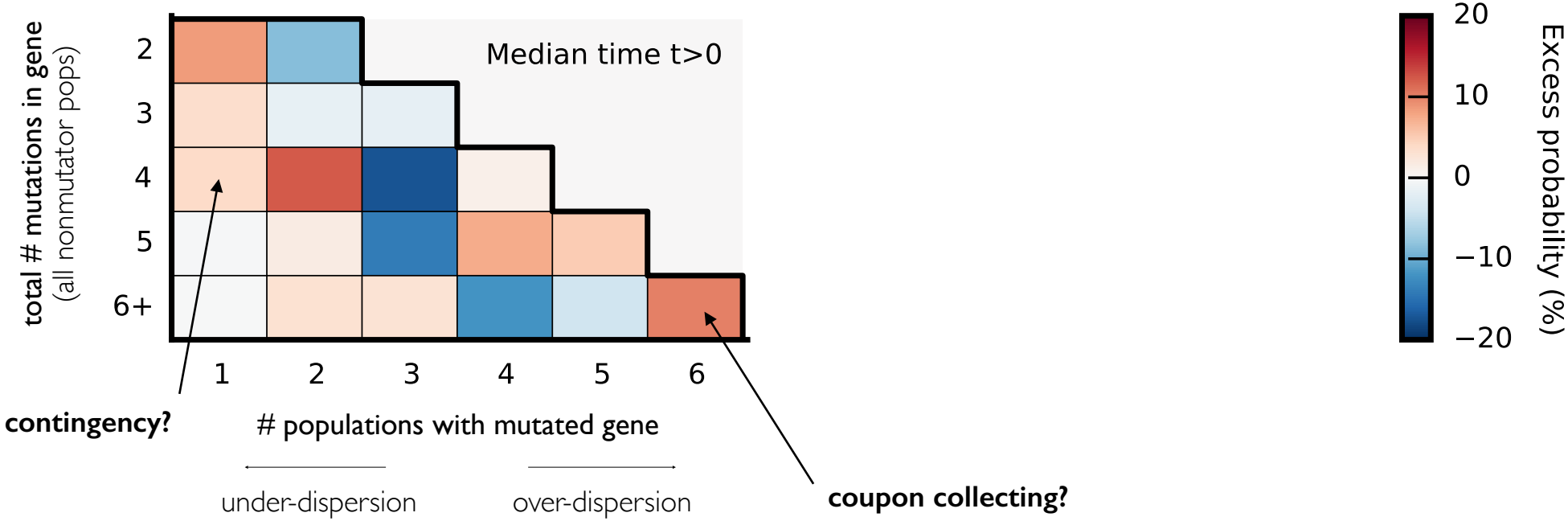

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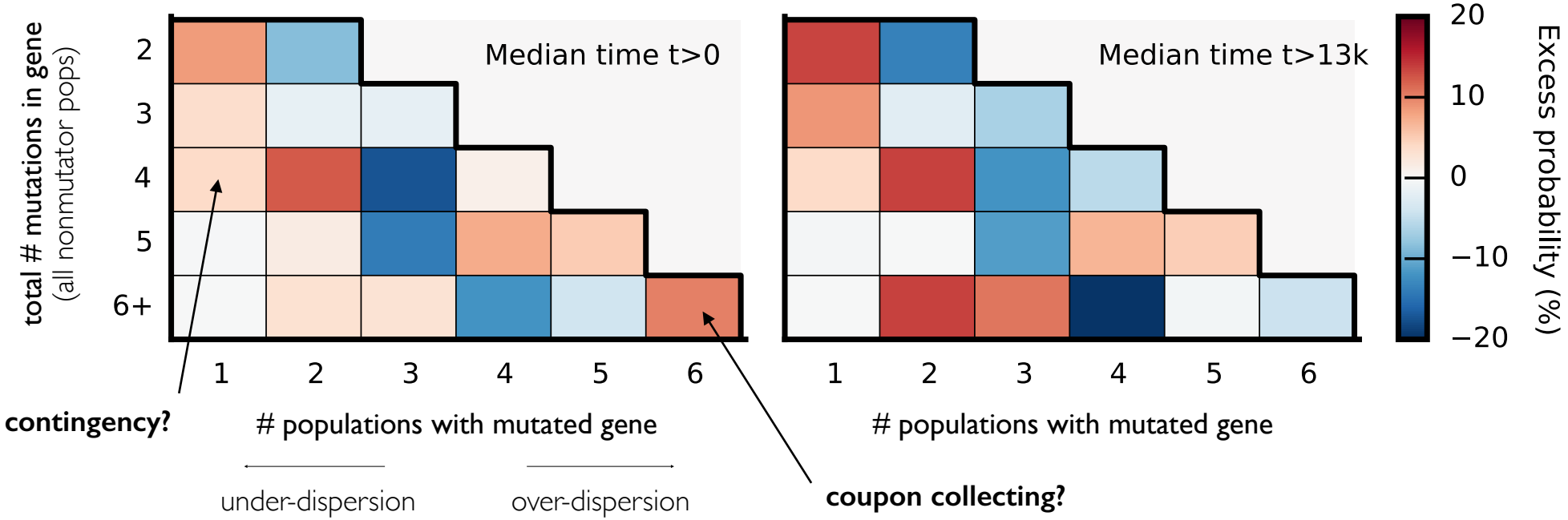

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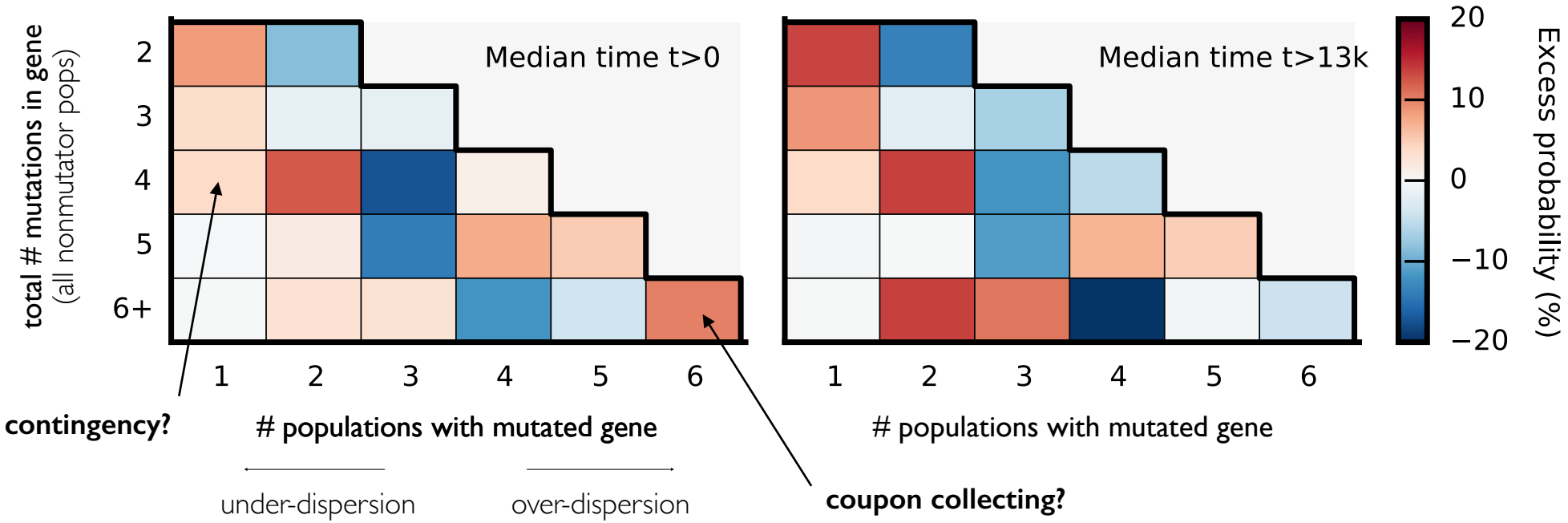


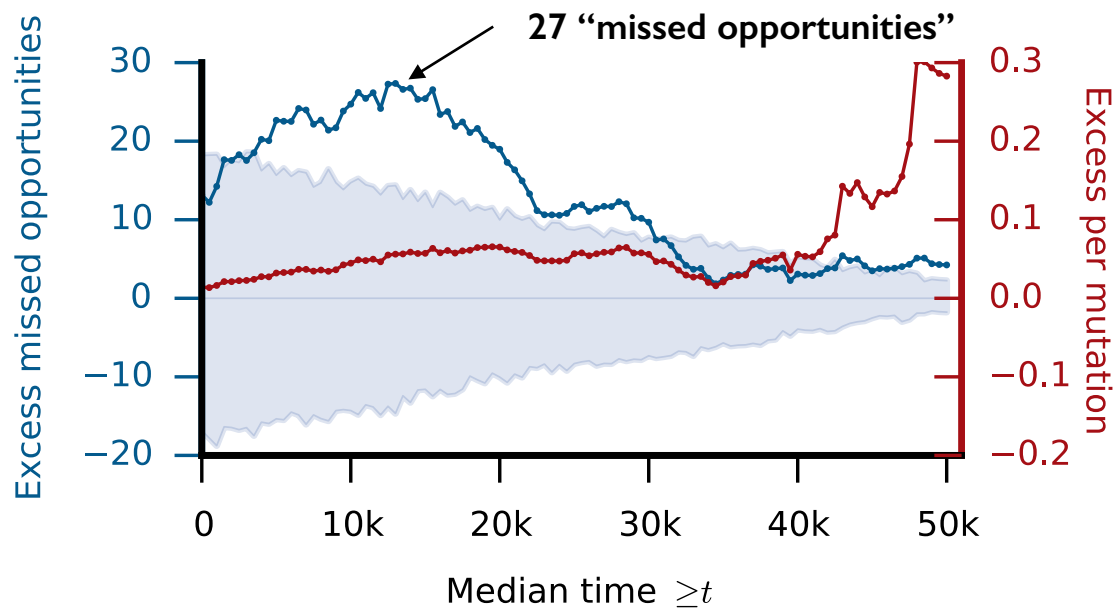
contingency?

under-dispersion

over-dispersion

coupon collecting?

sum across tiles to look at global signal



What about sex? Back to yeast!

We can maintain yeast sexually or asexually in the lab

Sexual yeast undergo periodic cycles of mating and sporulation

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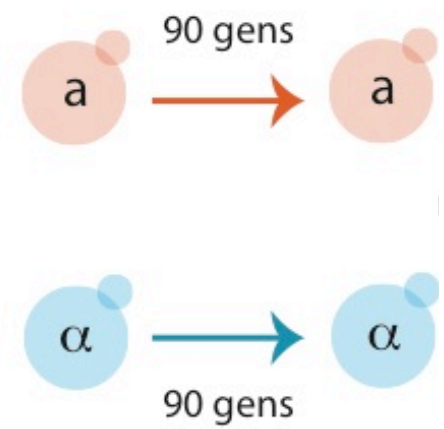

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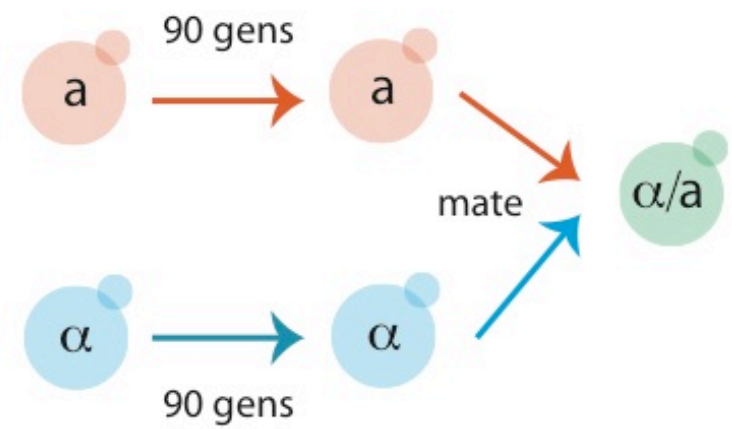

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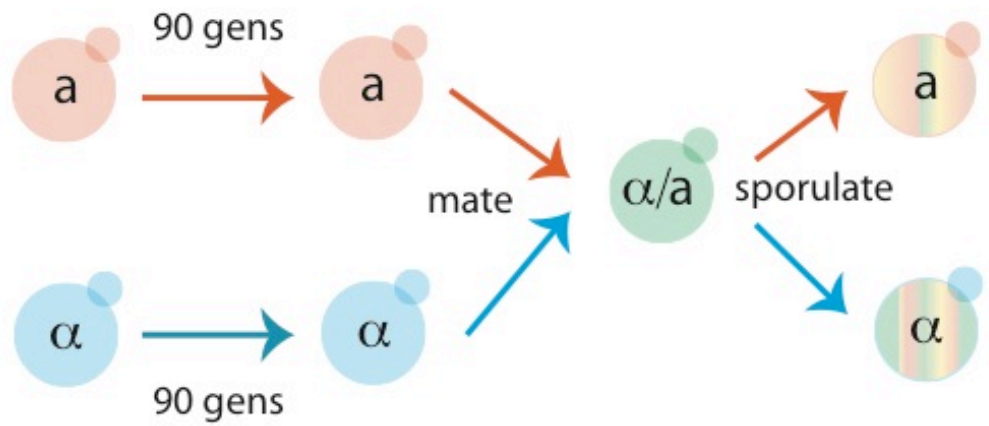

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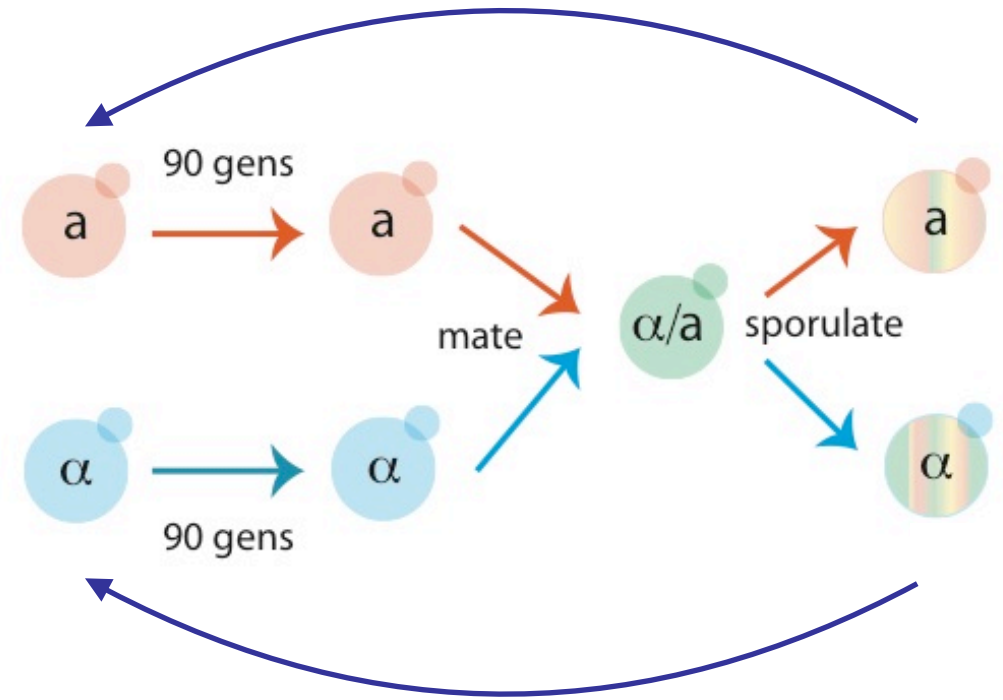
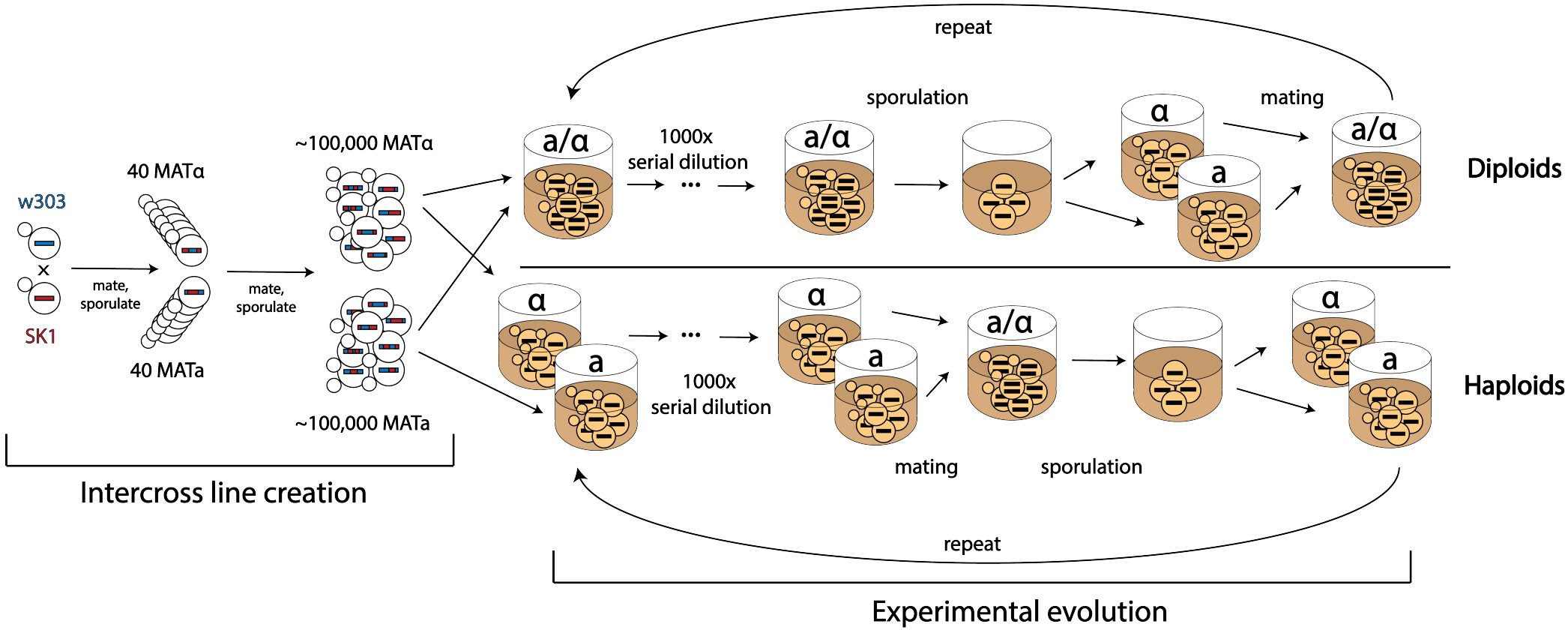
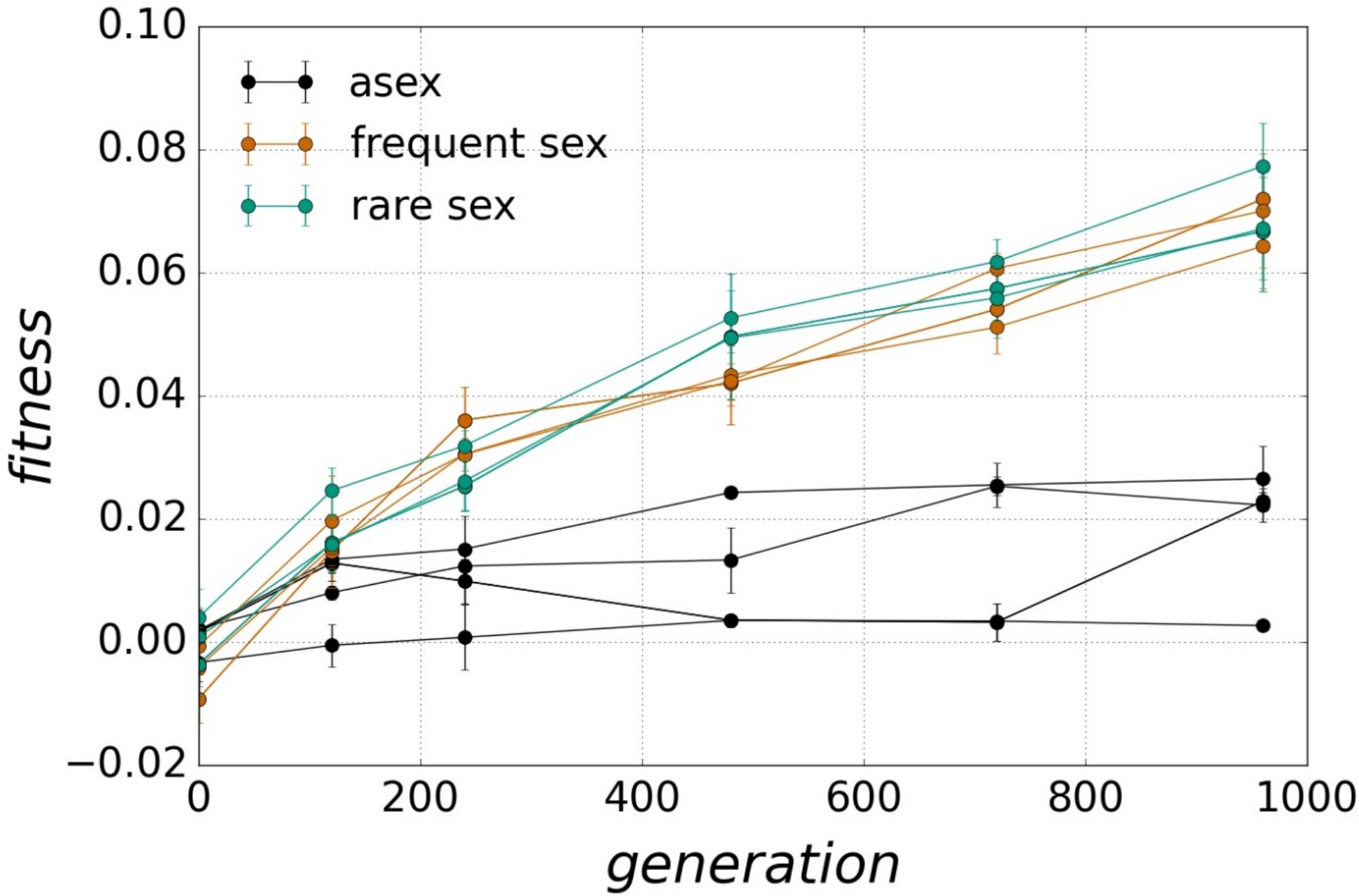


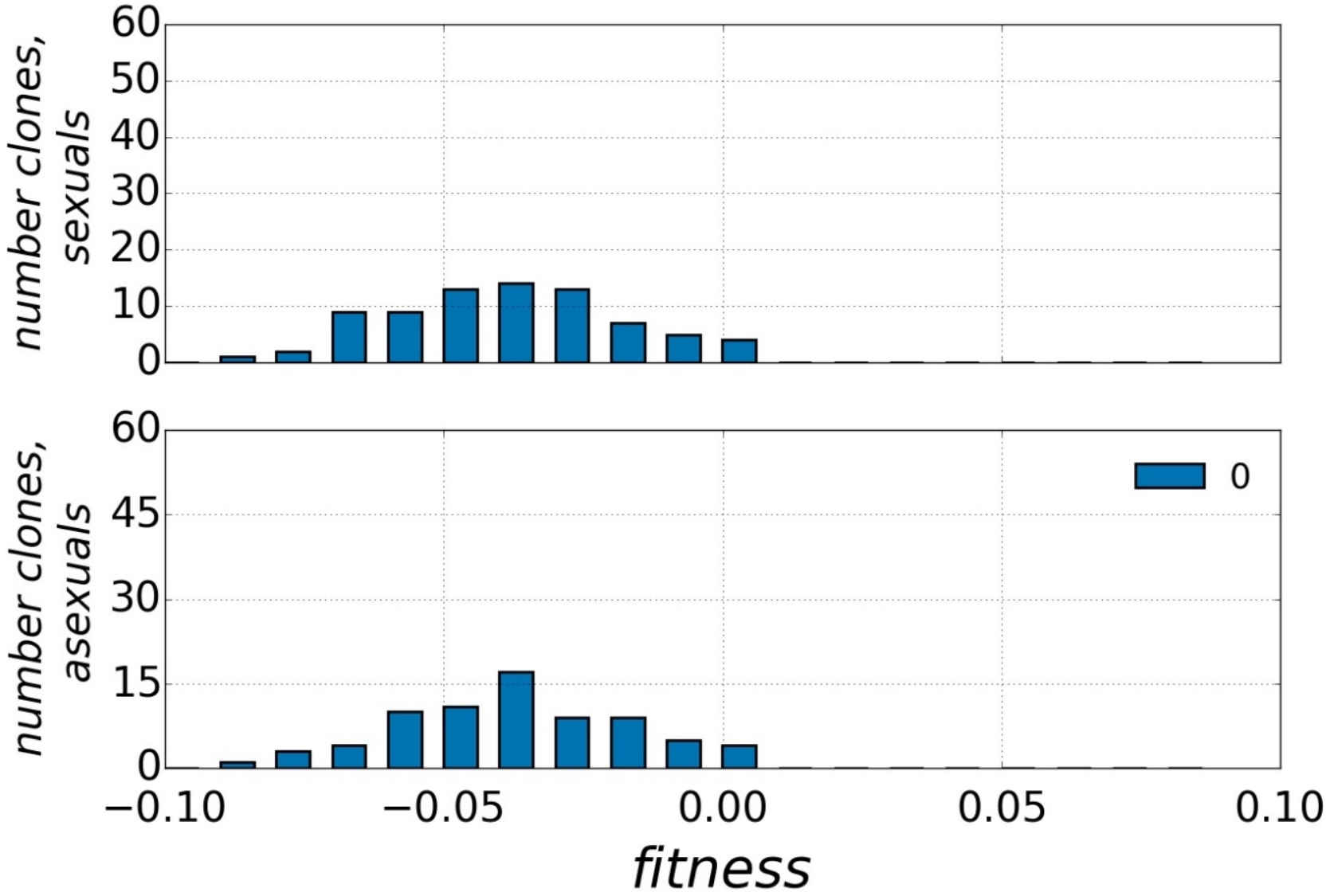
Evolution on Standing Variation in Budding Yeast



Sexual Populations Continue Adapting



Sex Maintains Fitness Variation



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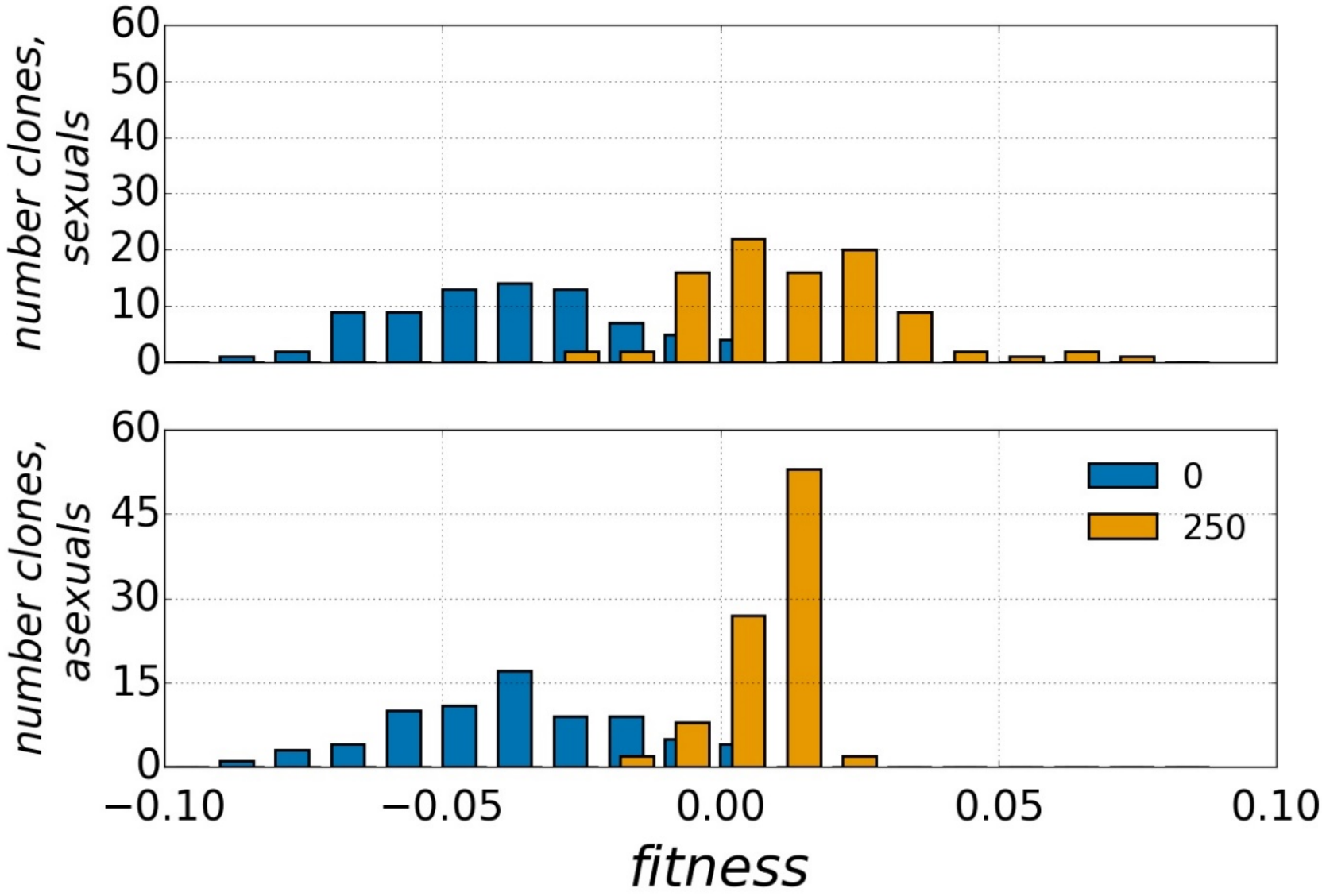

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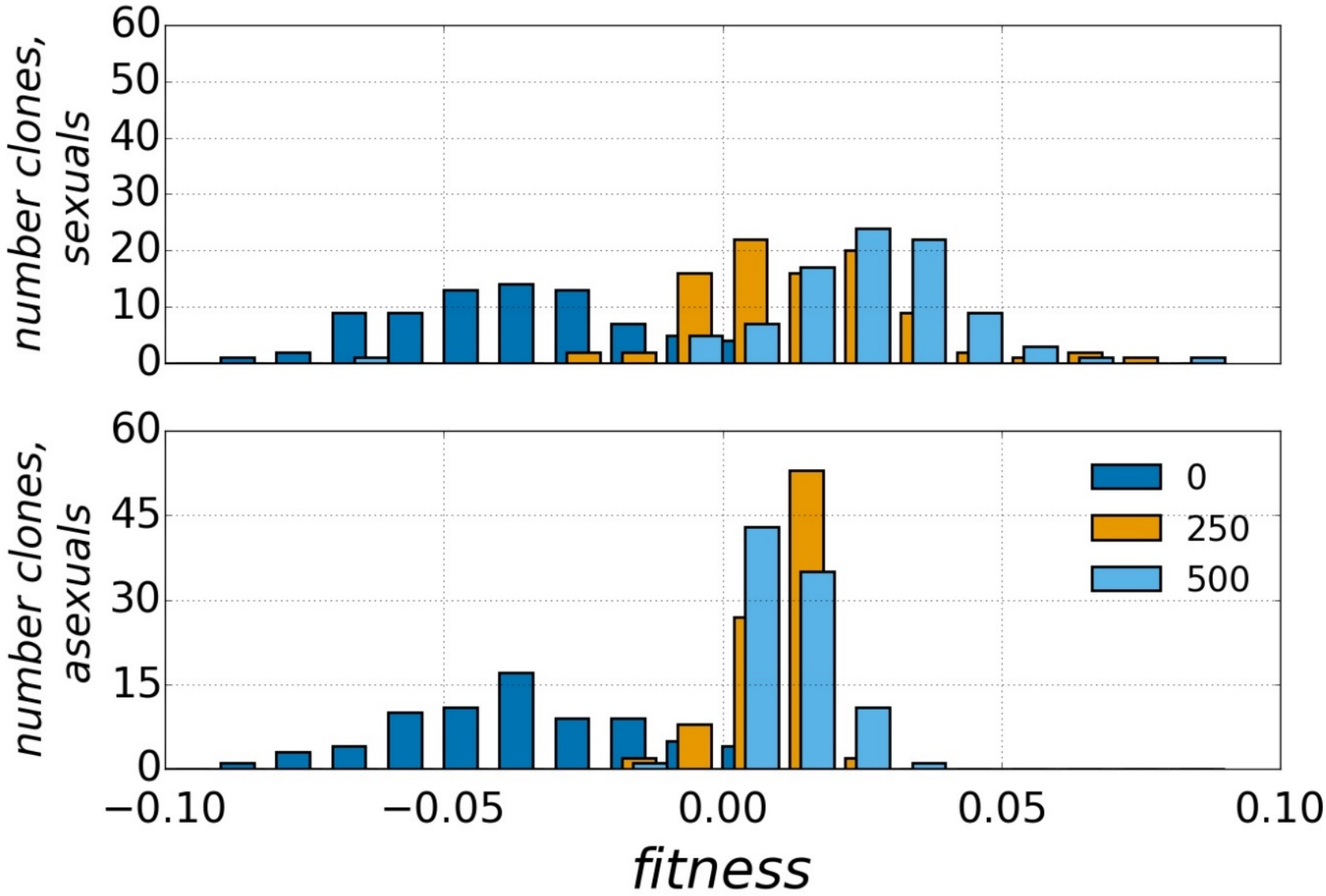

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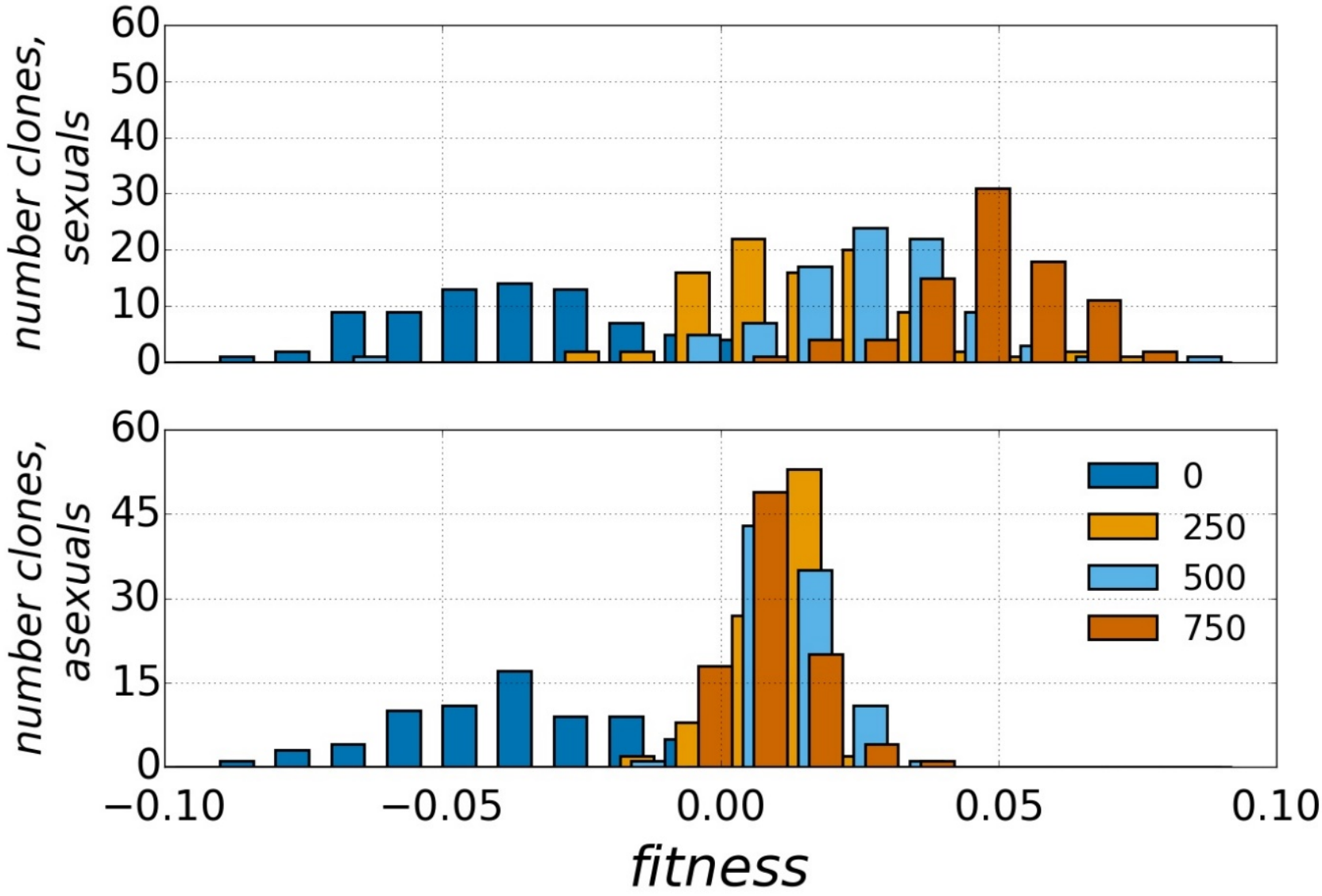
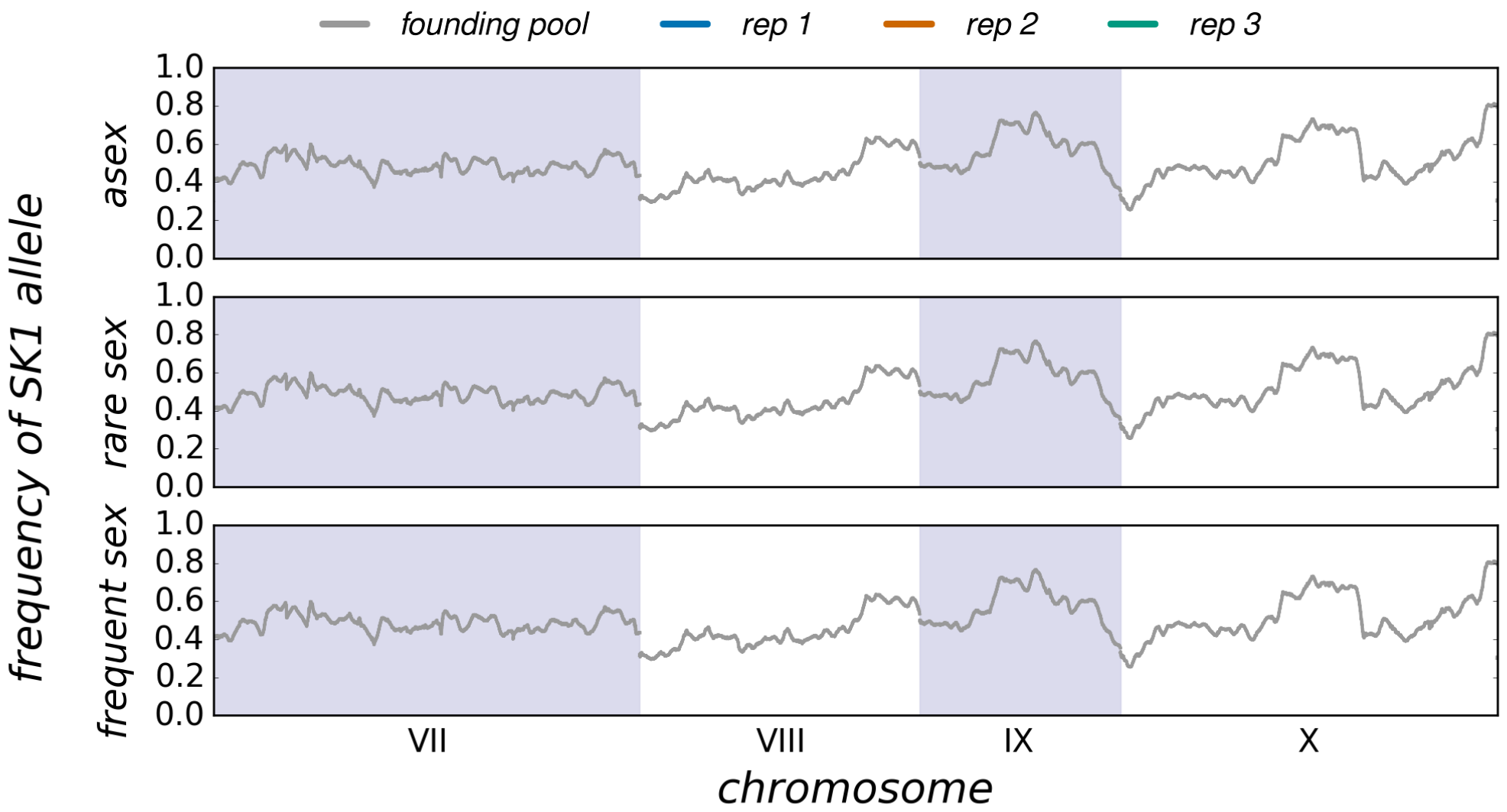


Evolution More Repeatable in Sexuals



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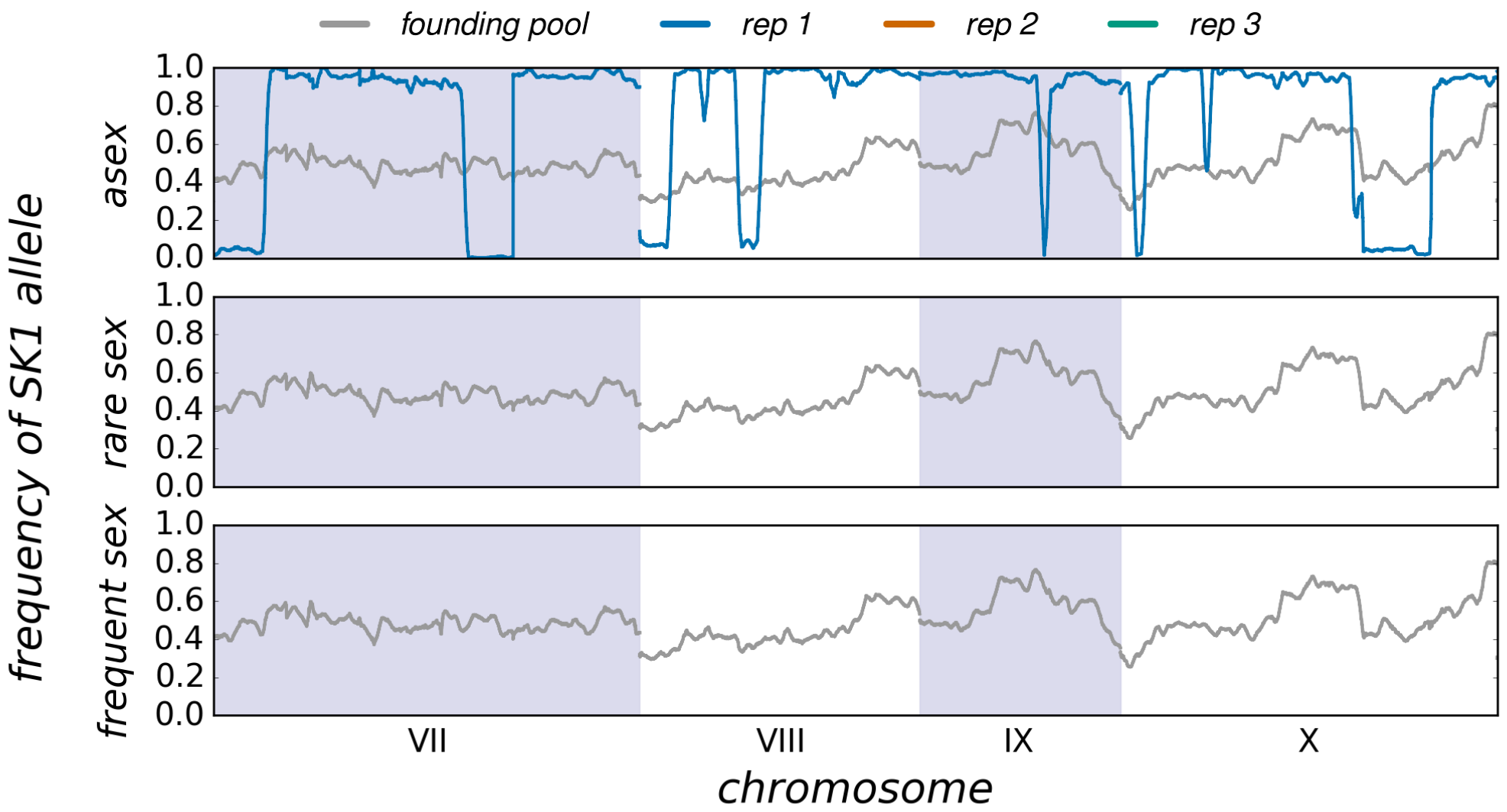

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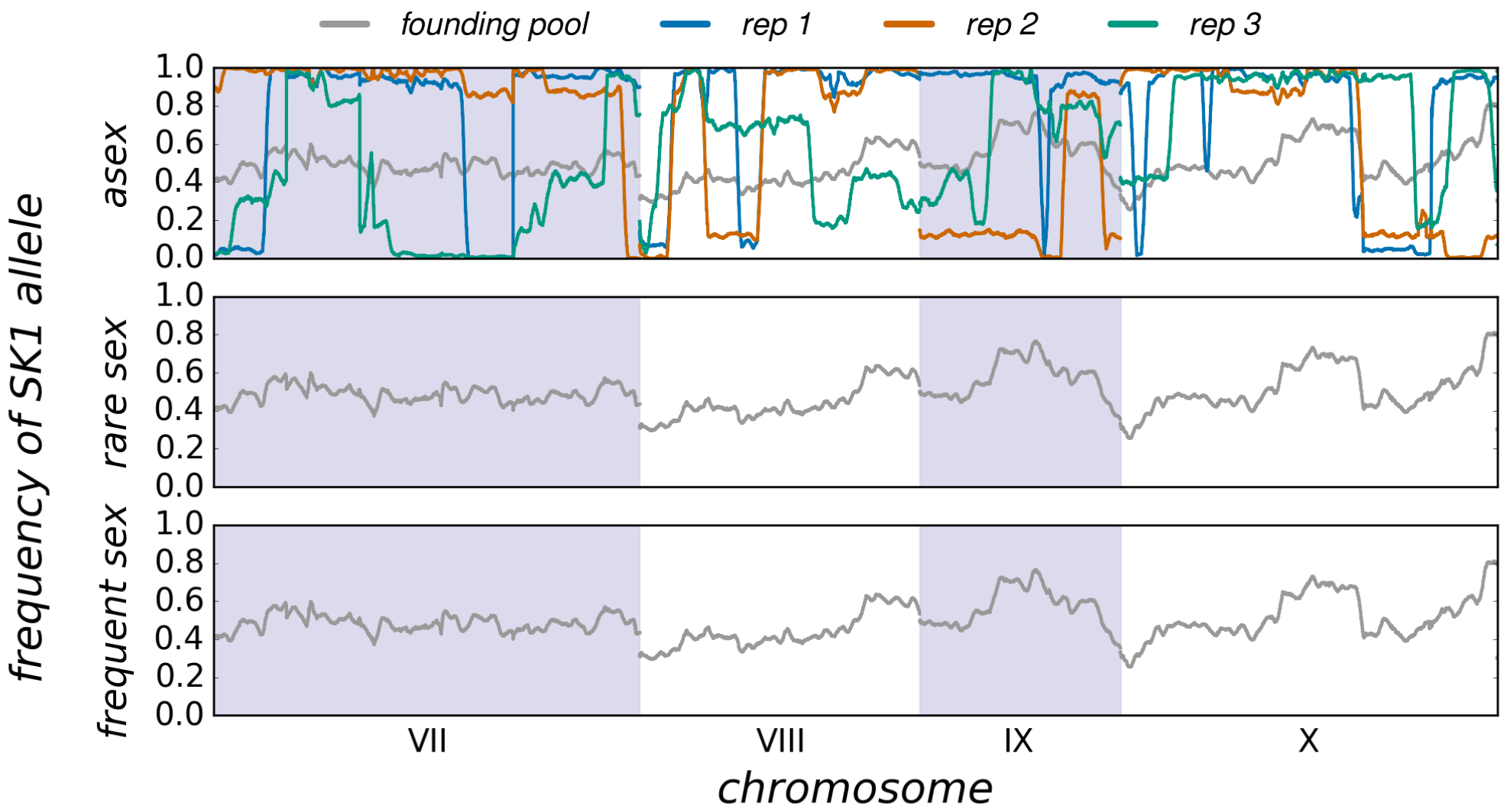

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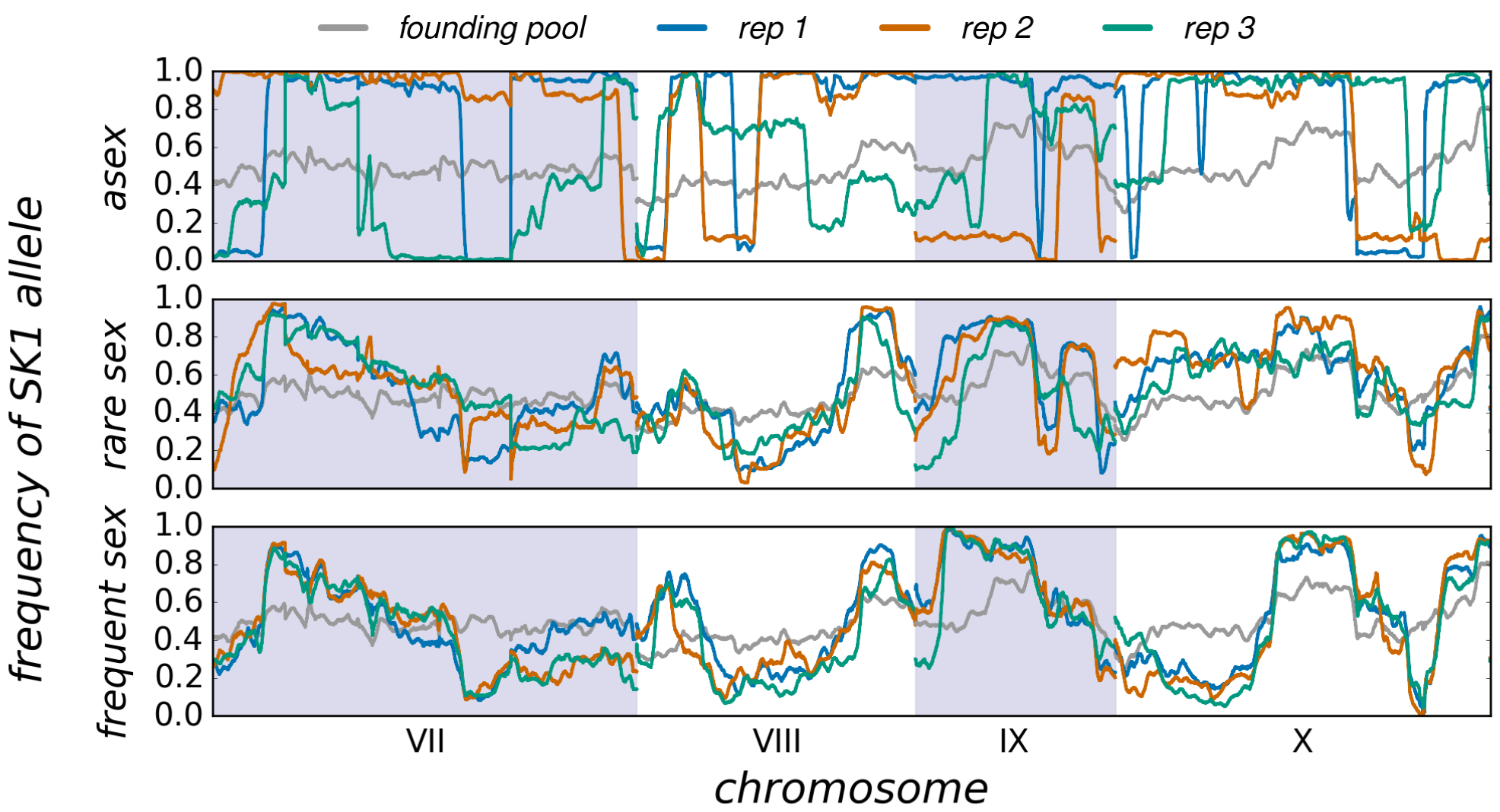

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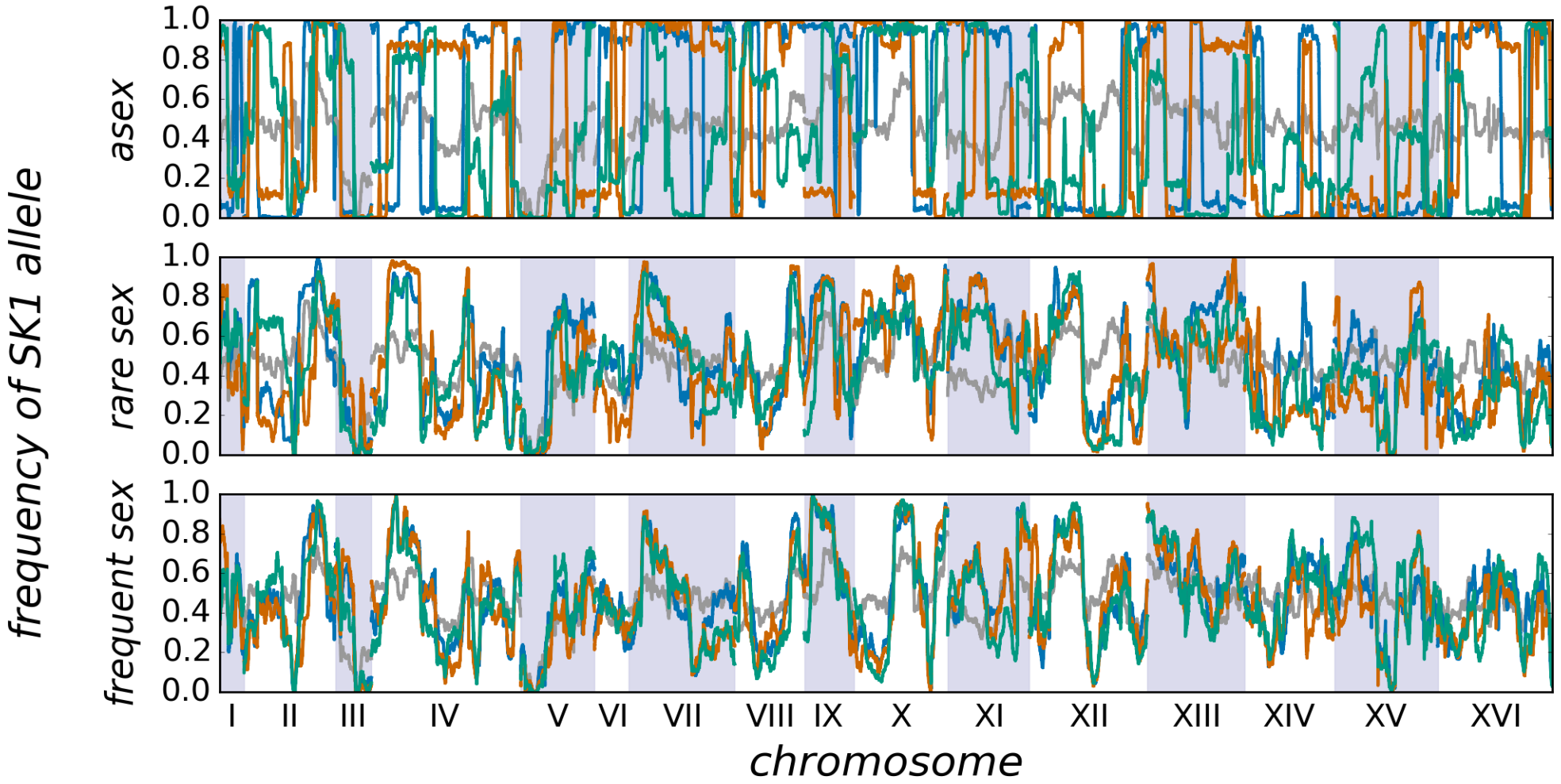
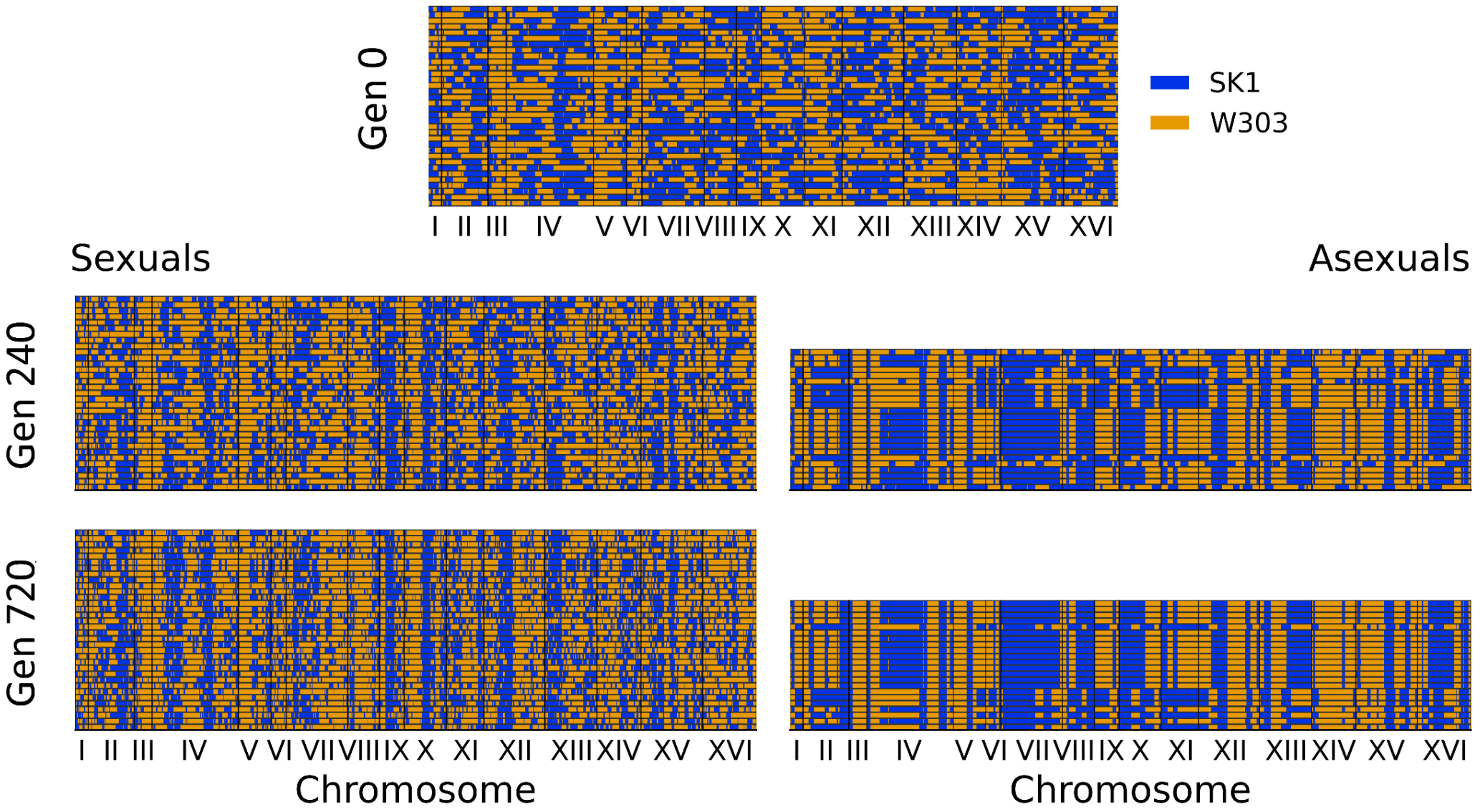
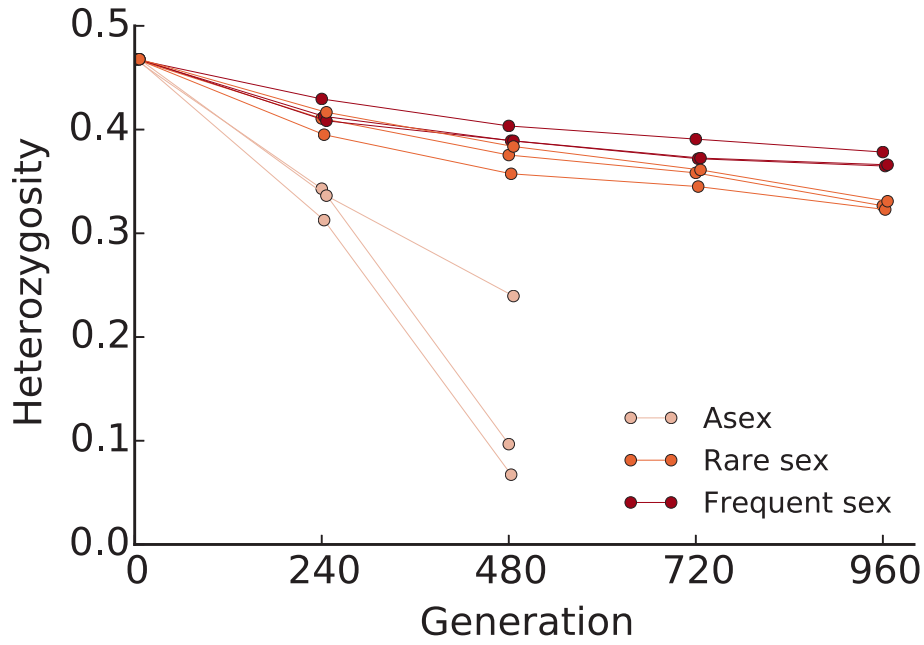


Selection on Alleles Versus on Genotypes



Intrapopulation versus Interpopulation Variation



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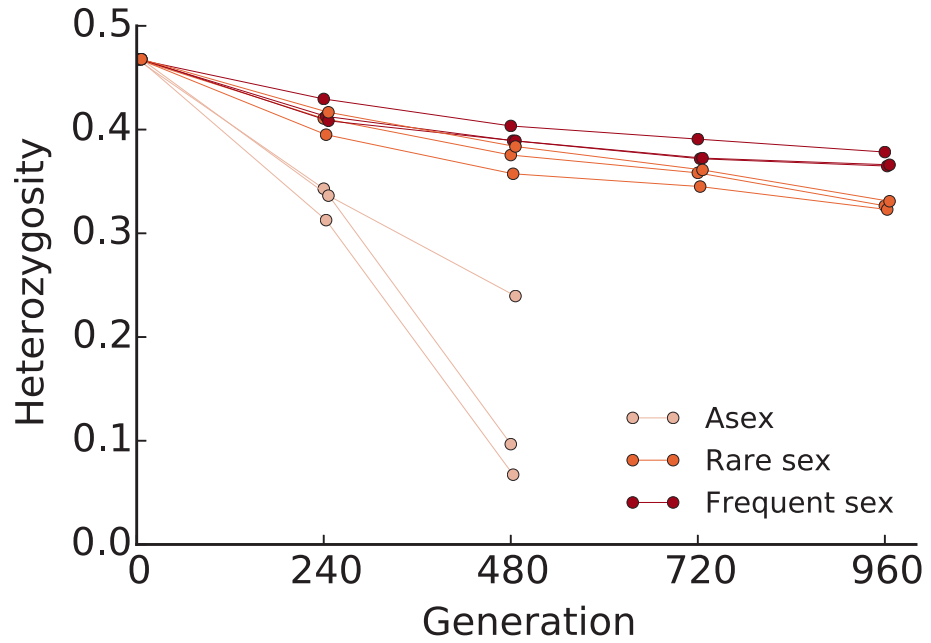

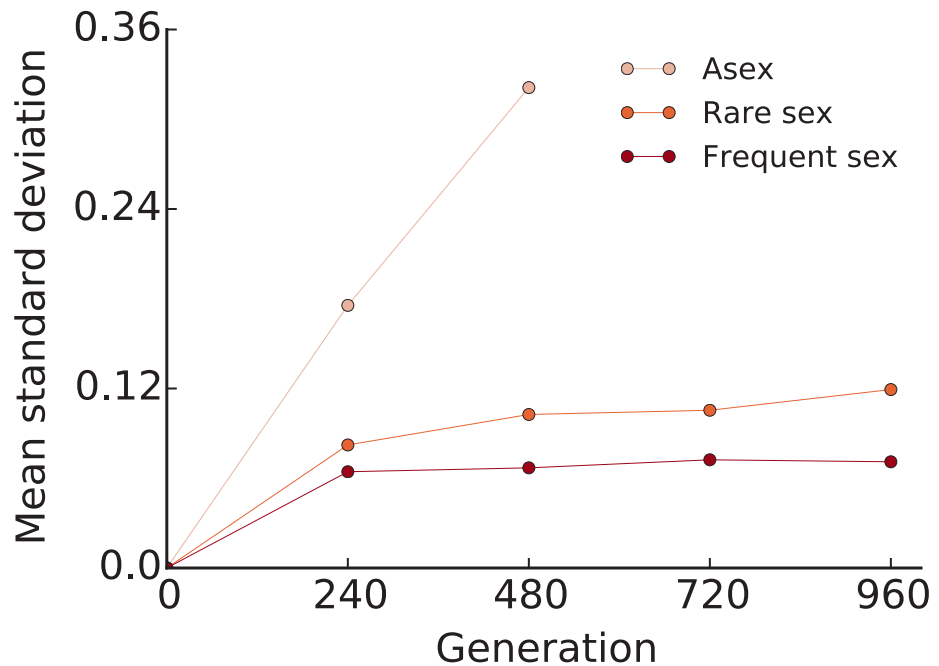

Allele Frequency Changes Stagnate Over Time

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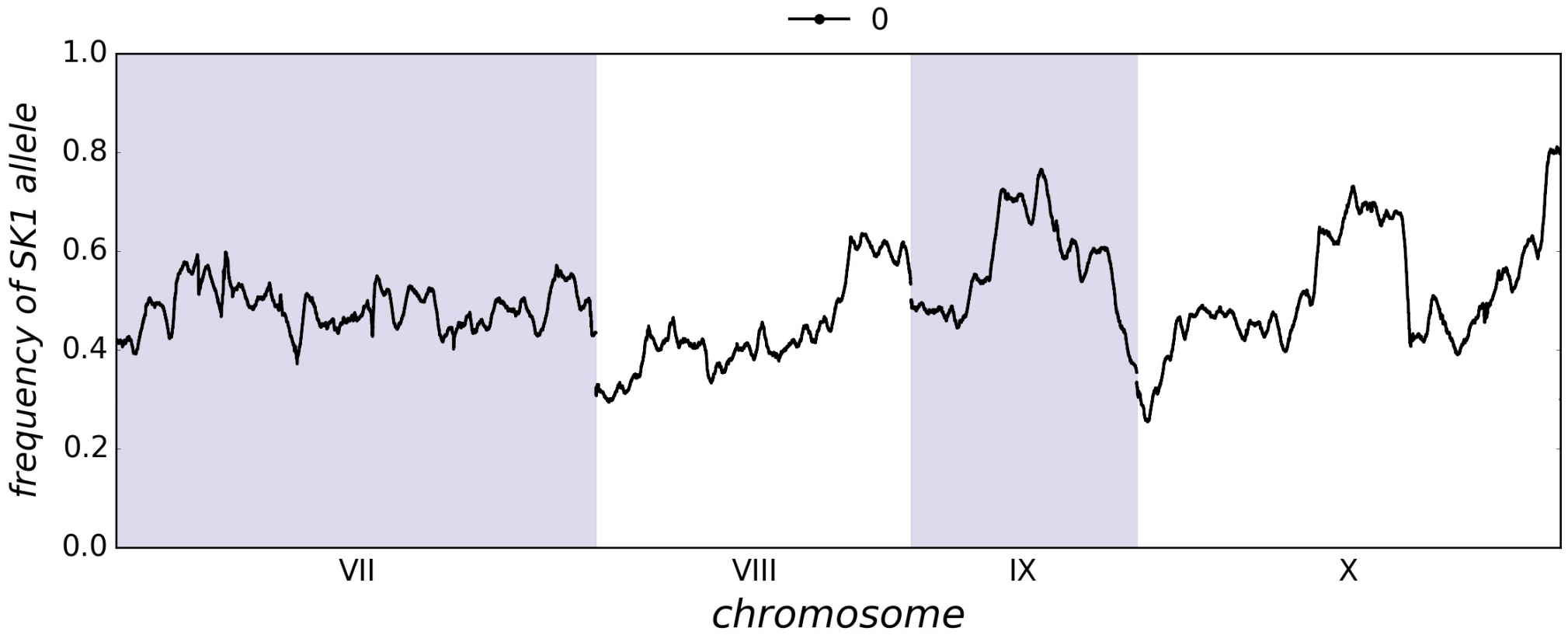

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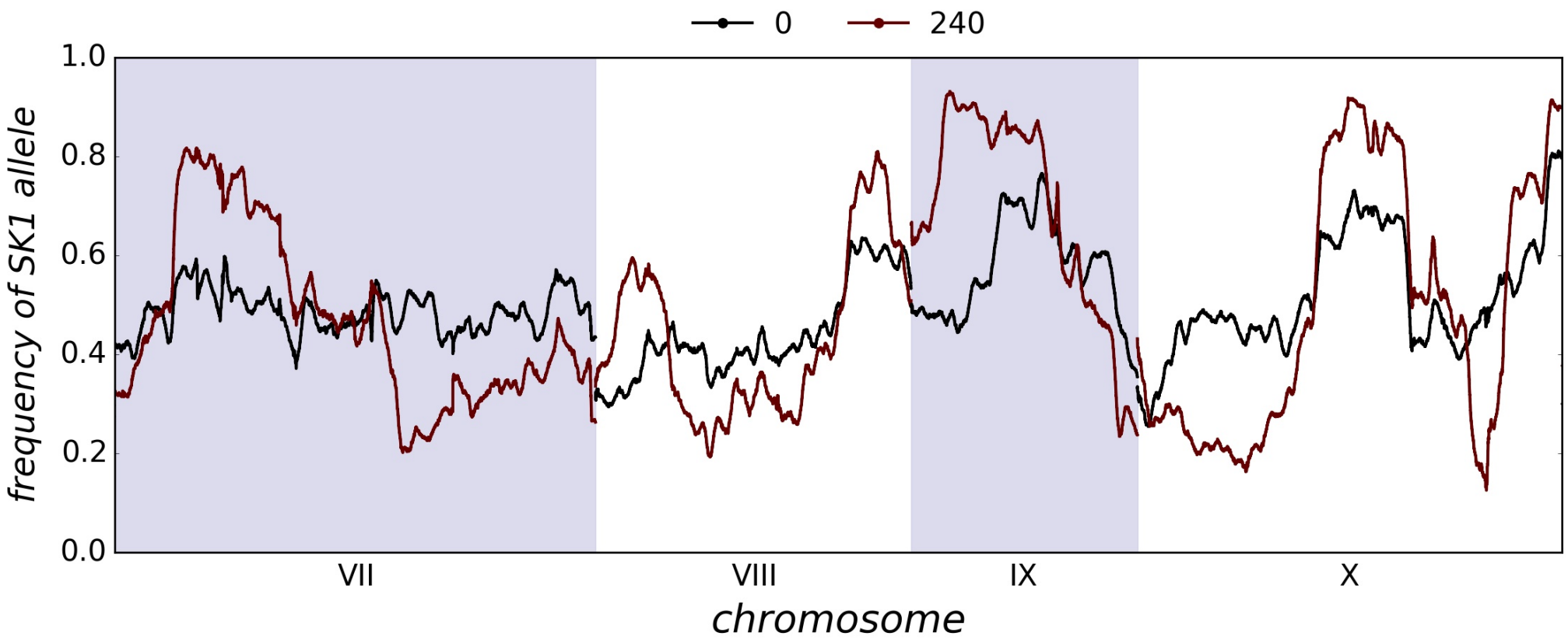

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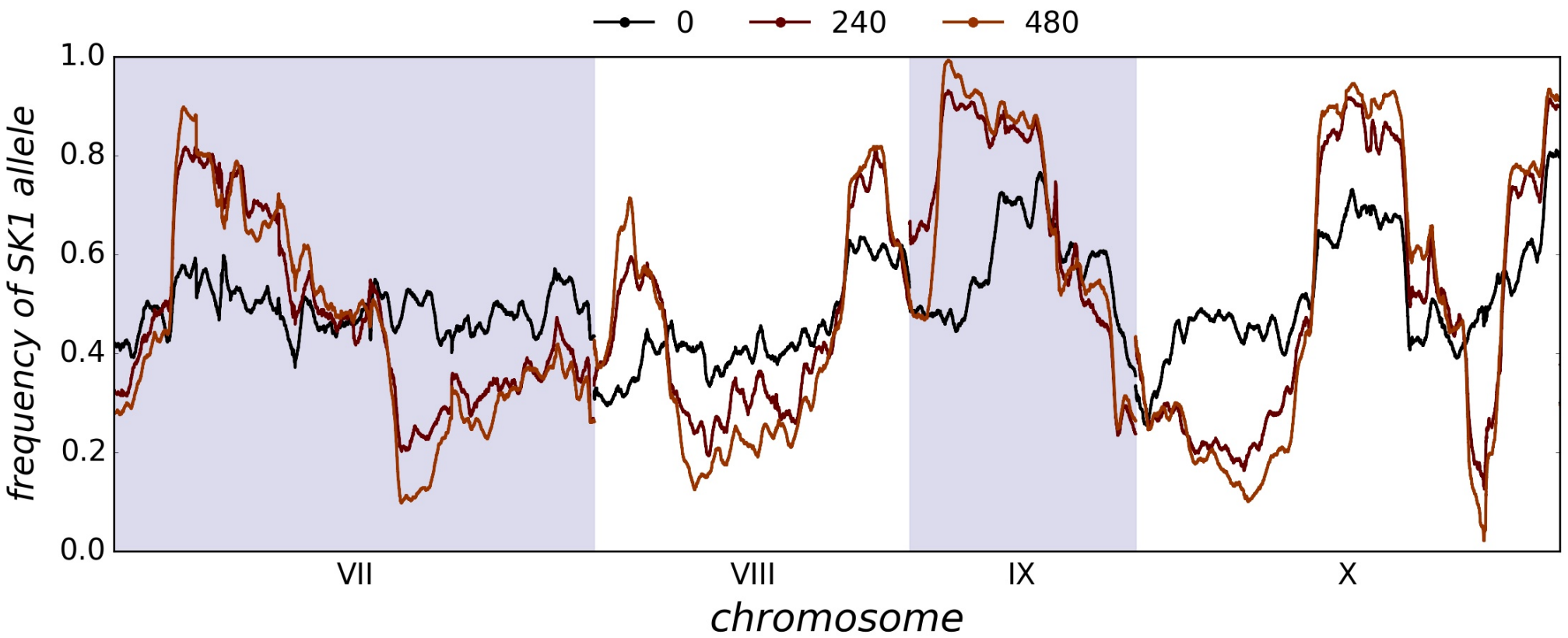

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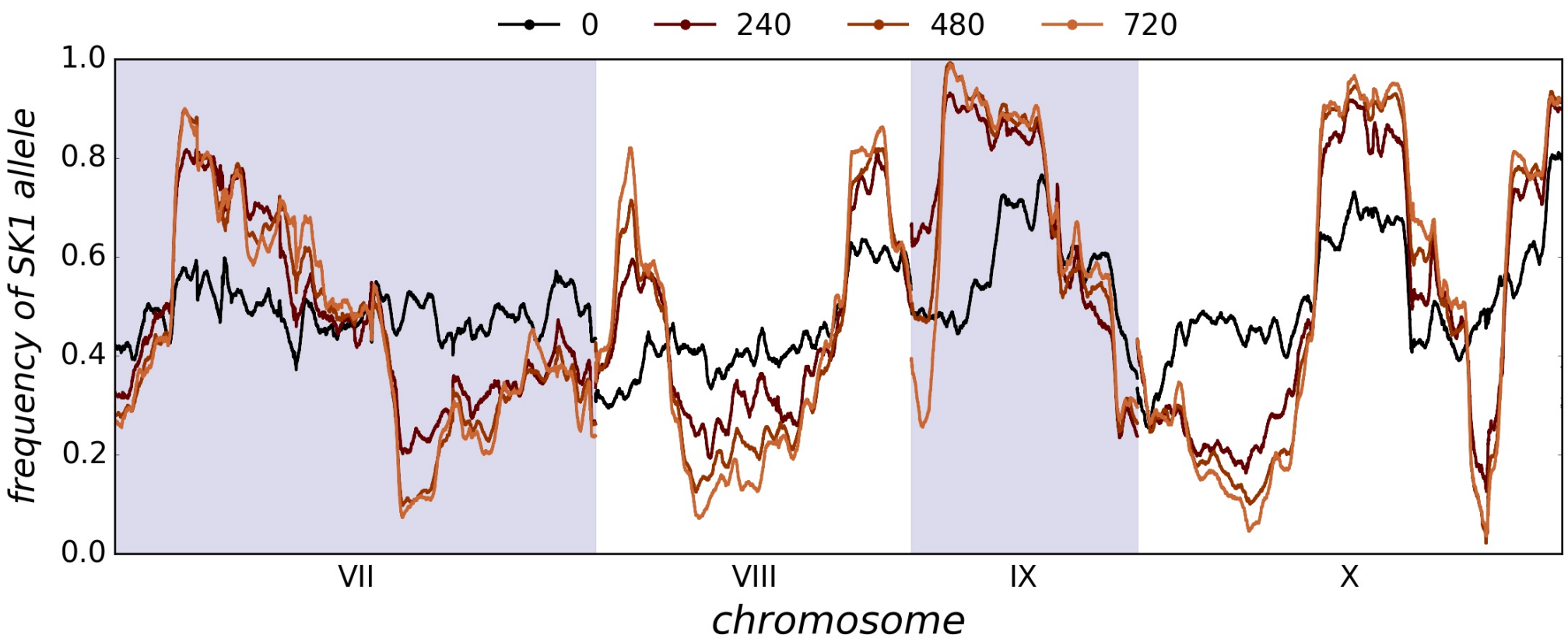

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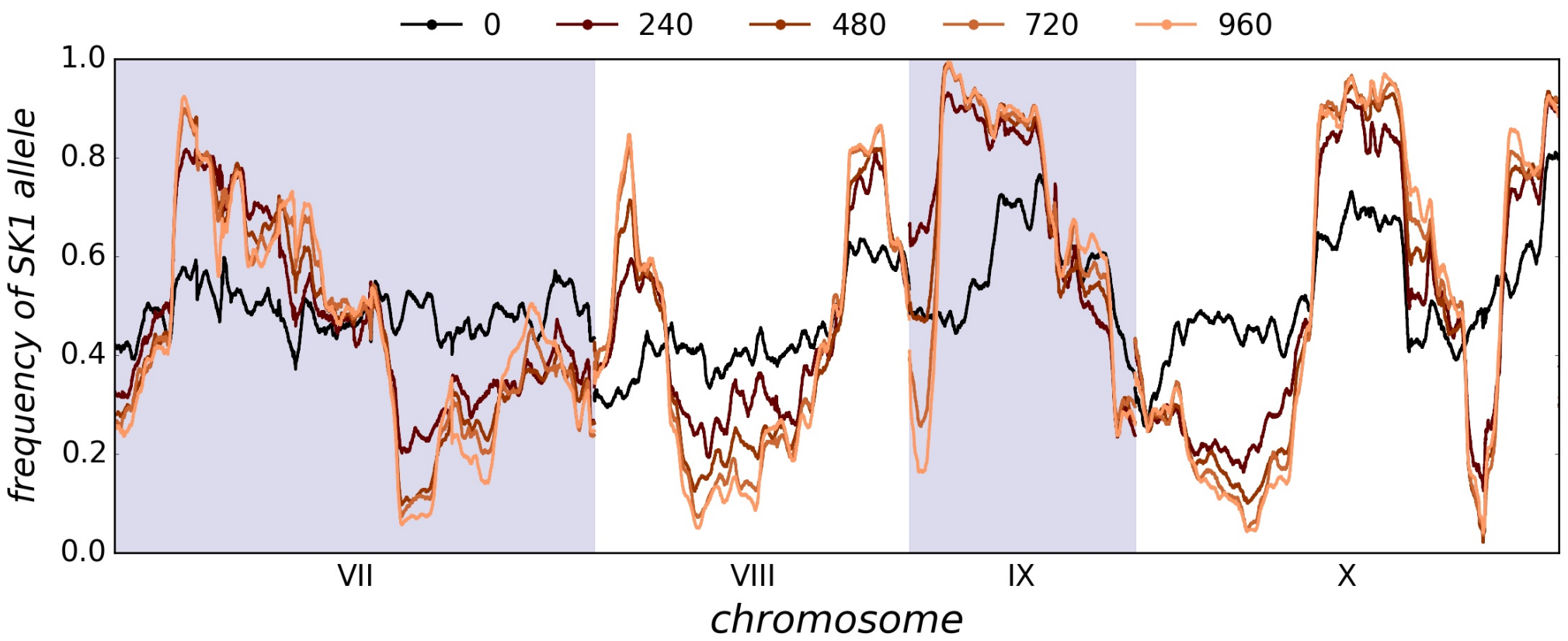

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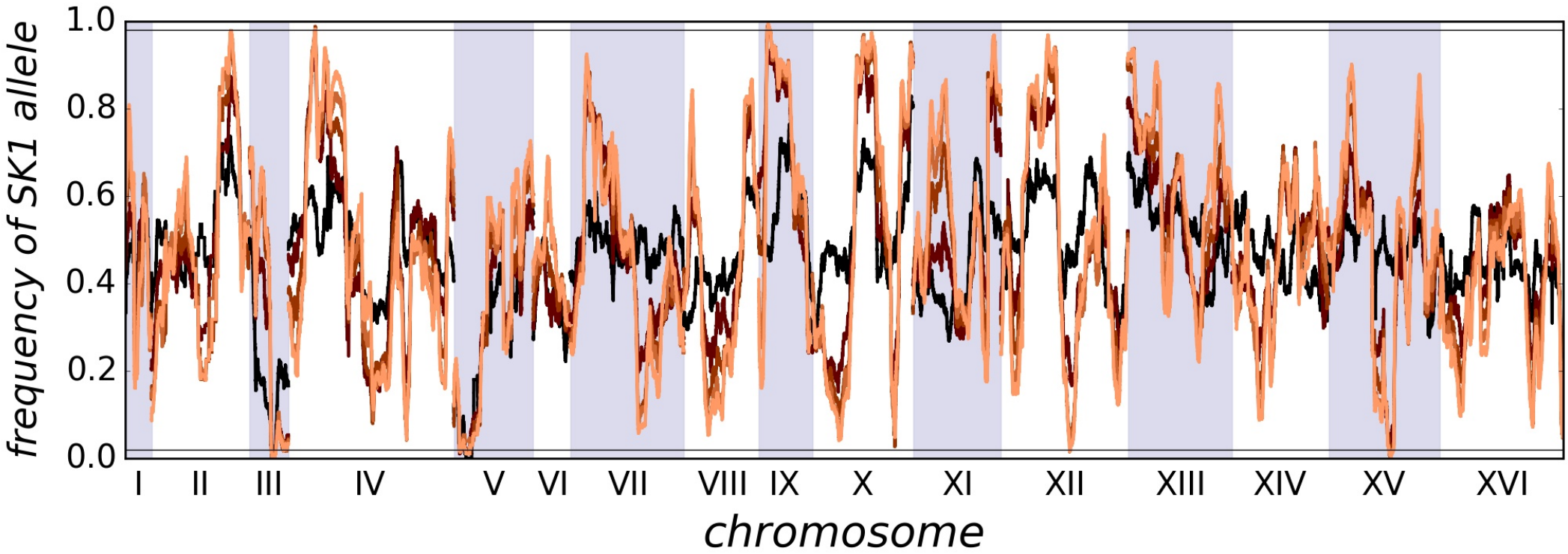

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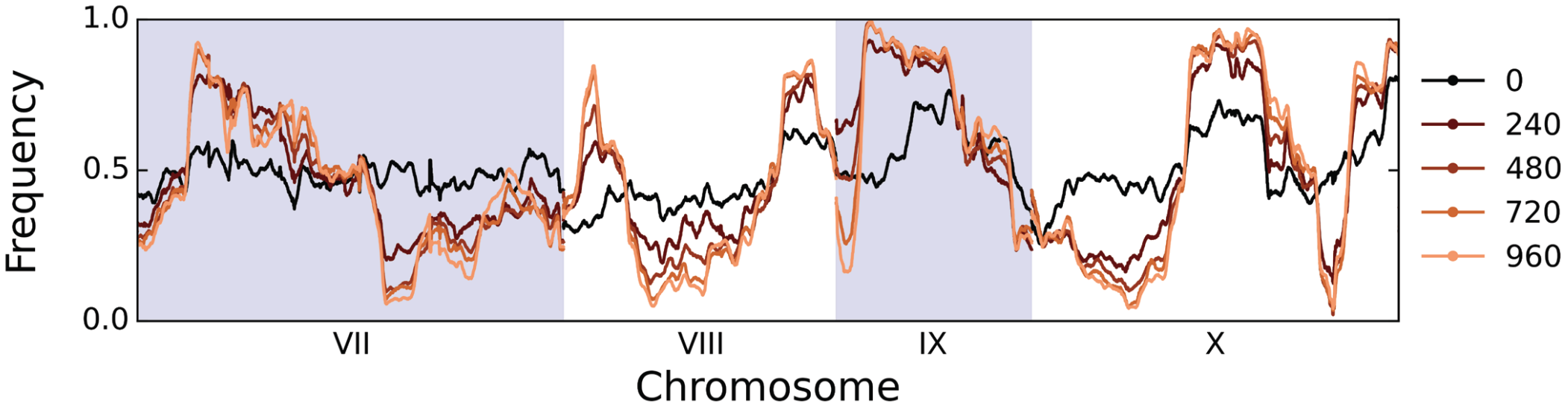

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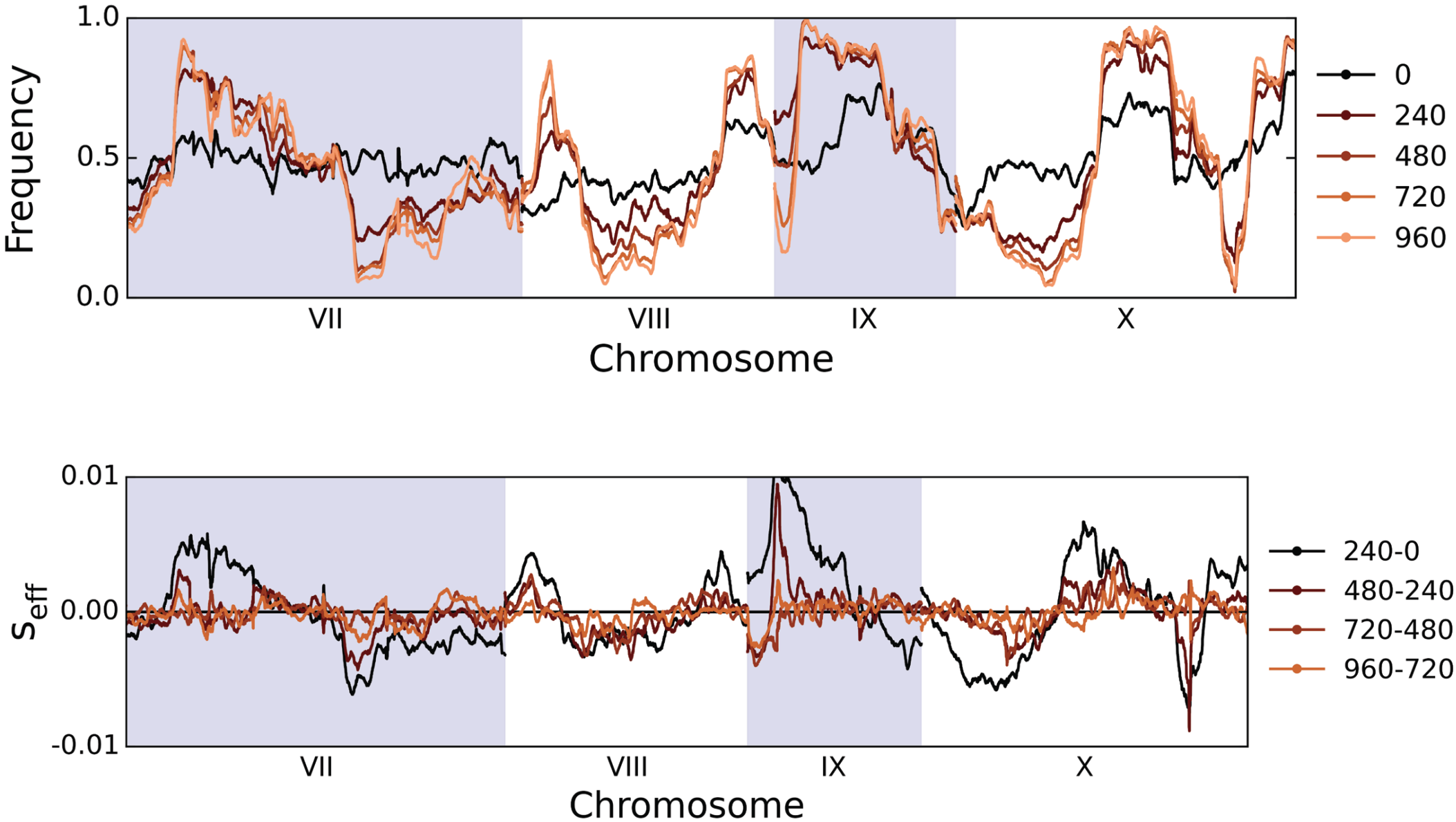
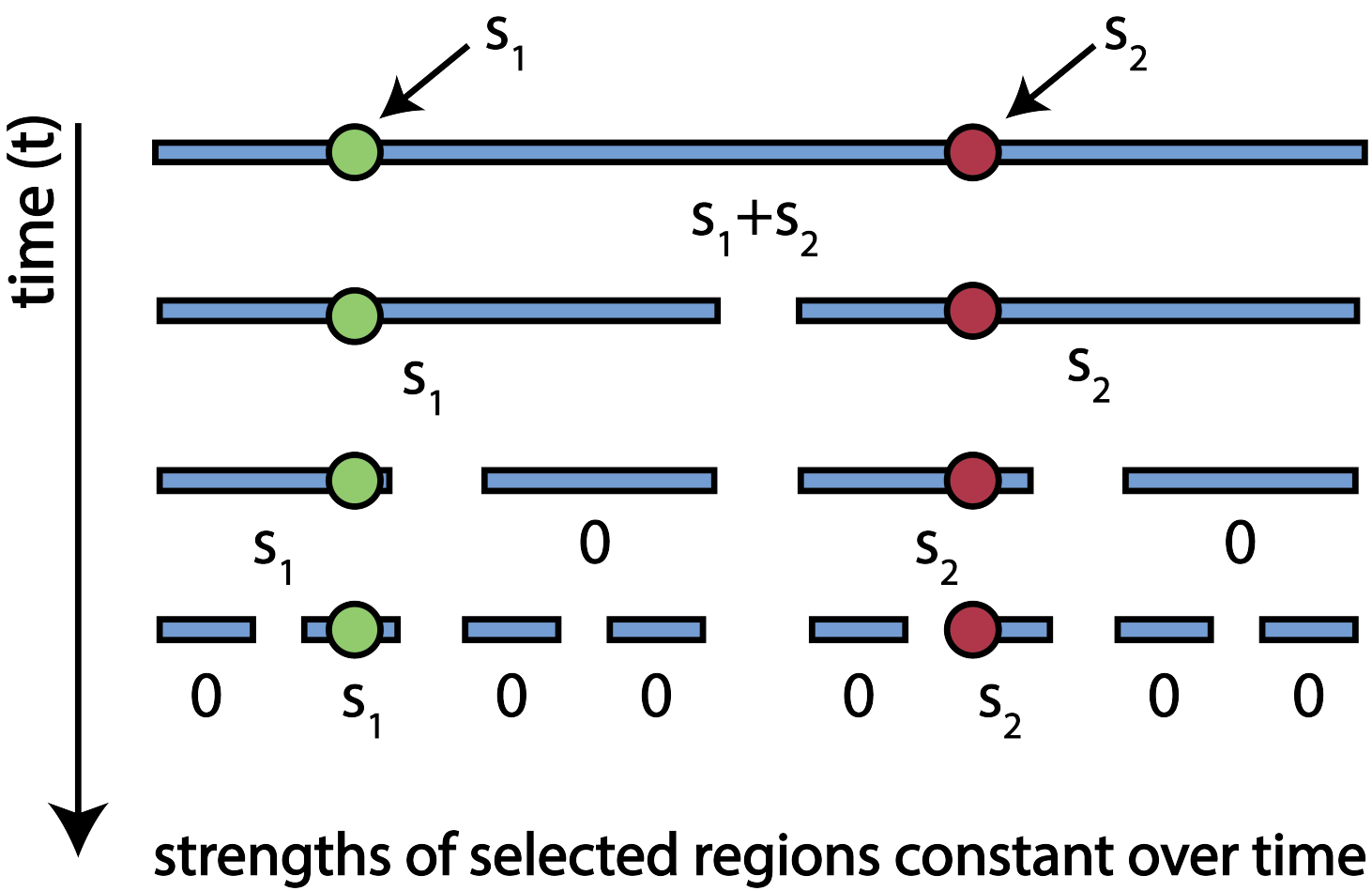
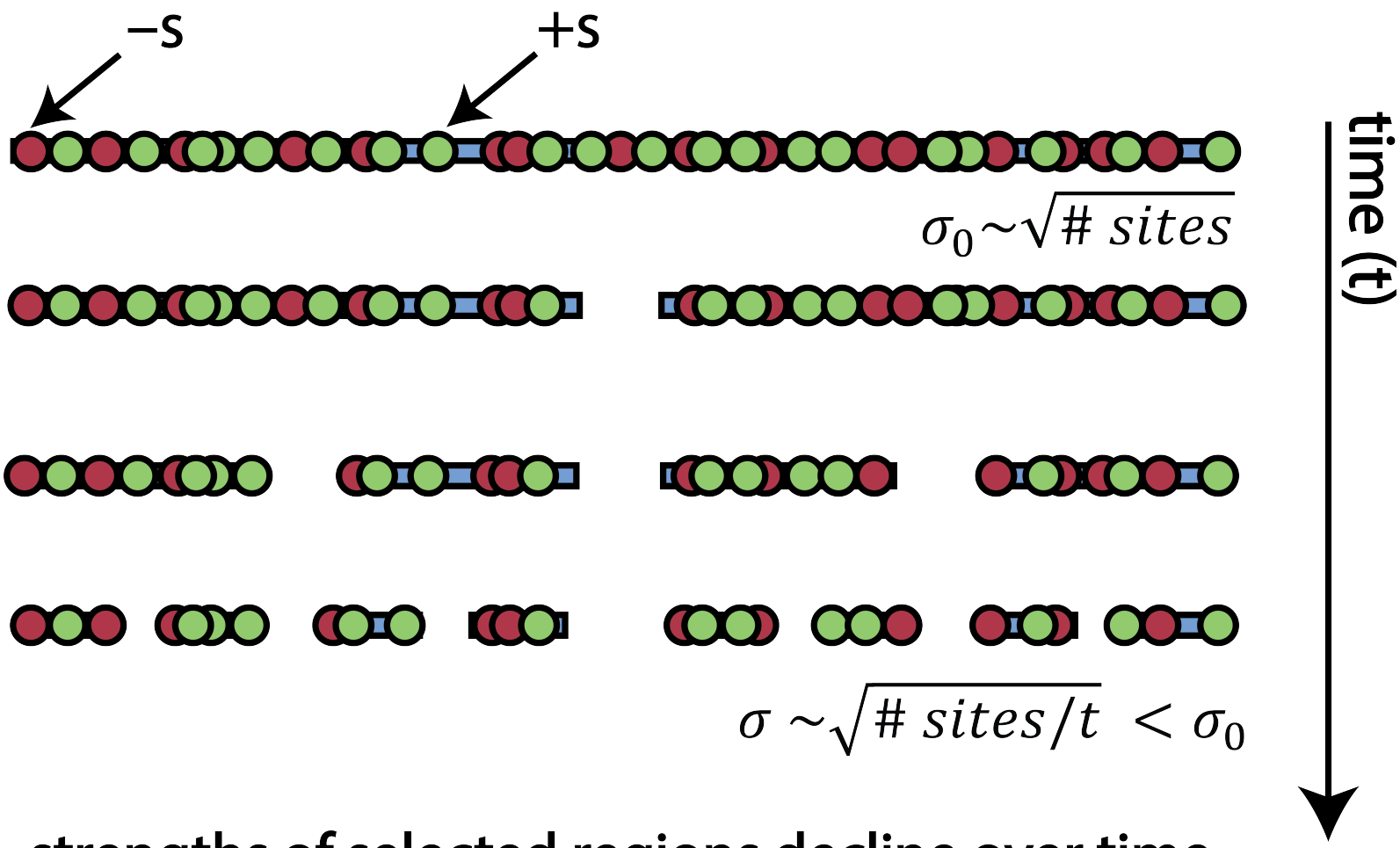


A Few Strongly Selected Loci

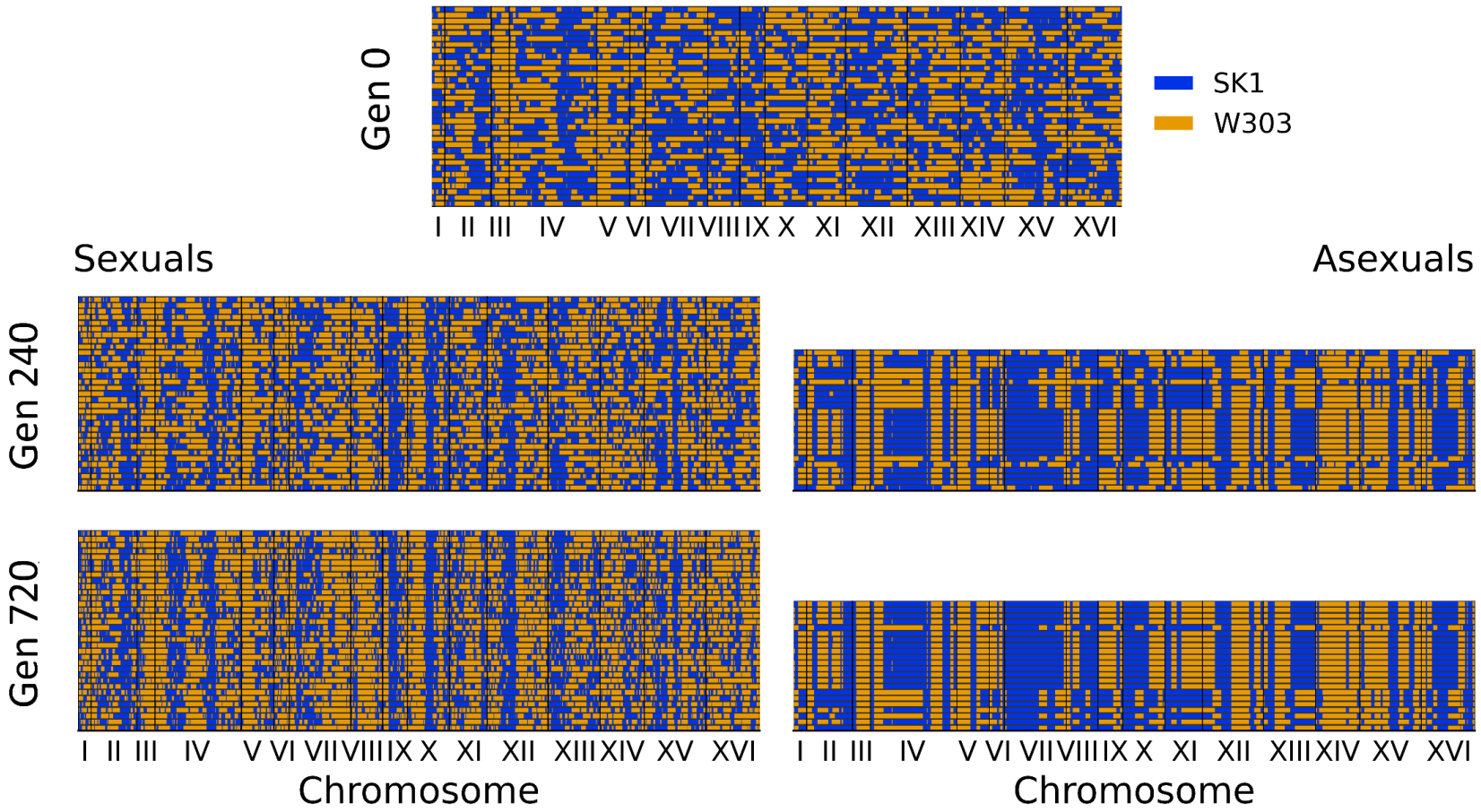


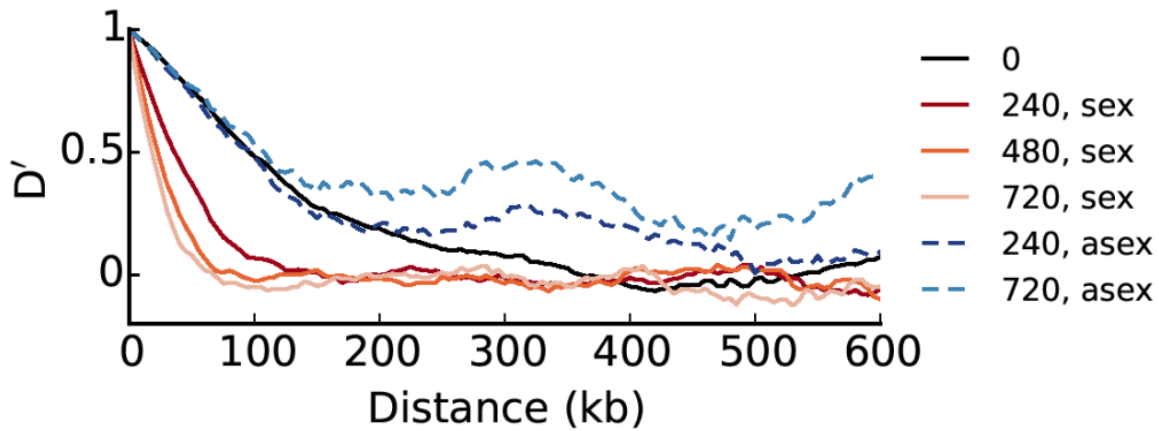
Dense, Weak Linked Selection



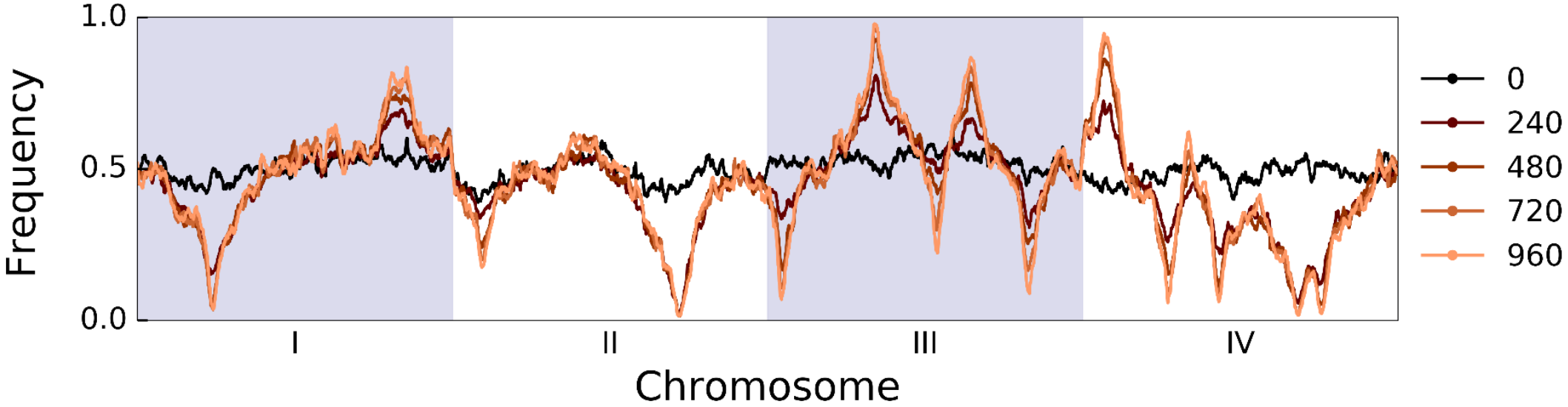
strengths of selected regions decline over time

More “Refined” Selection in Sexuals Over Time?





Simulations Support Dense Weak Selection



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