Genetic redundancy fuels polygenic adaptation in *Drosophila*

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Adaptive traits

- Most molecularly characterized traits have simple genetic basis
  - pigmentation (Hoekstra 2006; Hof et al. 2016, Jones et al. 2018)
  - lactose persistence (Tishkoff et al. 2007)
  - resistance to
    - viruses (Magwire et al. 2012)
    - insecticides (Daborn et al. 2002)
    - malaria (Hamblin and Di Rienzo 2000)

https://www.lalpathlabs.com/blog/what-is-malaria-fever/

https://catherinephamevolution.weebly.com/the-british-peppered-moth.html

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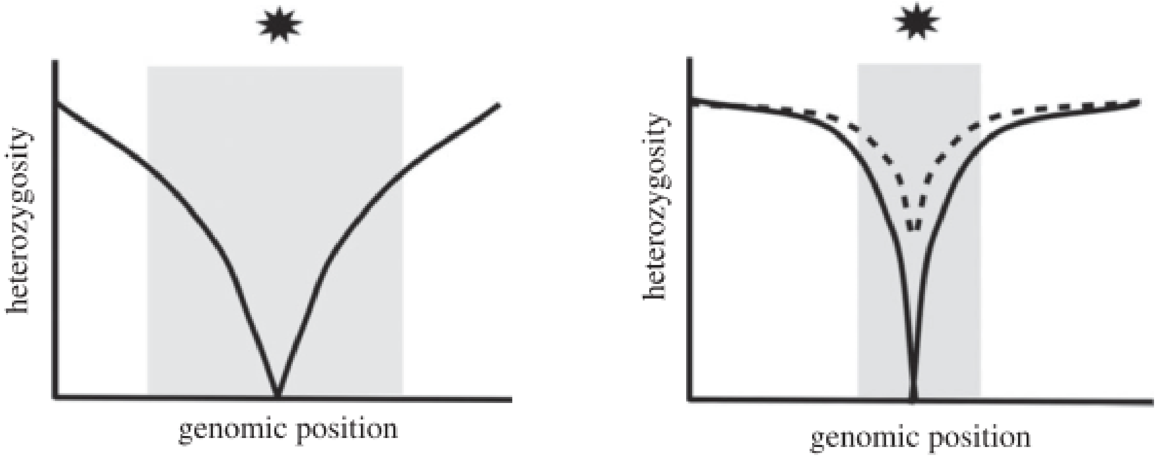
- Selective sweep



Burke 2012

Adaptive traits

- Most adaptive traits are polygenic
- Prediction: small allele frequency changes across many contributing loci

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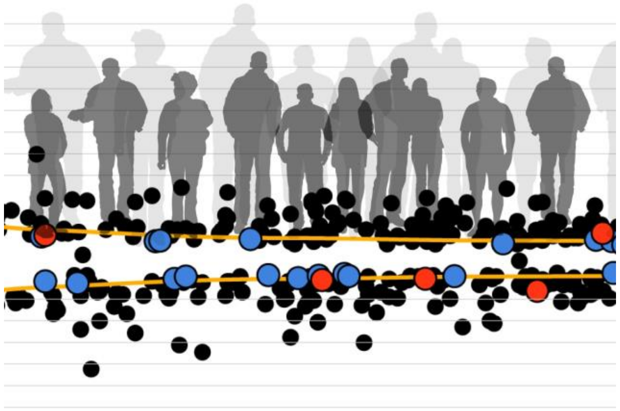
  - Artificial selection experiments and QTL studies in *Drosophila* (Yoo 1980; Weber 1996; Gilligan and Frankham 2003)

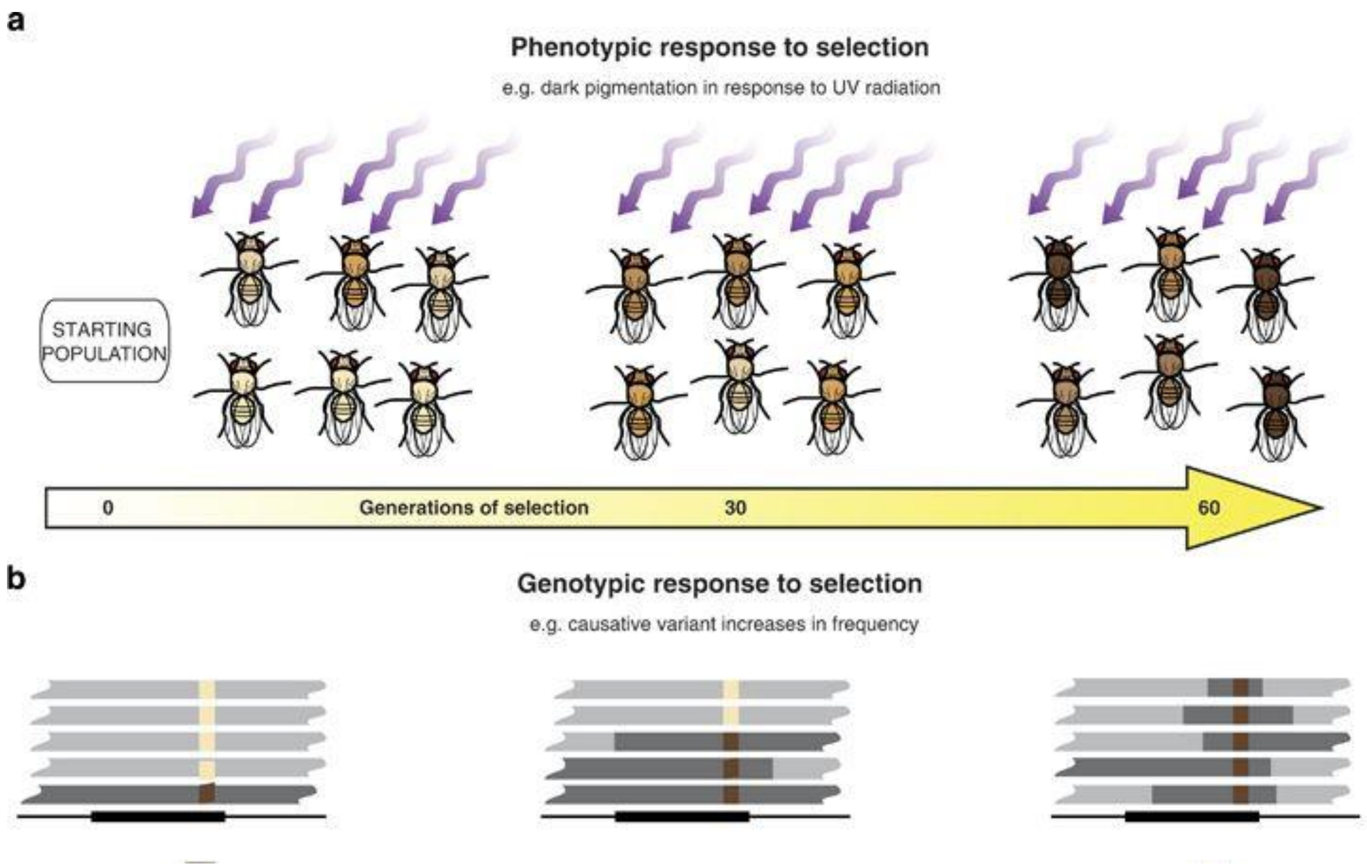
  - Human height (Yang et al. 2010; Wood et al. 2014)
  - blood lipid levels (Willer and Mohlke 2013)
  - basal metabolic rate (Eijgelsheim et al. 2017)

https://www.yourgenome.org/stories/fruit-flies-in-the-laboratory



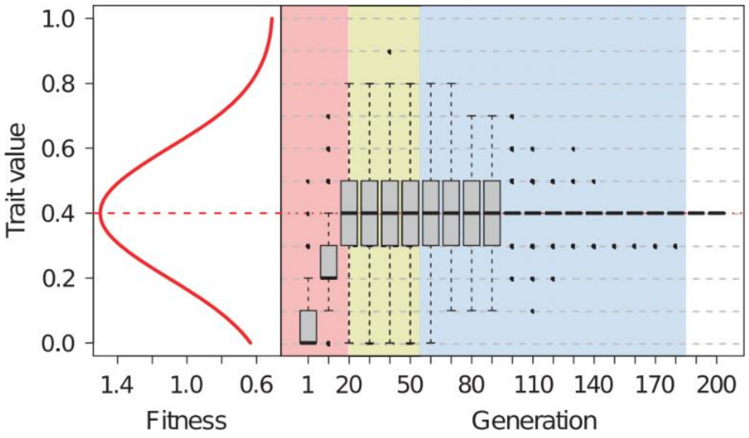
https://medicalxpress.com/news/2017-02-genes-height-revealed-global-people.html

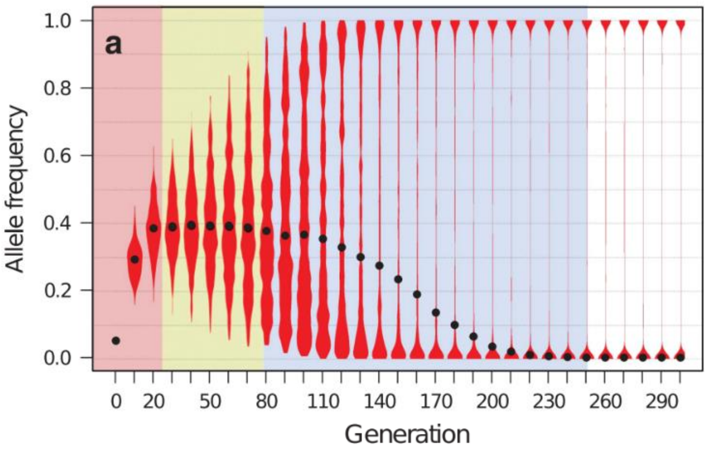
Experimental evolution



Franssen et al. 2015

Polygenic adaptation of a quantitative trait after a shift in trait optimum





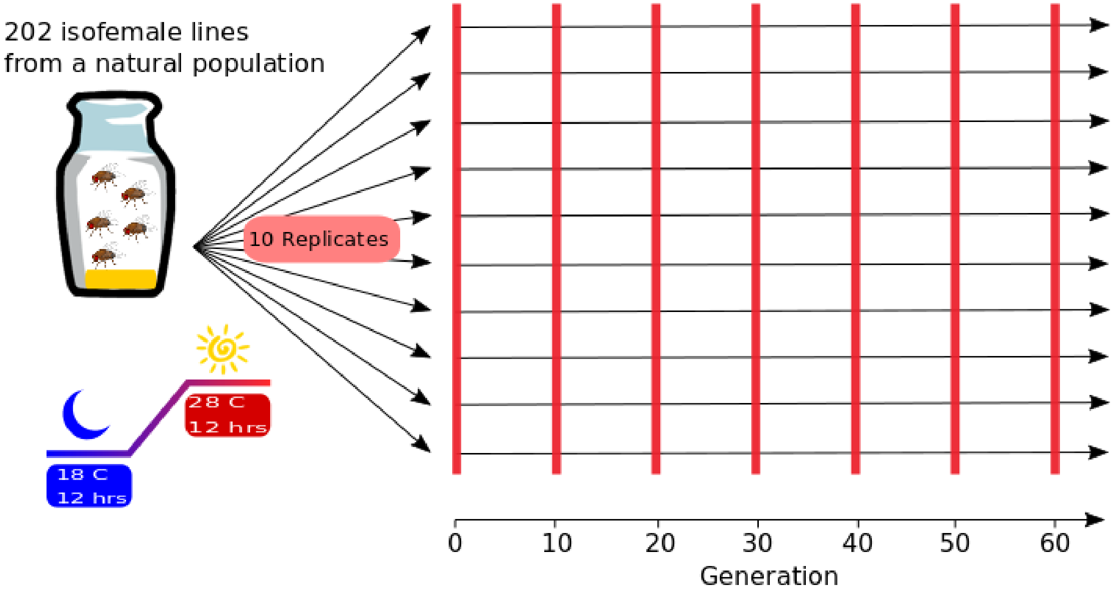
Franssen et al. 2017

Laboratory natural selection to a new temperature regime

https://gcocs.org/map-of-florida-gulf-coast-beaches/

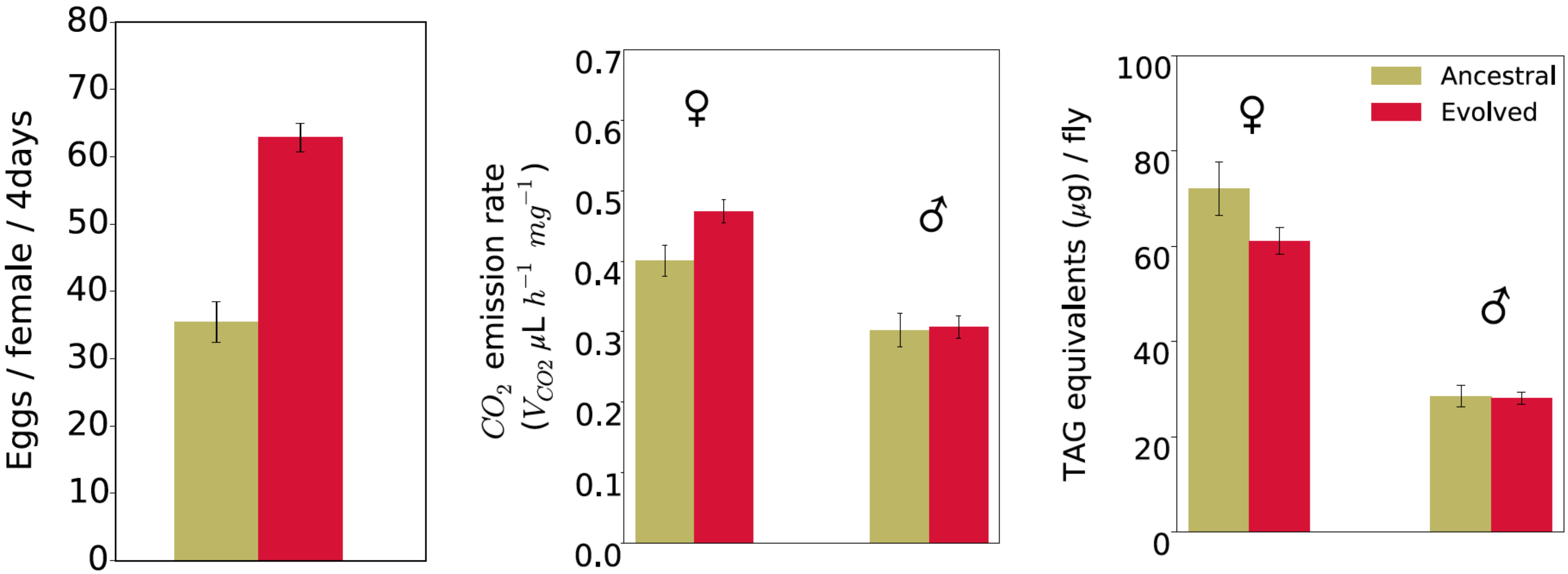
Tallahassee, Florida, USA

Pool-Seq

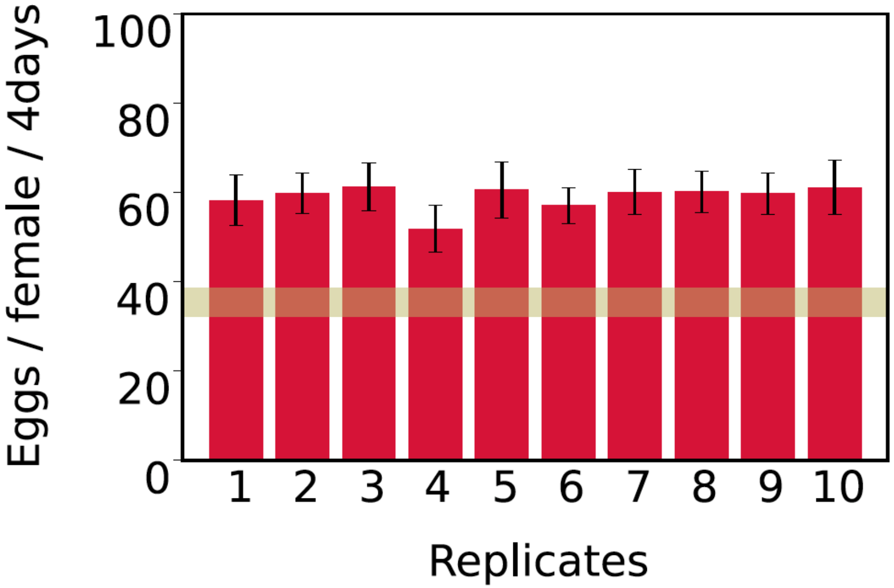


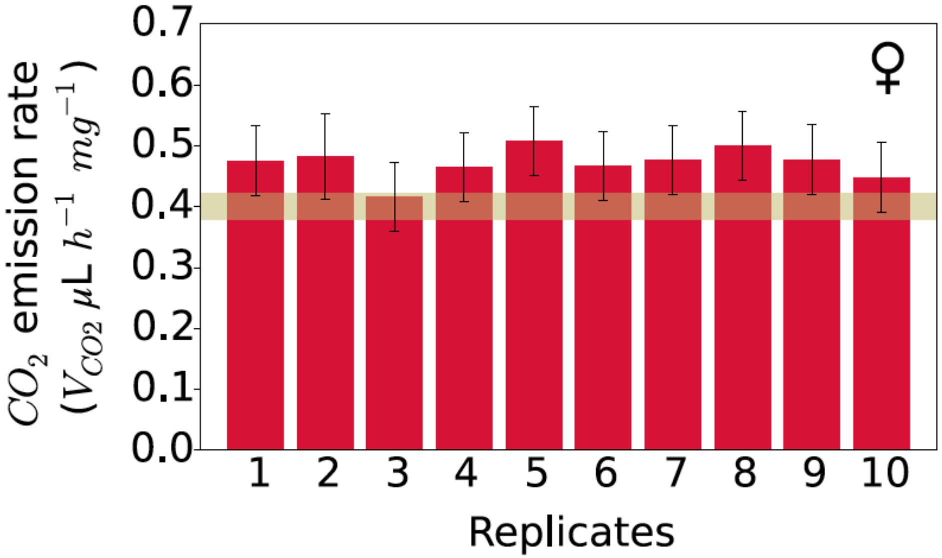
N = 1000

Evolved replicates have higher fitness, higher metabolic rate and lower fat content

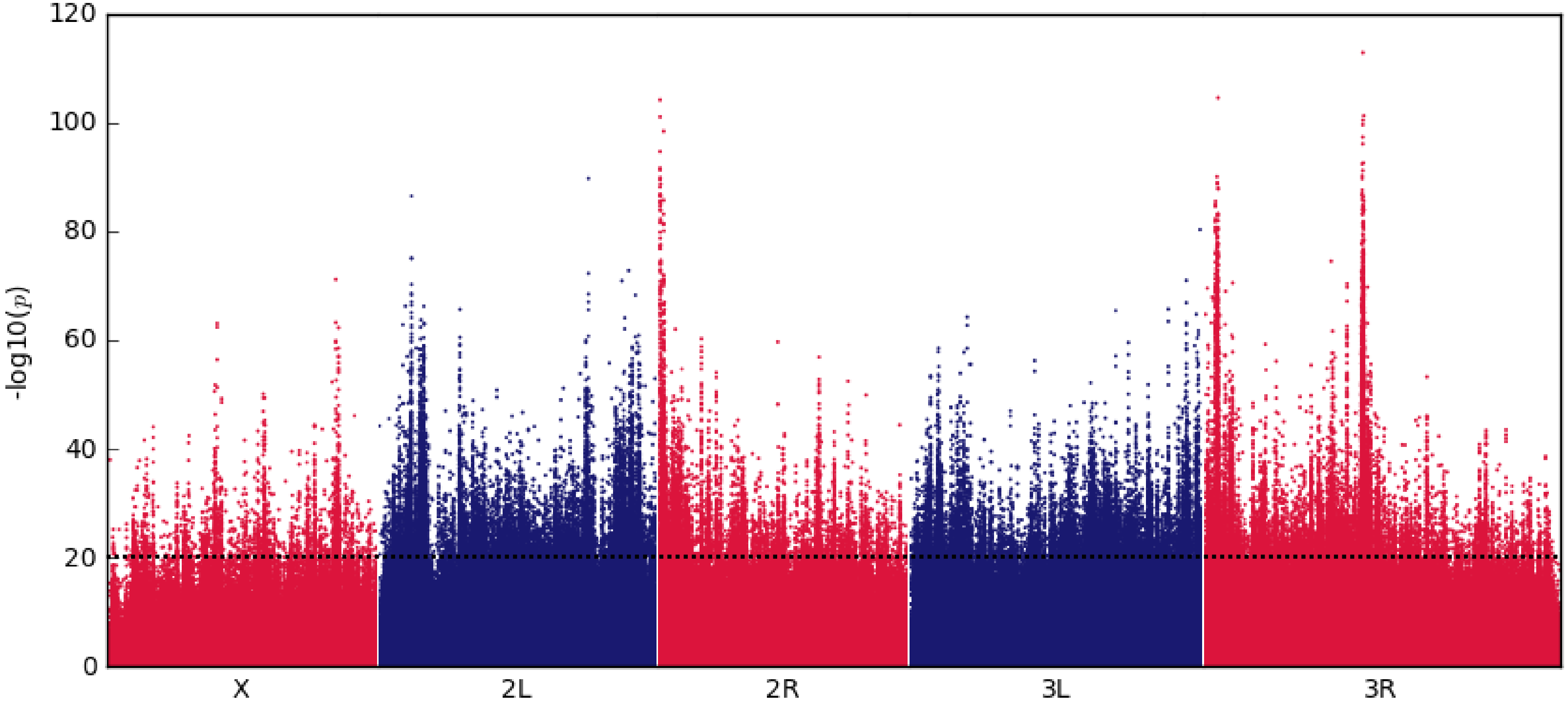


Phenotypic convergence among evolved replicates





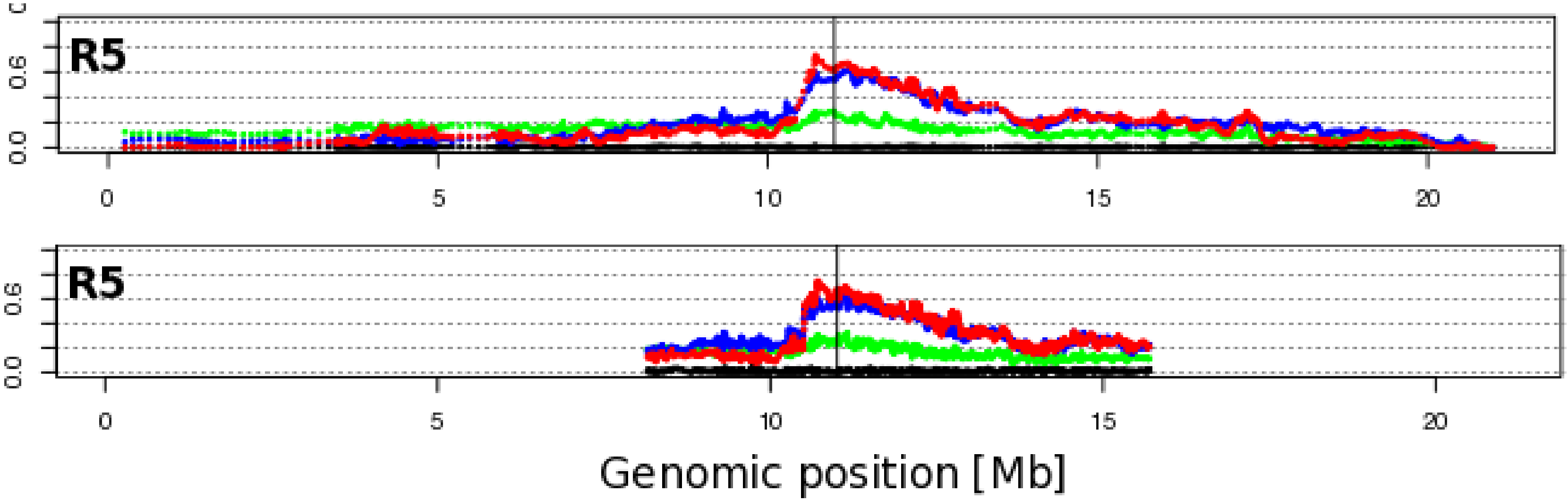
First glance; many putative targets of selection



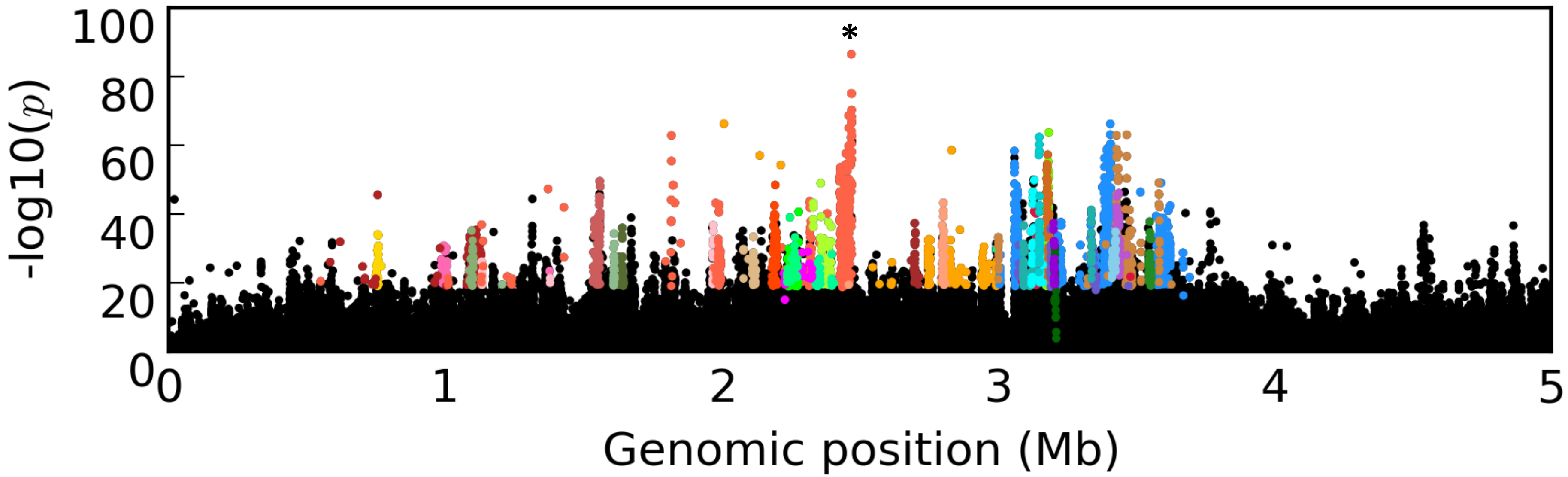
Significant allele frequency change between the founder and F60 populations (Cochran-Mantel-Haenszel: CMH test)

Reconstruction of haplotype blocks from Pool-Seq

- In haplotypes starting from low frequencies, allele frequency trajectories of selected and hitchhiking SNPs are correlated across time and replicates (*Franssen et al. 2016*)

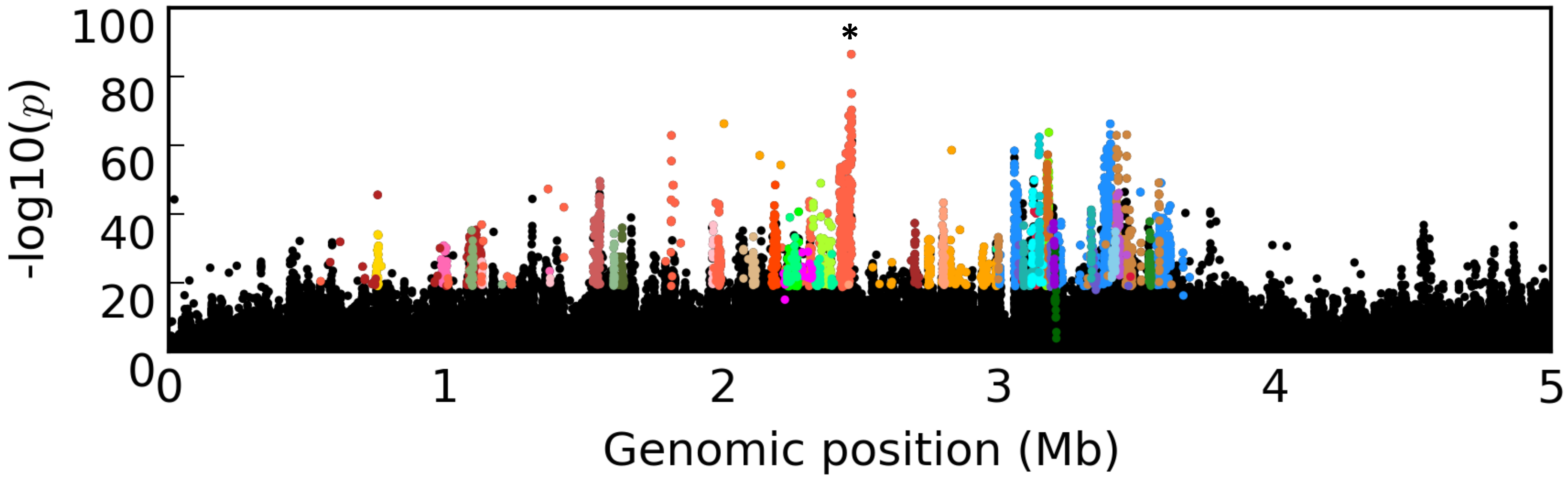


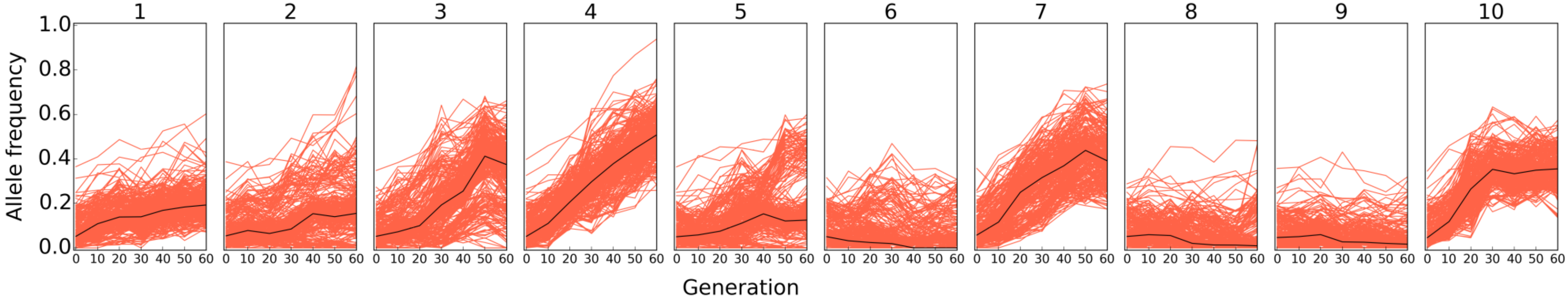
Multiple adjacent haplotype blocks



- 52,199 candidate SNPs (5% FDR–corrected q-values of CMH and Fisher's exact tests)
- Minimum allele frequency change 0.2 in at least 2 replicate, Window size 1Mb, correlation coefficient 0.75

Multiple adjacent haplotype blocks





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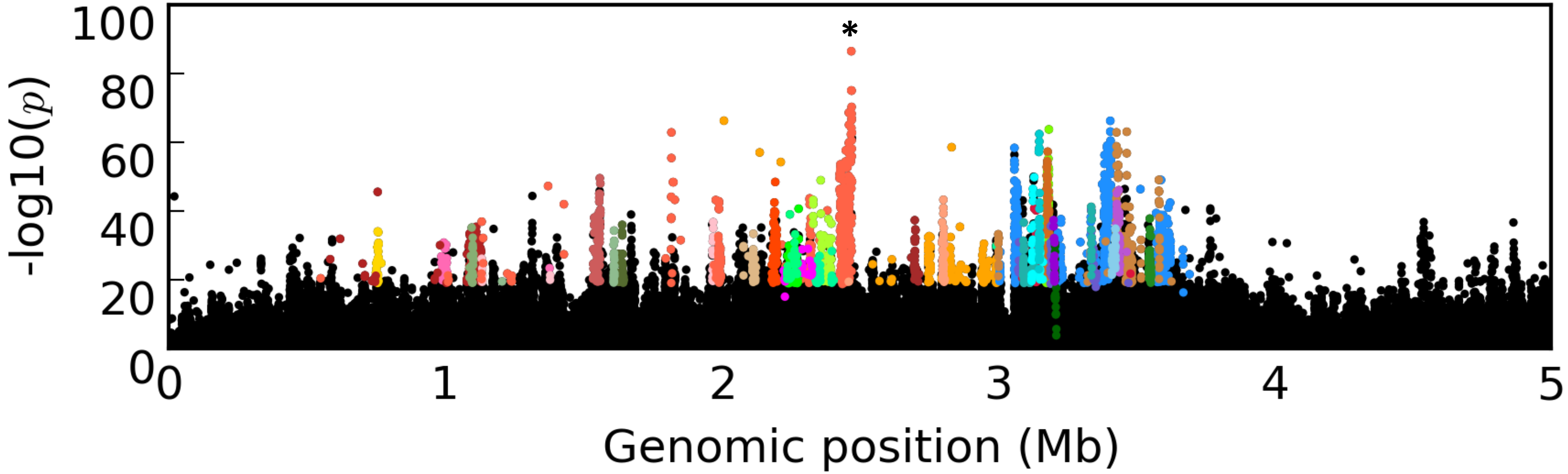
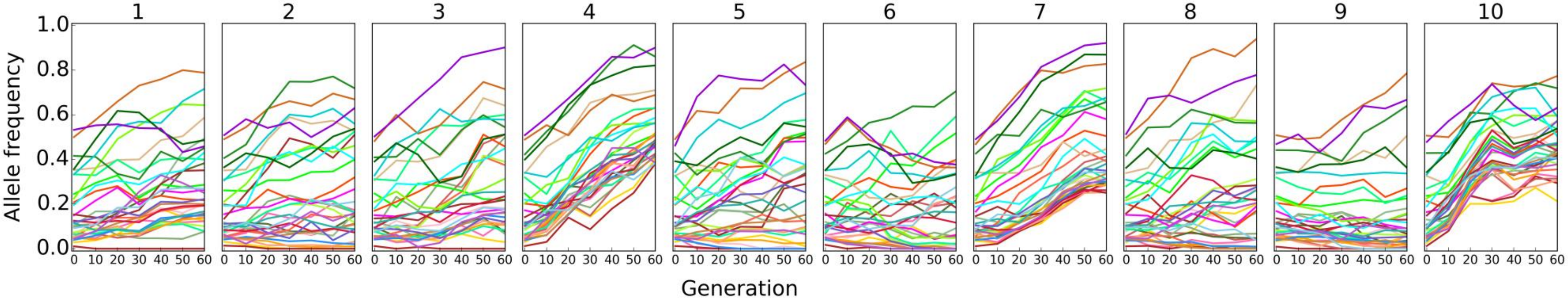
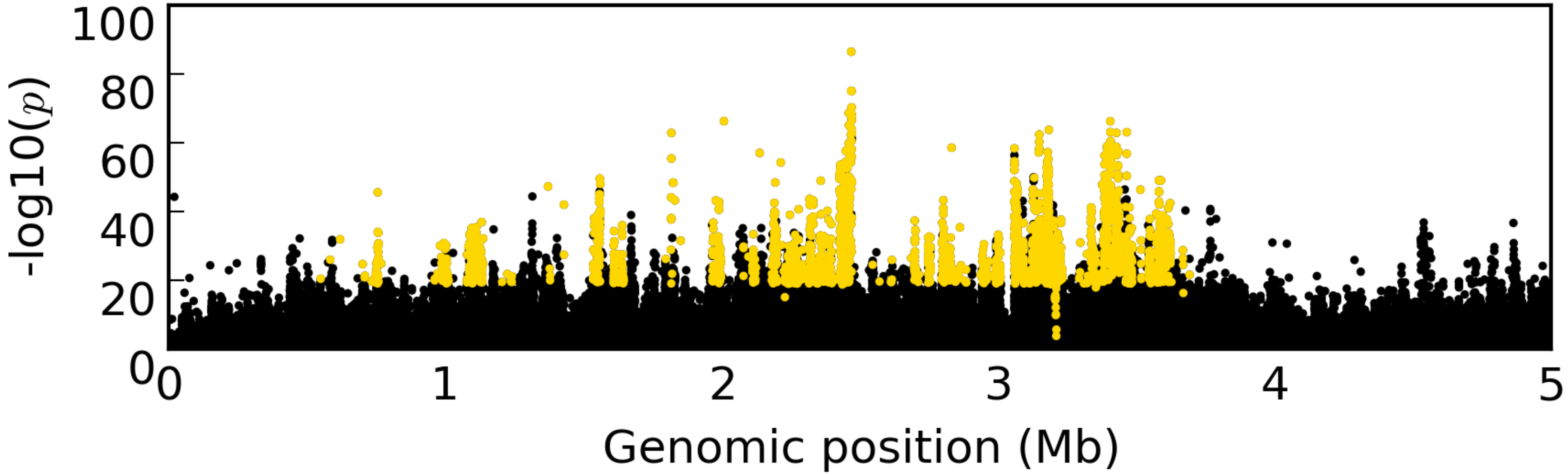
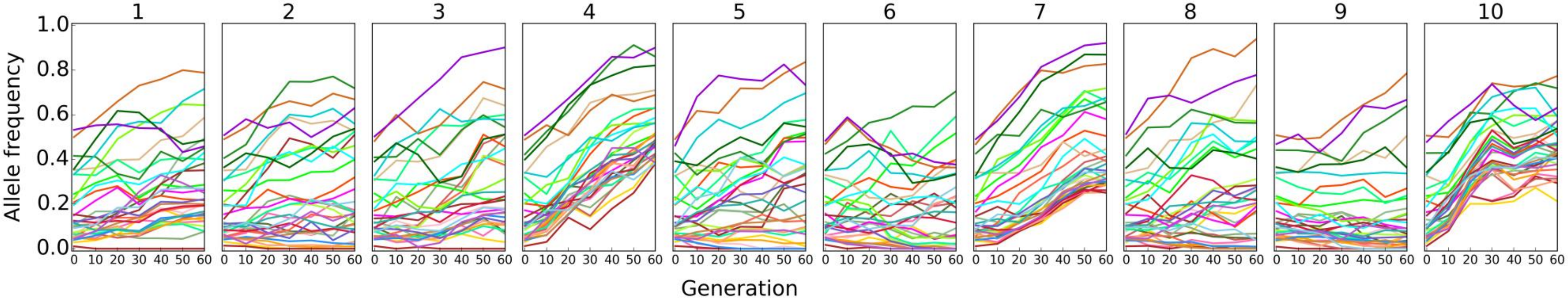


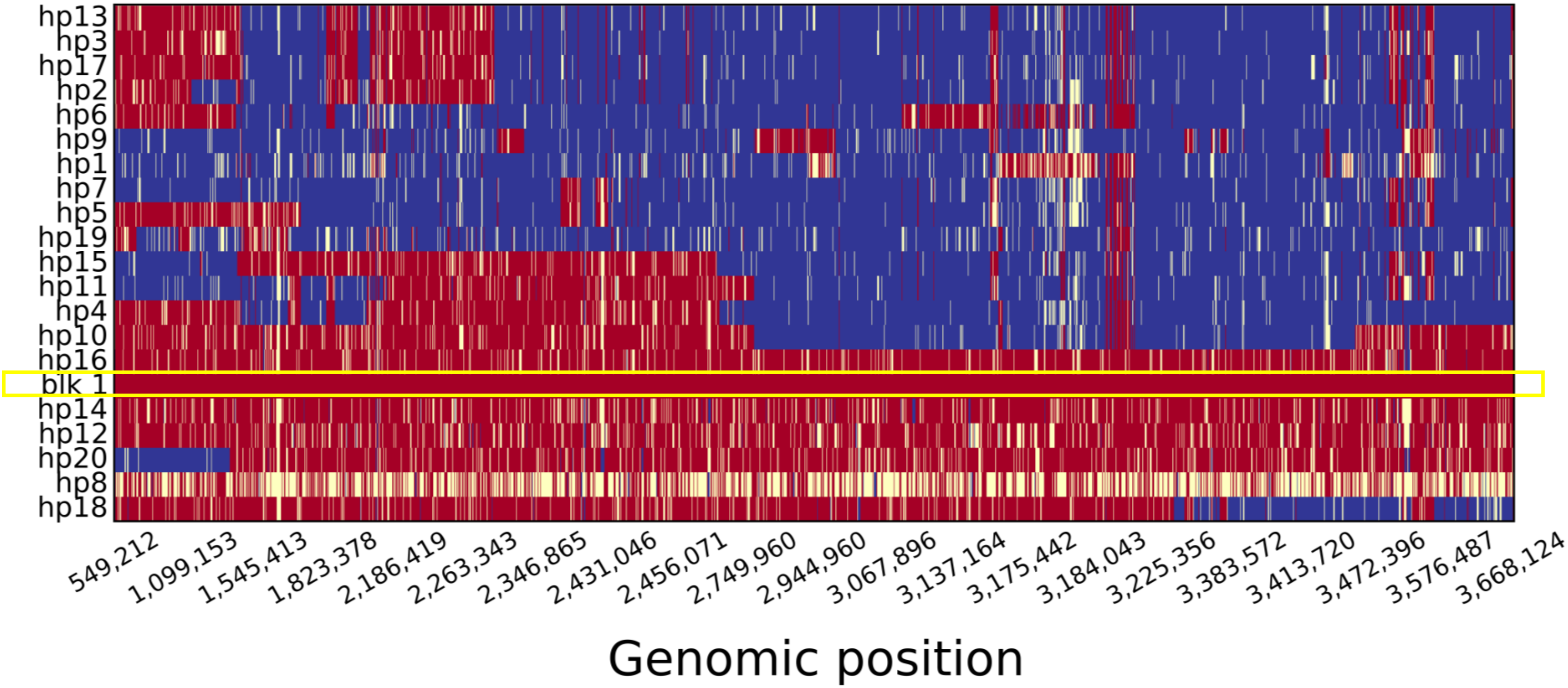


Reconstruction of a large haplotype block from multiple haplotype blocks

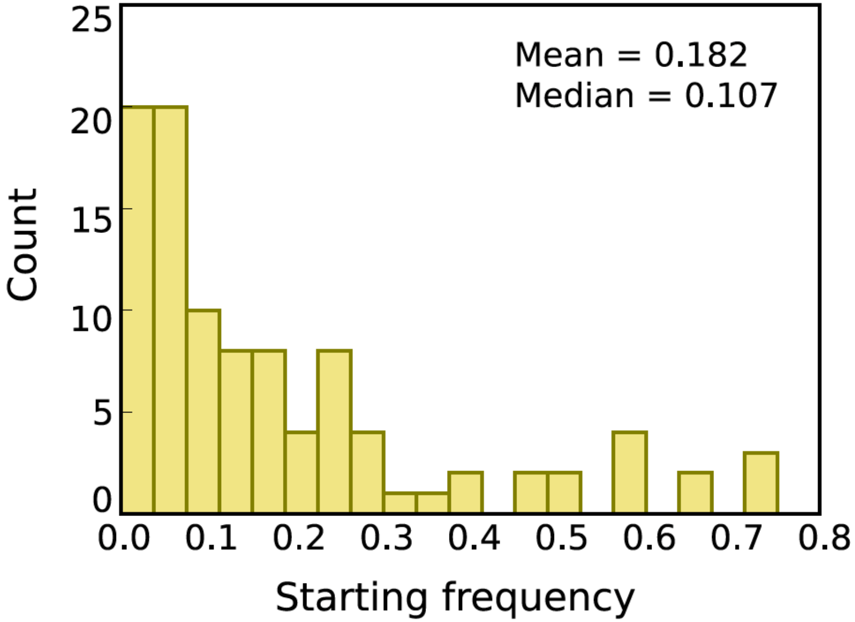


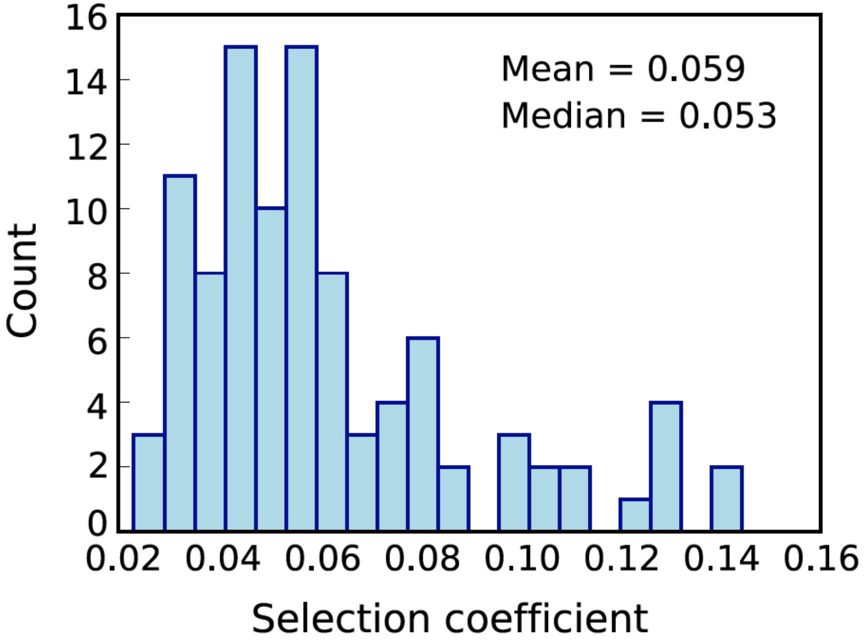


Validation of reconstructed haplotype blocks

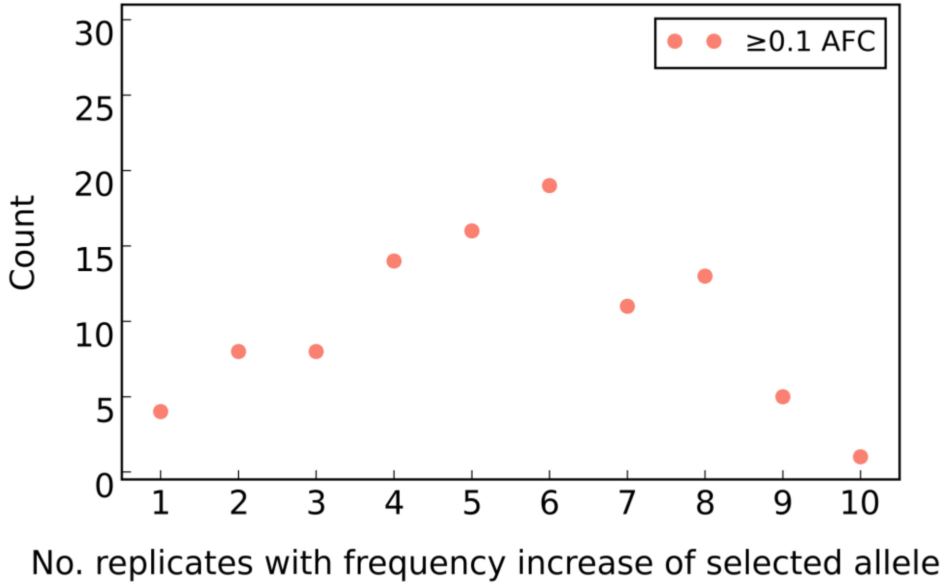


Characteristics of 99 selected alleles





Genomic heterogeneity among evolved replicates



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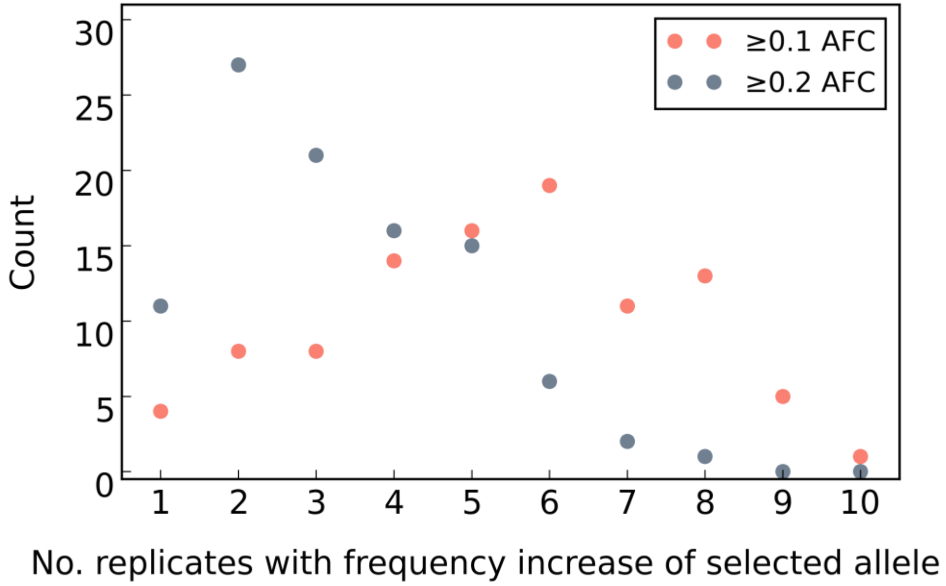

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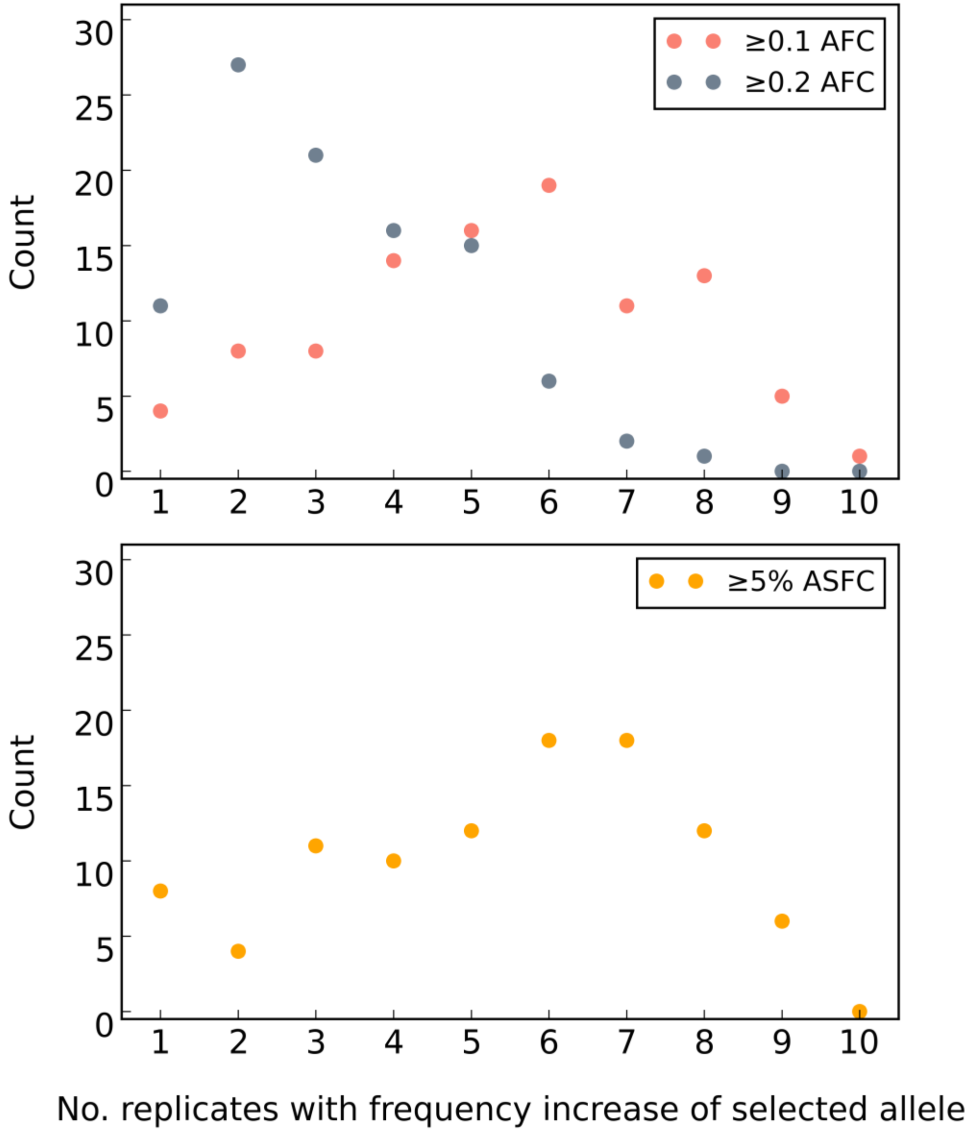

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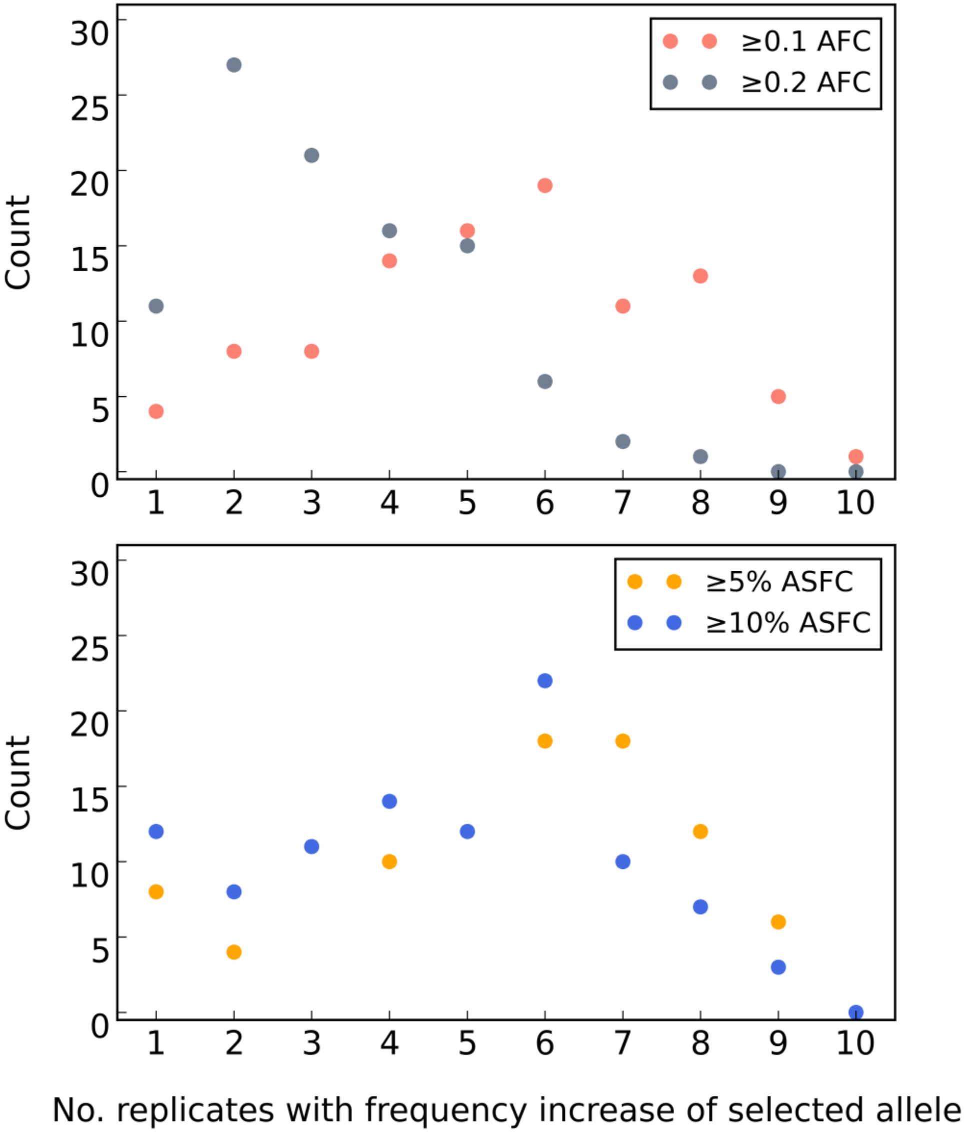
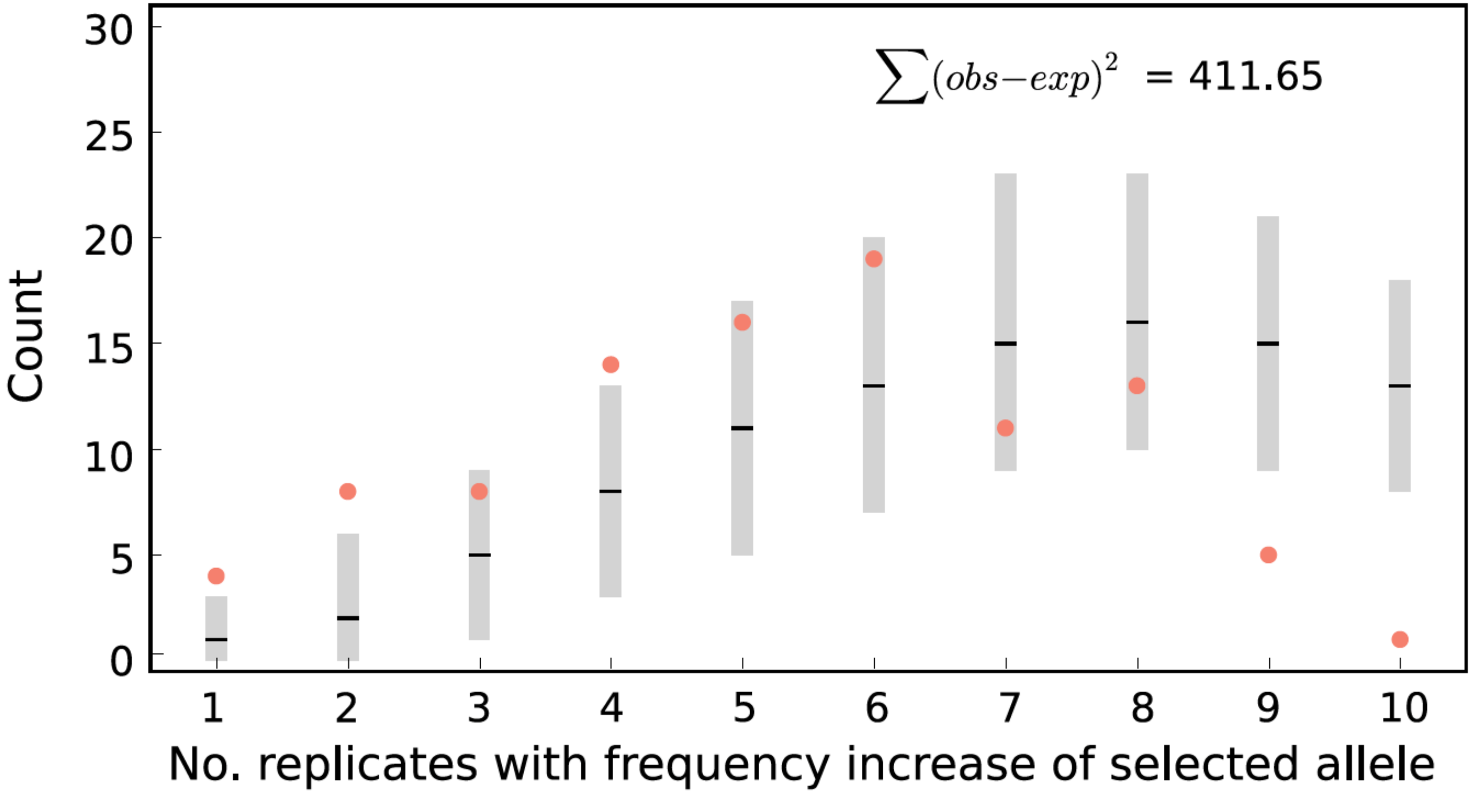


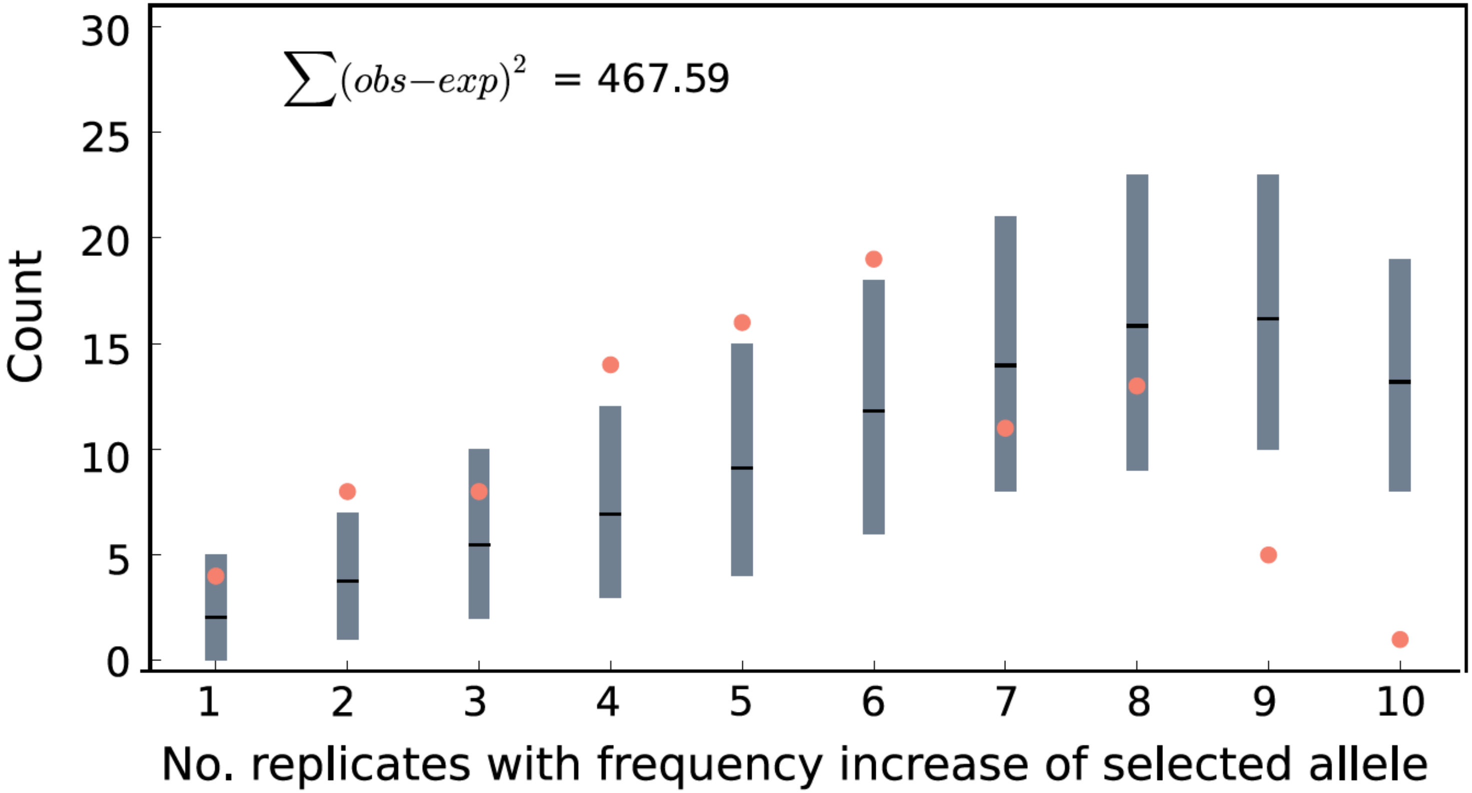
Genomic heterogeneity doesn't fit the sweep paradigm

Constant *s* across replicates and no linkage

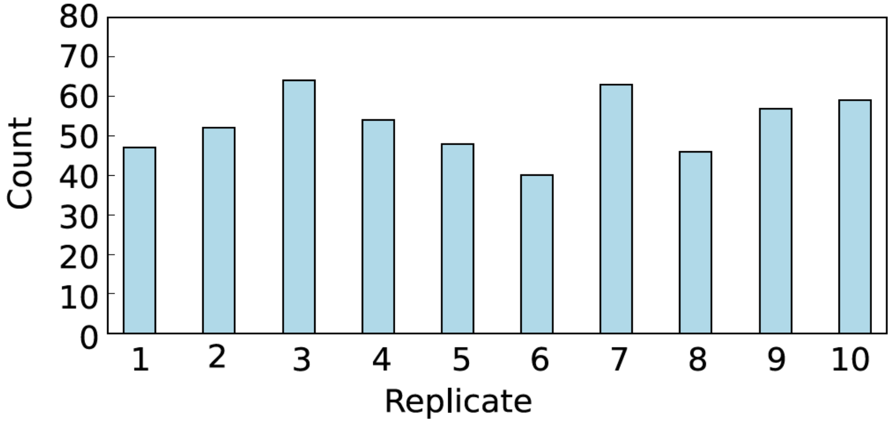


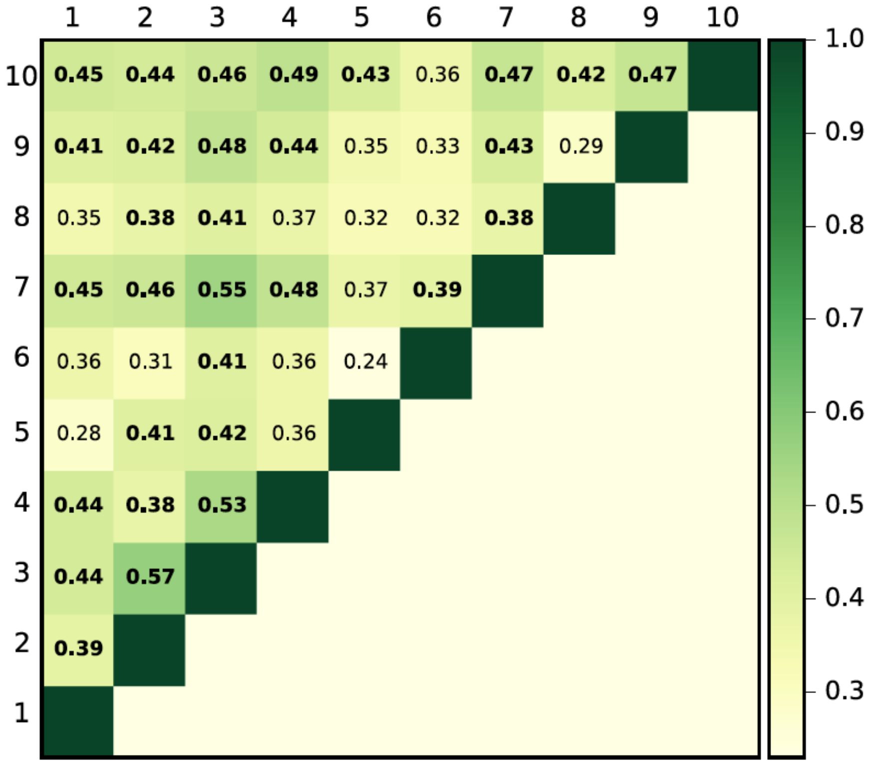
Genomic heterogeneity doesn’t fit the sweep paradigm

With linkage and a constant *s* across replicates



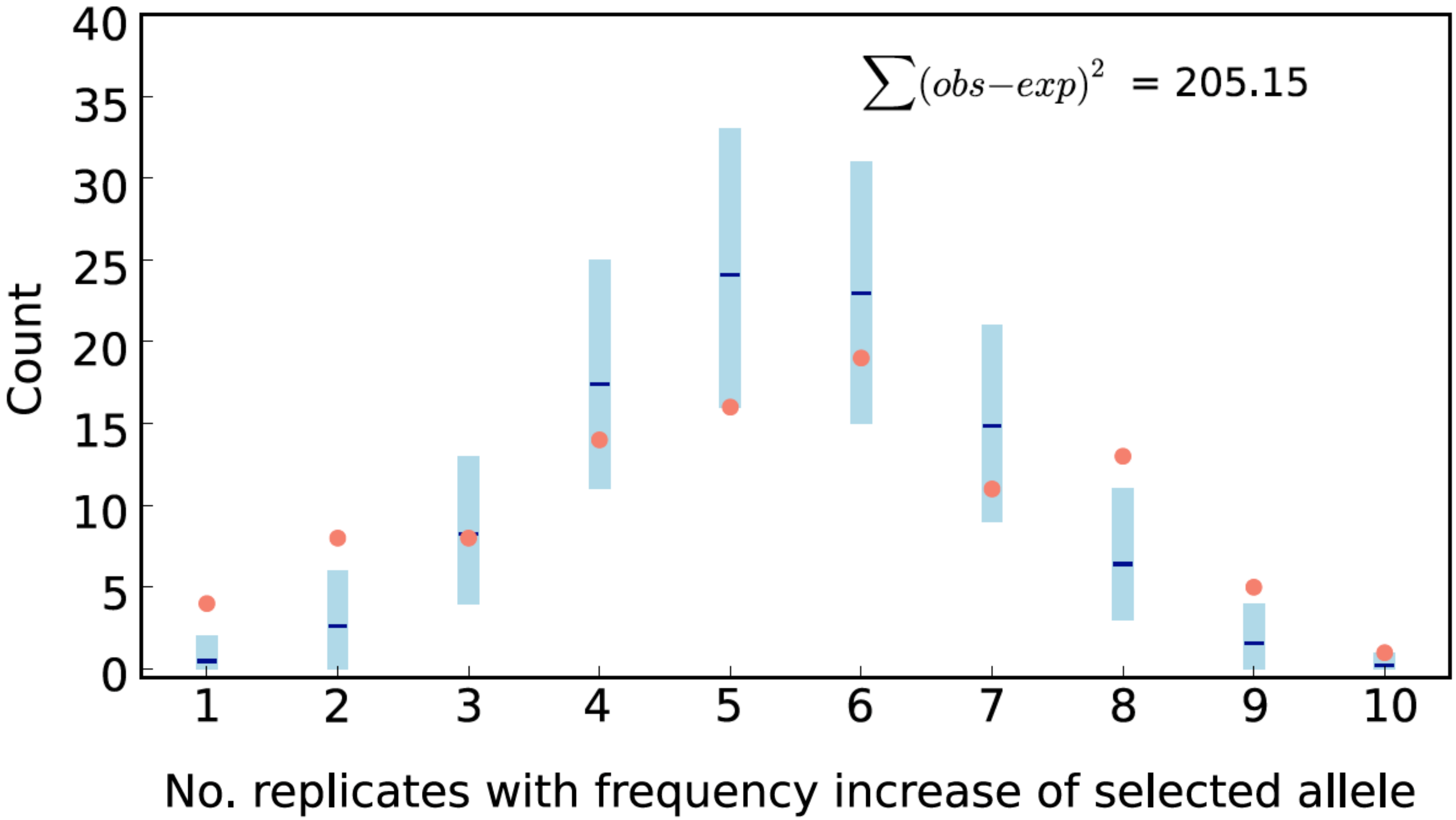
Low genomic similarity among evolved replicates



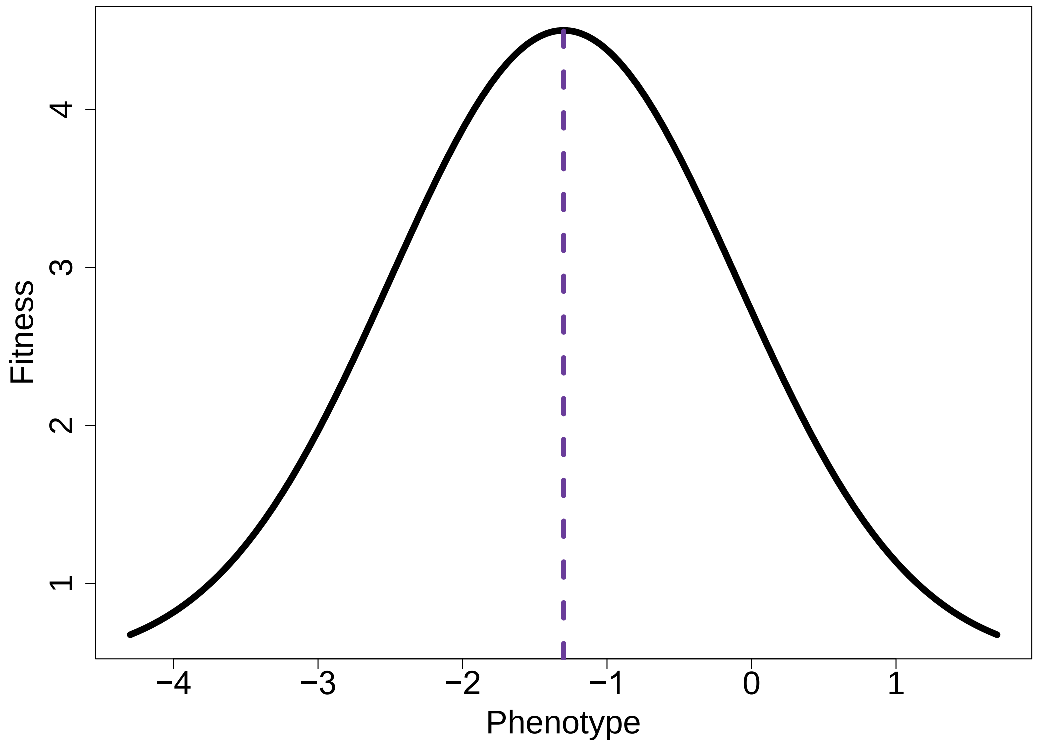


	1	2	3	4	5	6	7	8	9	10
10	**0.45**	**0.44**	**0.46**	**0.49**	**0.43**	0.36	**0.47**	**0.42**	**0.47**	
9	**0.41**	**0.42**	**0.48**	**0.44**	0.35	0.33	**0.43**	0.29		
8	0.35	**0.38**	**0.41**	0.37	0.32	0.32	**0.38**			
7	**0.45**	**0.46**	**0.55**	**0.48**	0.37	**0.39**				
6	0.36	0.31	**0.41**	0.36	0.24					
5	0.28	**0.41**	**0.42**	0.36						
4	**0.44**	**0.38**	**0.53**							
3	**0.44**	**0.57**								
2	**0.39**									
1										

Genomic heterogeneity fits genetic redundancy paradigm



Quantitative trait after a shift in trait optimum



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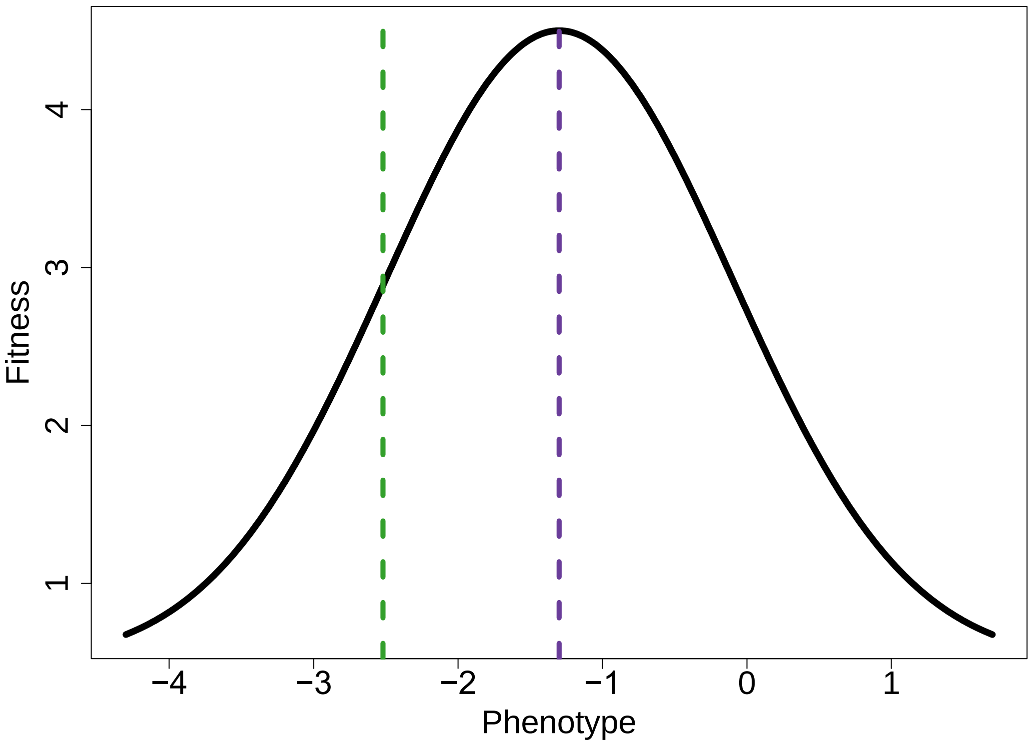

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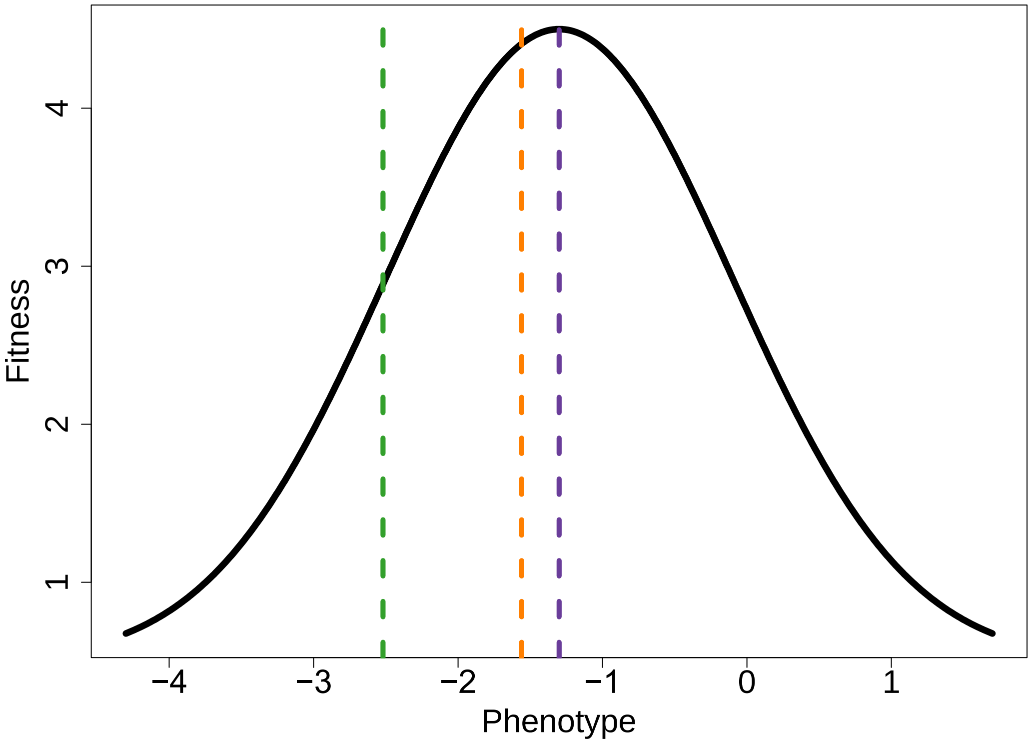
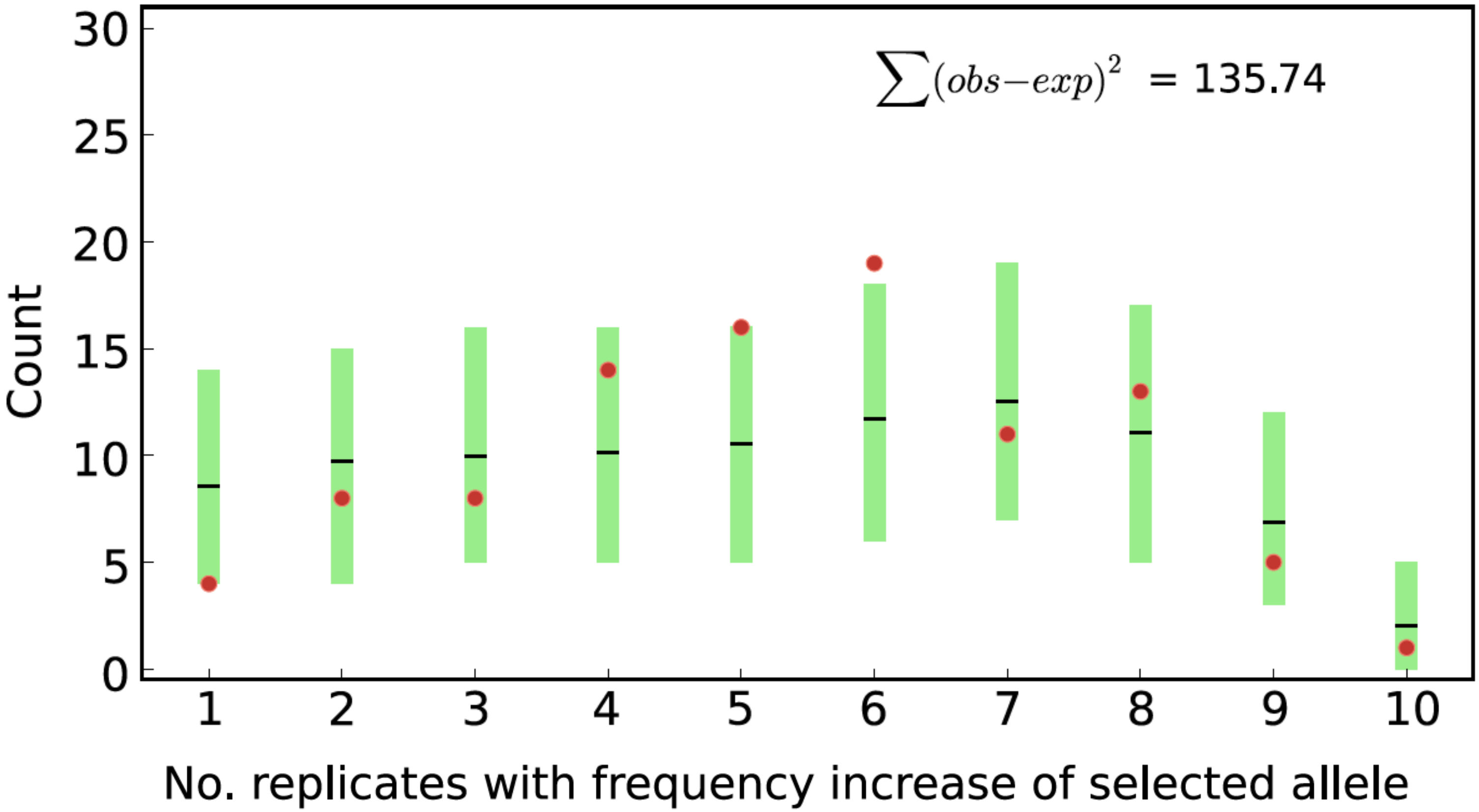
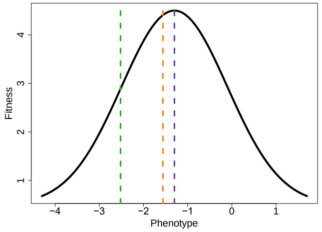


Genomic heterogeneity fits a quantitative trait paradigm

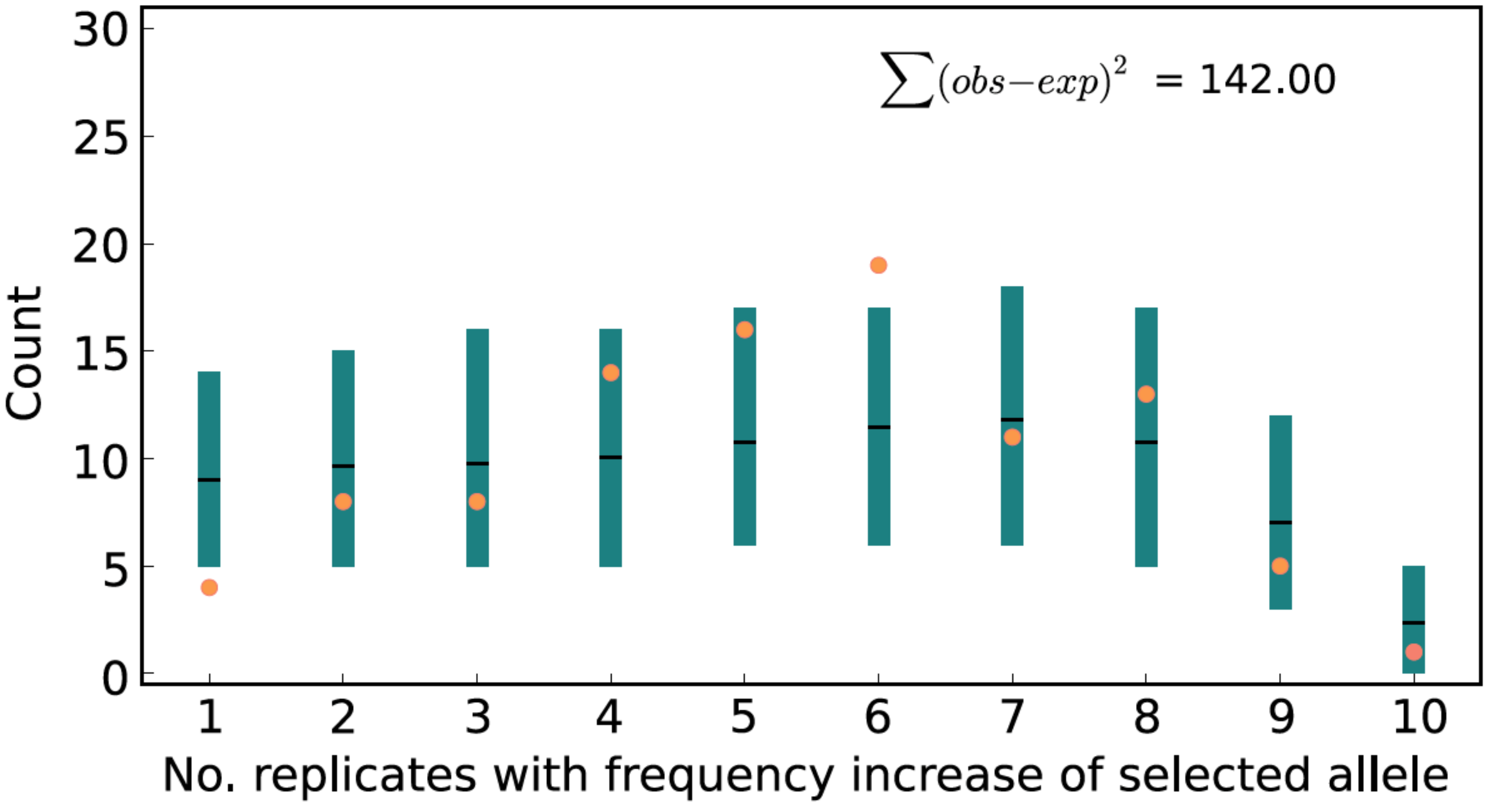
QT paradigm without linkage

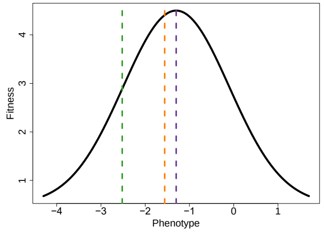




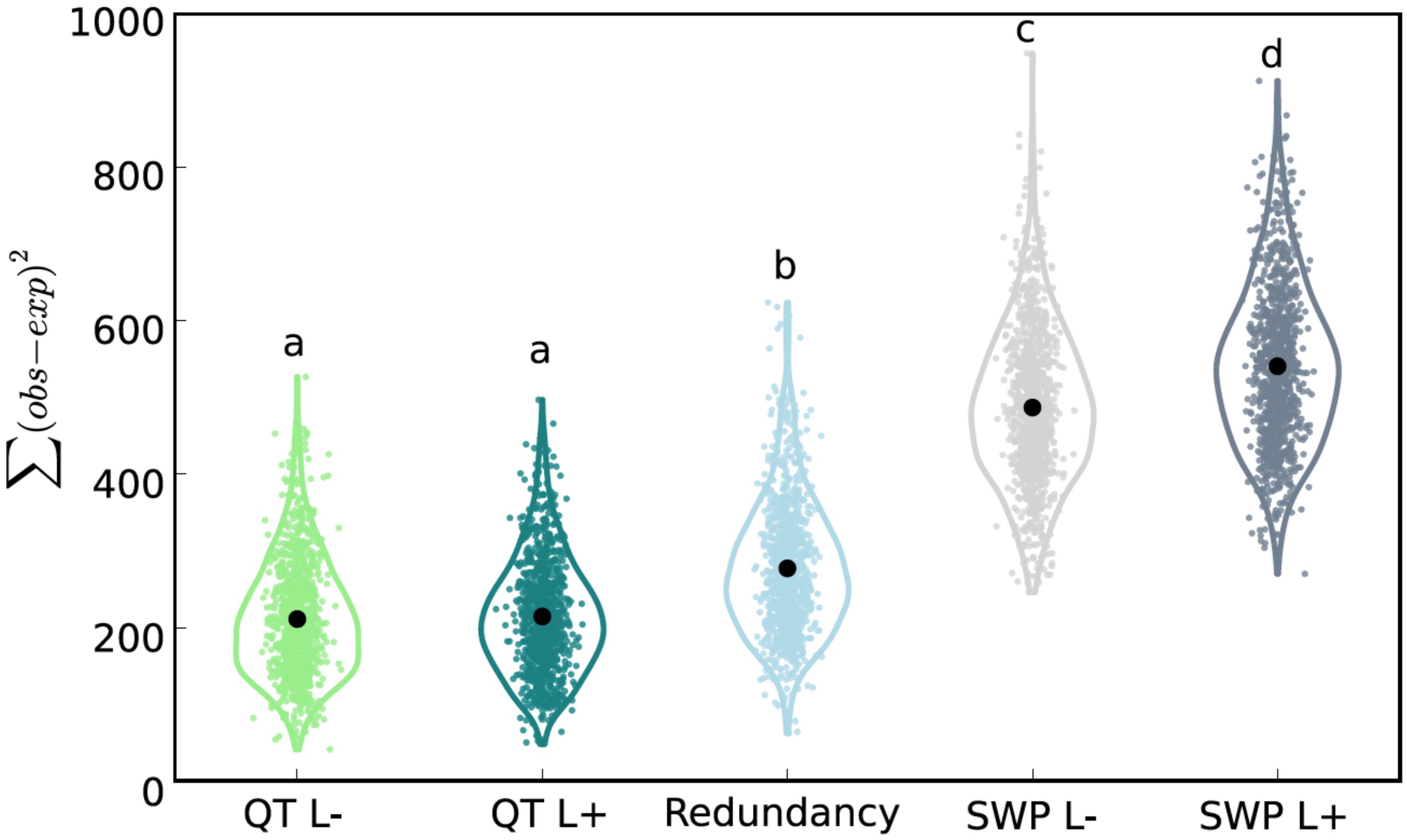
Genomic heterogeneity fits a quantitative trait paradigm

QT paradigm with linkage

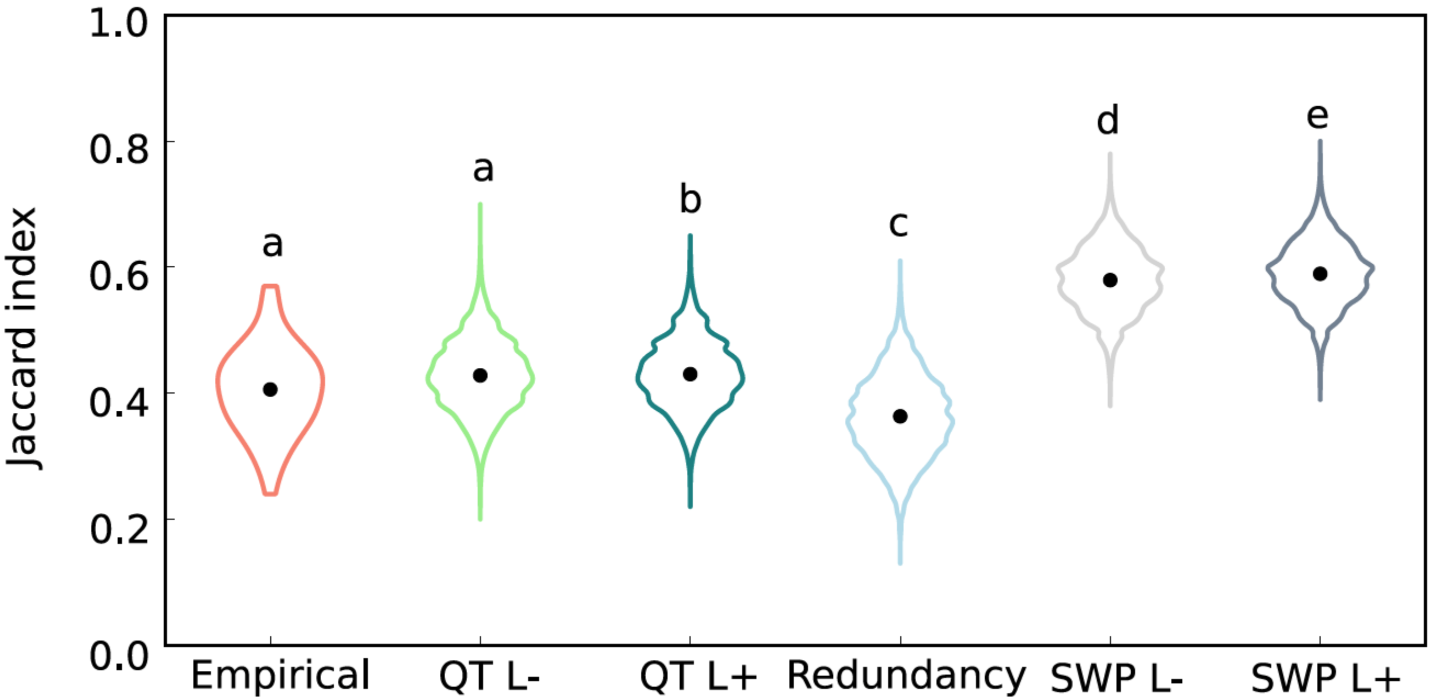




QT and redundancy paradigms fit the RFS of the empirical data better than selective sweep paradigm



Replicates in selective sweep paradigm are more similar than the empirical data and QT paradigm



Summary

- Natural *D. simulans* populations harbour a vast reservoir of adaptive variation facilitating rapid evolutionary responses.
- Genomic heterogeneity fits polygenic adaptation with quantitative trait paradigm.
- Genetic redundancy provides multiple genetic pathways leading to phenotypic convergence.
- No evidence of strong genetic constraint

PLOS | BIOLOGY

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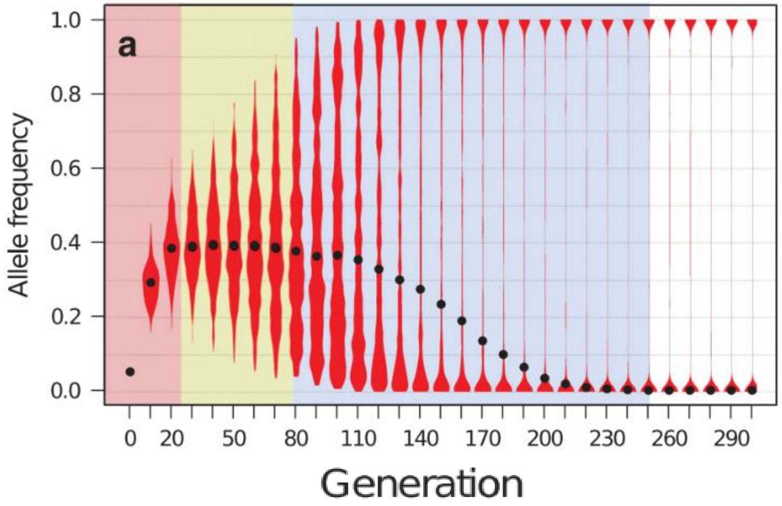
Following the predictions of QT paradigm, the median frequency of selected alleles plateau



Franssen et al. 2017

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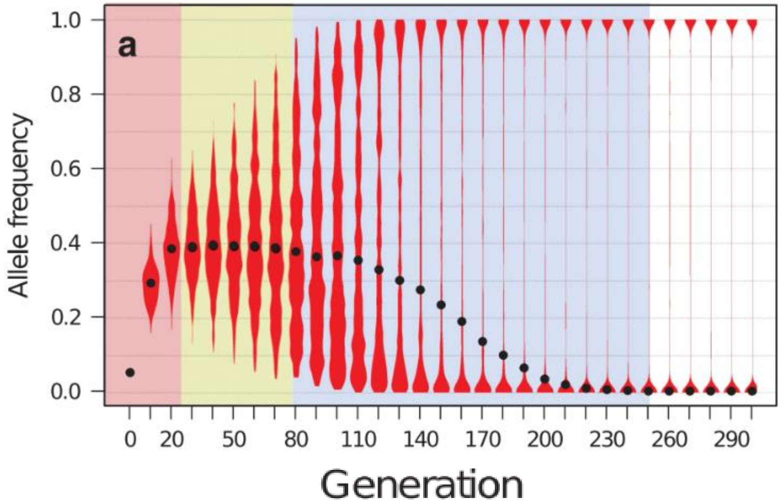

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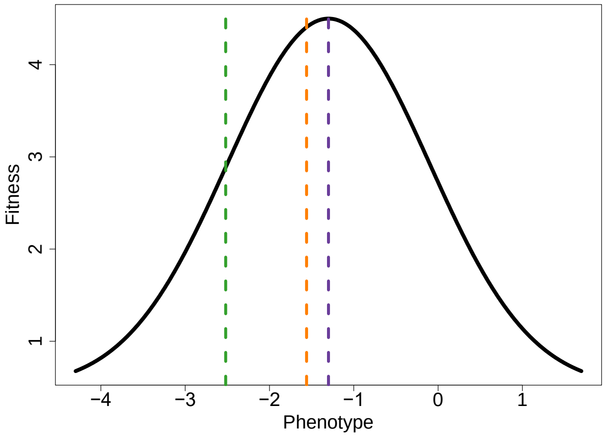

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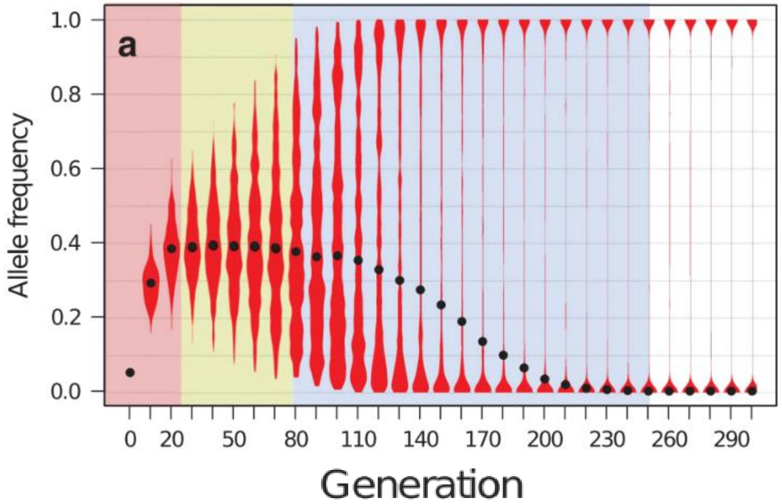

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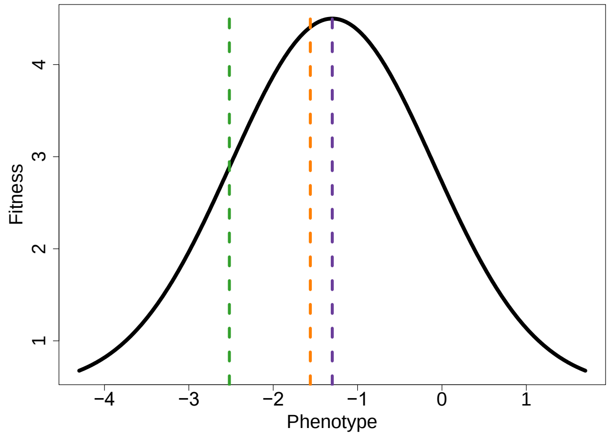
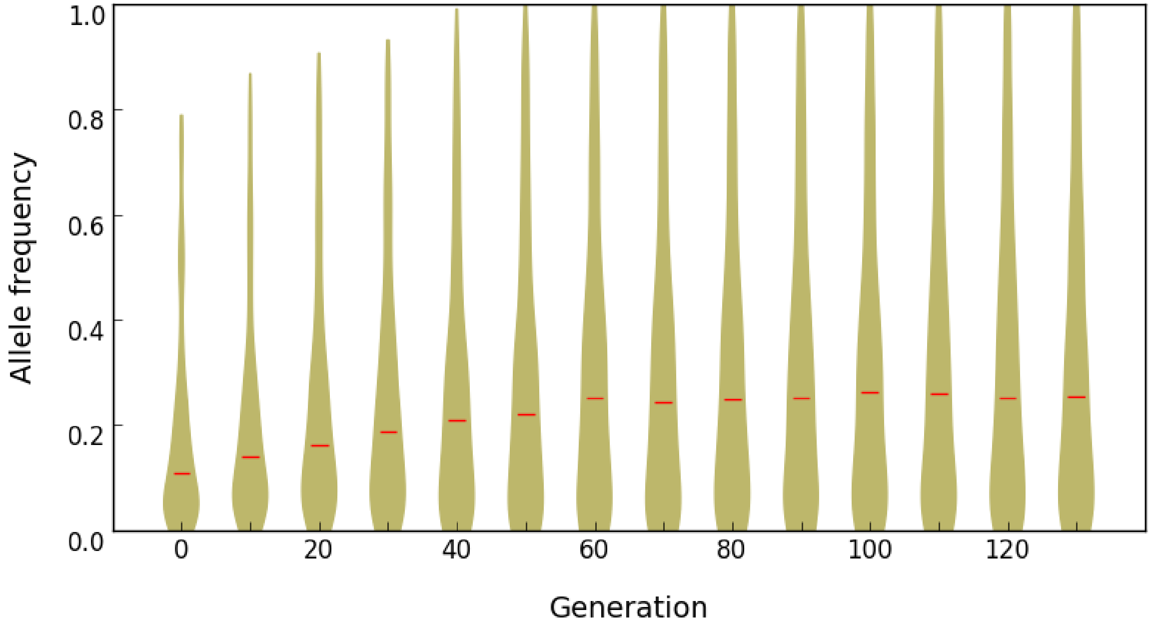
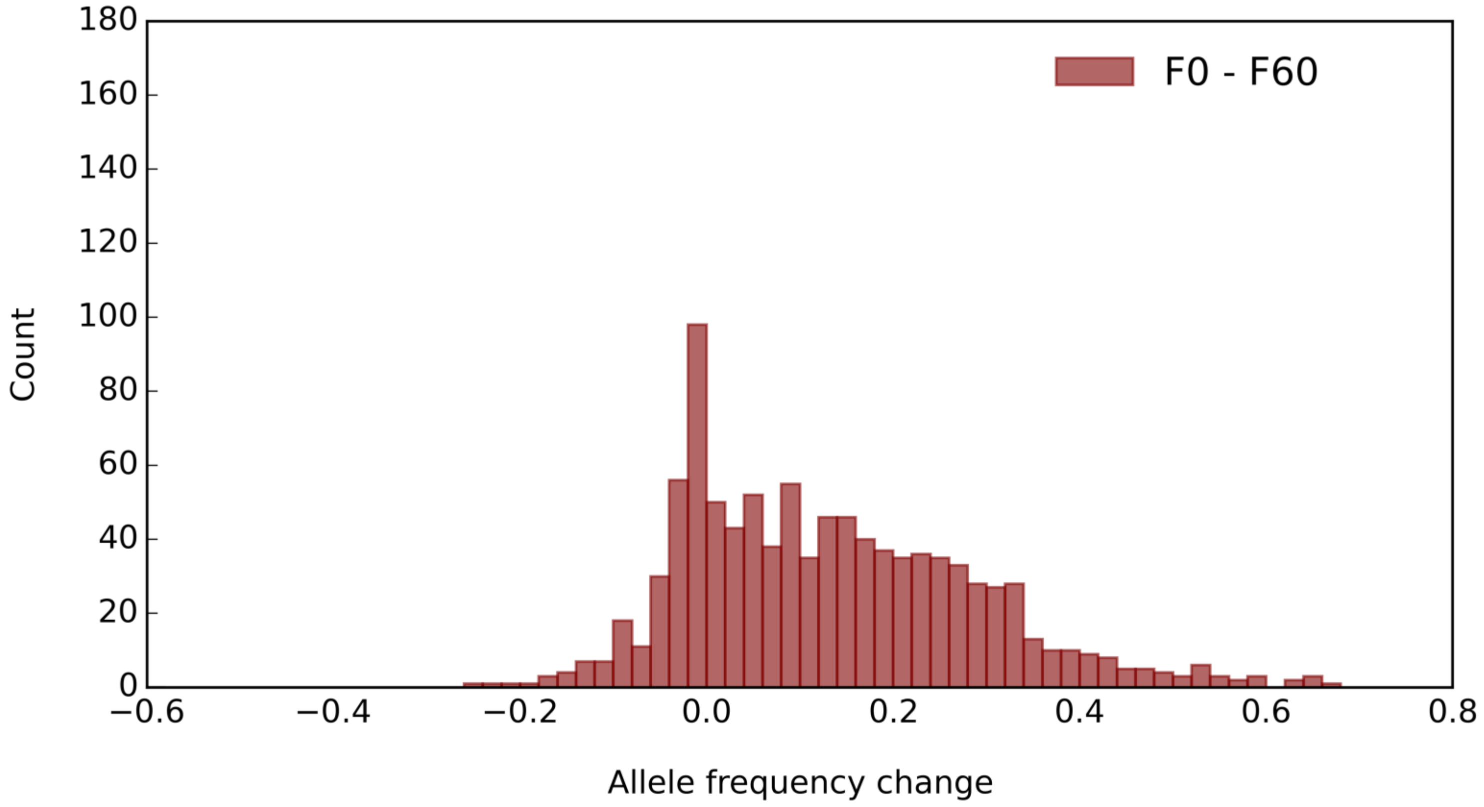
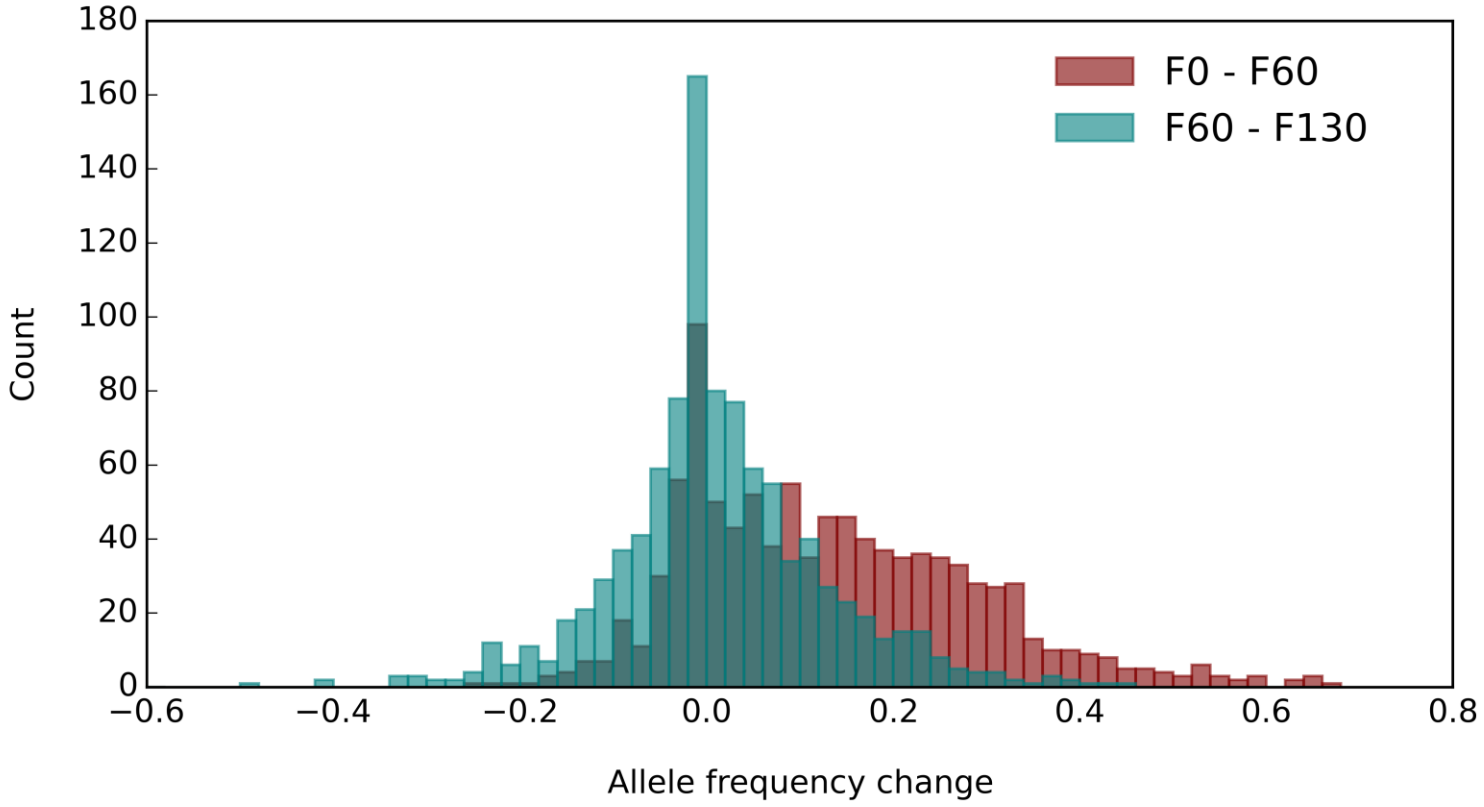




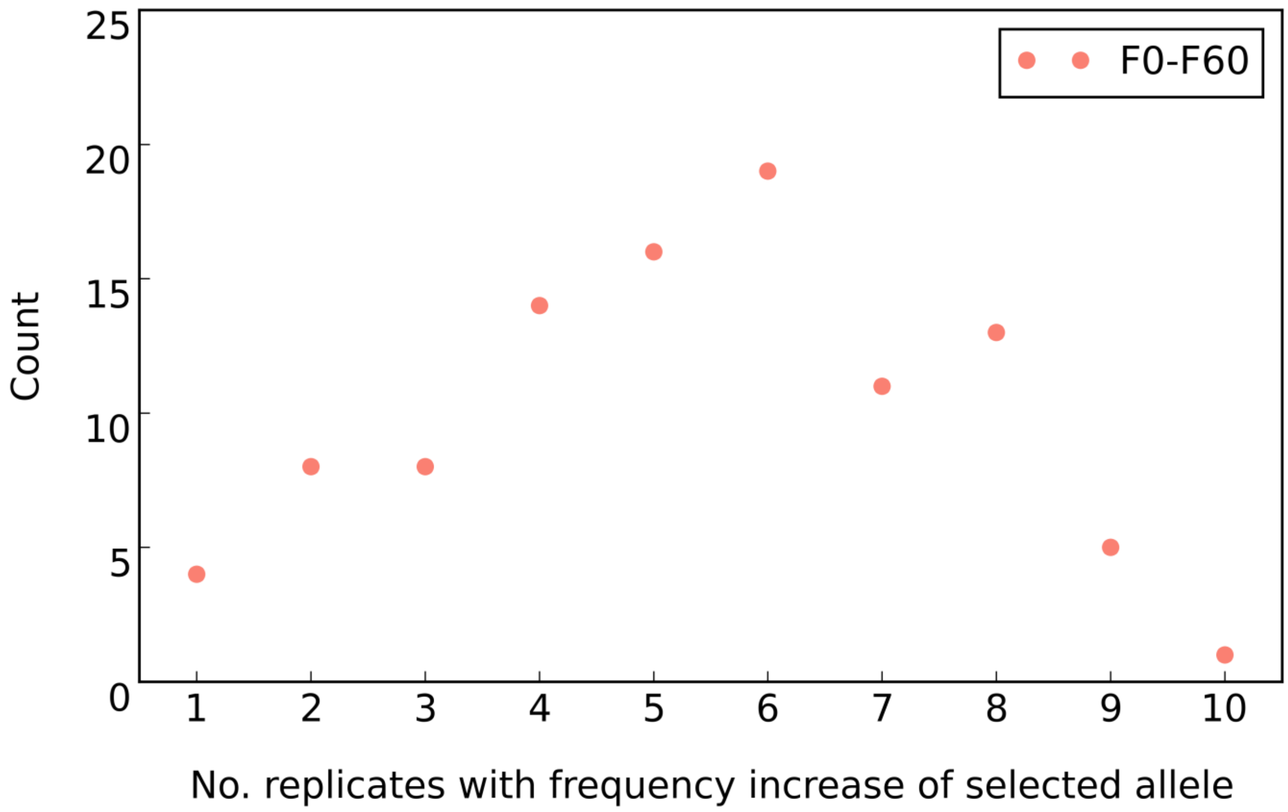
Prominent allele frequency shift in early generations of adaptation



Plateau and drift in allele frequencies in later generations of adaptation



Genomic heterogeneity persists even after 130 generations of adaptation



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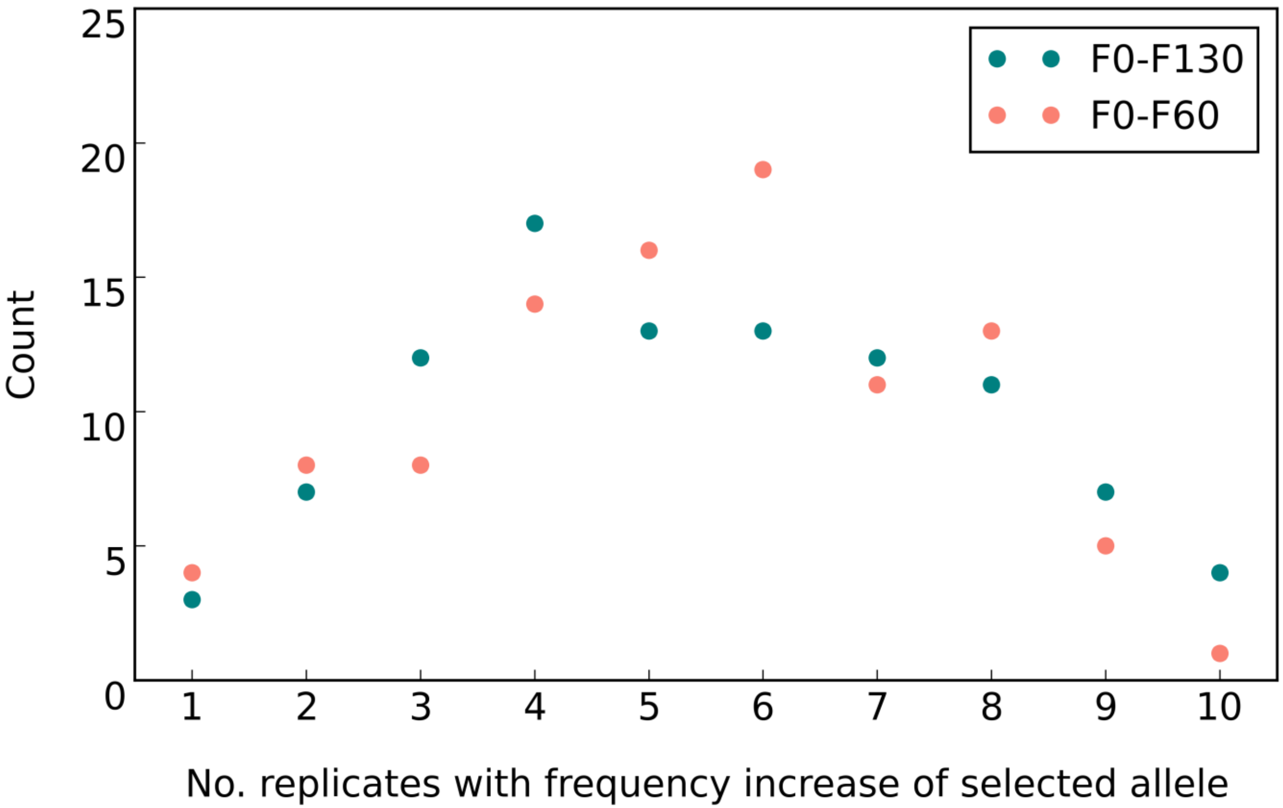

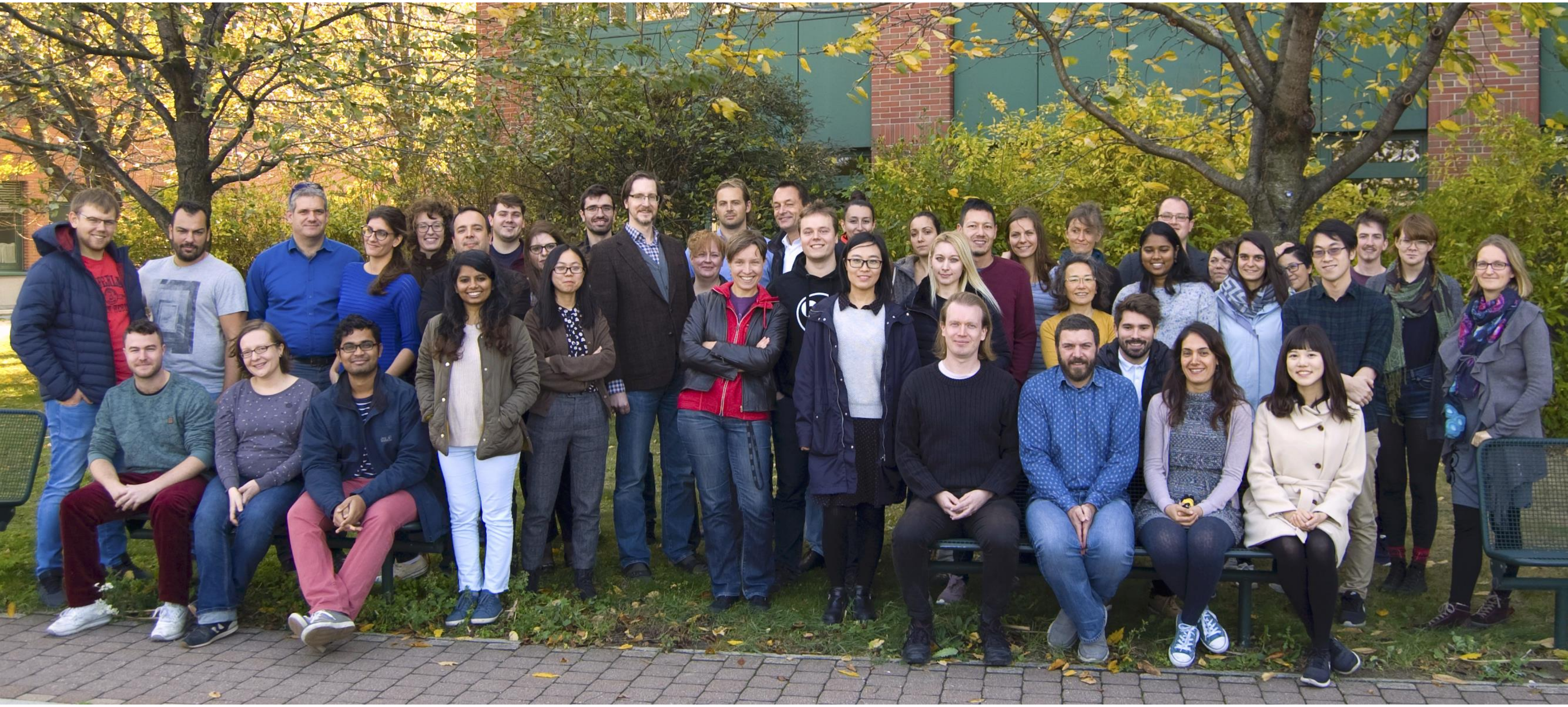

Der Wissenschaftsfonds.

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