# Introduction

Quantitative genetics aims to quantify genetic diversity; this diversity has broad implications for adaptation, it is well described how diversity enhances efficiency of adaptation; adaptation with more Va = faster, more efficient; particularly seen in the case of quantitative genetics, where stabilizing selection is often assumed; different story with the maintenance of variation around a fitness optimum, i.e. after the adaptive walk what happens?; several models have appeared over the last 50 years to explain the maintenance of variation; continuum of alleles vs diallelic; within continuum of alleles, the approximate distribution of allelic effects depends on the relative mutation rate to selection strength; in other words, the strength of new mutations to standing genetic variation; models over the last 50 years have failed to explain natural diversity observed in populations;

Much of the variation between and within populations is the result of continuous variability in traits individuals in those populations possess. Differences in such quantitative traits lead to adaptation and speciation. Underpinning adaptation by quantitative traits is additive genetic variance (VA), the heritable component of variation; the amount of which has mystified quantitative geneticists for close to 100 years. Predicting levels VA is reliant on mutation rate and selection strength: both of which are notoriously difficult to estimate in natural populations. Many quantitative traits are subject to stabilizing selection, where intermediate trait values have maximum fitness. Theory suggests that adaptation via stabilizing selection should be more efficient with higher standing VA, and that the selective fixation of this standing variation should decrease VA as adaptation takes place (Fisher 1930; Lande 1975). However, these expectations have not always coincided with observed data.

Depletion of VA with stabilizing selection has been shown both experimentally , and analytically, however increasing amounts of more modern work show no effect of selection strength on VA. Sztepancz and Blows (2017) showed that there was no relationship between genetic variation and the strength of stabilizing selection in *Drosophila serrata­­­.* More modern analysis of Fisher’s (1930) geometric model (upon which stabilizing selection is built) has shown that when the individual effect of selection in alleles is weak, stabilizing selection has a minimal effect on VA, as drift at any individual locus may compete with selection to adjust allele frequencies (Barton 2017). Discrepancies such as these can perhaps be explained by the relative effect of stabilizing selection, depending on where a population is relative to the optimum. When populations are far from the optimum, mutations act under a directional selection model, where larger mutations that bring an individual closer to the optimum are more beneficial (Zhang 2012). However, as populations approach that optimum, large effect mutations become costly as they are more likely to drag populations further away from the optimum.

Barton 2017: selection negligible when individual allles is weak and comparable to drift

Thornton 2019: when phenotypes approach optimum, strength of selection on indivual muts decreases effect on Va under infinitesimal model, selection gets more info when selection on

Zhang 2012: when phenotypes near optimum, selection is stab, while far away, closer to dir sel

Sztep: dir sel more common in nature? Populations more commonly maladapted?

At the heart of the evolutionary sciences is the need to understand the natural world’s diversity. Darwin’s (1863; SOURCE) introduction of natural selection some 140 years ago led to increasingly accurate glimpses into the units of evolution, genes, and their movement through a population in response to selection (SOURCE). However, these movements, particularly in a multivariate trait space, become a challenging realm to predict (SOURCE; Lande 1979, 80 etc.). To navigate this space, it is necessary to reduce the predictors of trait trajectories to their principles: how they affect additive genetic variance, the heritable component of trait variability.

Additive genetic variability, VA, is regarded as the most important predictor of a population’s adaptability (Lynch and Lande 1998; Aguirre *et al.* 2014; Careau *et al.* 2015), and hence it’s trajectory through time towards a phenotypic optimum. Although a multitude of stochastic and deterministic processes also contribute to the population’s total trait variability, VA is heritable, and therefore predictive of a population’s trajectory over micro-evolutionary time. The VA of a population determines the phenotypic space that population can explore. Hence, it is predicted that populations with large amounts of VA are best suited to adapting to novel environments (Barton and Charlesworth 1998). Such an example is X. However this is not always the case, standing genetic variation is characterized by a variety of architectural and population-level constraints such as rates of pleiotropy, selection strength, additive effect size, linkage, and deleterious mutation/background selection (SOURCE). For example, under infinitesimal models, selection has a trivial impact on standing variation (Barton 2017).

including genetic drift, selective pressures, additive effect sizes, between- and within-gene interactions, and heritability (SOURCES).

* Natural diversity, population movements in trait space
* Heritable variation
* Stabilising selection, effect on variation/need for variation vs drift
  + Expected to remove variation, mutation alone can’t explain why in natural populations we see so much variation: why?
* Additive effect sizes, effects on variation
* Background selection, effect on variation
* Population genetics expectations of variation under bkg sel, additive effects

# Methods

Using the forward-genetics modelling package SLiM 3.4 (Haller and Messer 2019), I constructed two models to explore a portion of the multivariate parameter space that explains genetic variability in natural populations. These parameters included genome wide recombination rate, the additive effect size distribution, the rate of universal pleiotropy, and the selection strength multiplier, (Table 1). The amount of mutational covariance between traits was also varied across models but was not considered for analysis. The relative rate of deleterious mutation compared to trait mutations was also varied across models. This parameter led to two alternate outcomes that could influence the response: either the reduction in QTL mutation rate due to increasing deleterious mutation rate could cause observed differences, or the effect of the deleterious mutations themselves could be attributed to the differences. Preliminary analyses indicated that the ratio of QTL mutations to deleterious mutations remained constant across increasing levels of this parameter (Figure S3). This suggests that a similar deleterious load was experienced across populations, and that the effects of increasing this rate are attributable to changes in QTL mutation rate. The highest QTL mutation rates were experienced in models with low rates of deleterious mutation, and vice versa. Thus, models with high mutation rate and low selection strength (deleterious mutation rate < 0.33; > 660) approximated the Kimura-Fleming-Lande Gaussian approximation of allelic effects (Kimura 1965; Lande 1975; Fleming 1979), while models with low mutation rates and high selection strength approximated Turelli’s (1984) House-of-Cards model. Among all parameter combinations, multiple conditions and assumptions were shared.

## Common model elements

Both of my experimental models consisted of a SLiM 3.4 model simulating a Wright-Fisher population of 8000 diploid individuals evolving over 100,000 generations. Populations first were subject to 50,000 generations of burn-in to build standing variation to mutation-drift balance (figure S1). Individuals were characterized by 8 traits, controlled by 100 loci each. Each trait had an identical effect on fitness, forming a ‘mega-trait’ with varying variance-covariance structures depending on pleiotropy rates. Each locus was assumed to have identical length, and each base pair within it mutationally independent. This assumption is supported by a study by Thornton (2019), which found that within-locus differences in linkage had no average effect on either genetic variance or the mean trait value, indicating within-locus independence. In addition, the average number of base pairs per locus is highly conserved within eukaryotes (Xu *et al.* 2006), indicating that the assumption of equal gene length is valid. Mutations were assumed to occur at an arbitrary position within the locus and was of arbitrary form. Mutations were assumed to be completely additive in effect, with no dominance or epistatic interactions, aside from additive epistasis occurring as a result of the fitness function (further explanation below). All loci were assumed to be on the same chromosome, with genetic distance being determined by the recombination rate parameter, r (Table 1). Both models had a genome-wide germline mutation rate of 8.045x10-6 per locus per generation, based on an average of five groups of eukaryotes (Aston *et al.* 2017).

The effective population size, Ne = 8000, was chosen to compromise between computational performance and the effect of genetic drift on populations under stabilizing selection. This value results in weak genetic drift in comparison with the strength of selection (under strong selection pressures), and appropriate standing genetic variation following burn-in to allow for adaptation (Lynch and Lande 1998).

Mutational effects on trait values were sampled from a normal distribution,

where λ is the additive effect size (Table 1). In the case of pleiotropy, a multivariate normal distribution was used, where n = 8, and

where **Σ** is a covariance matrix with diagonal values equal to λ and non-diagonals pulled from a normal distribution:

where is the parameter value of mutation correlation. **Σ** was ensured to be positive definite by multiplication with its transpose,

Non-trait deleterious mutations had fitness effects sampled from a gamma distribution:

Where and (SLiM Manual). This describes a distribution of fairly weak deleterious mutations on average.

All models were subject to 50,000 generations of burn-in, where mutations accumulate until the population reaches mutation-drift equilibrium. This is tracked as heterozygosity through the simulation, where mutation-drift equilibrium occurs when:

where µ represents the per-locus mutation rate per generation (Kimura and Crow 1964). A population at equilibrium was assumed sufficiently burnt in. Trials indicated that 50,000 generations of burn-in was sufficient for our population size (Figure S1). Deleterious mutation/mutation rate lowered the value of away from expectation in initial burn-in tests, however an alternative equilibrium was reached, satisfying the requirements of burn-in regardless of the parameter (Figure S1). During the simulation run, trait variances, covariances, and trait means were collected every 500 generations to track distances from the optimum and trait variability over time. At the end of the simulation, the allelic effects of segregating mutations in all populations were collected.

## Model specific characteristics

After reaching equilibrium, populations evolved for 100,000 generations of neutral drift or stabilizing selection, depending on the treatment. Neutral drift entailed no change from the properties of the burn-in, whereas stabilizing selection imposed a fitness function on phenotypes, invoking a multivariate optimum a fixed distance from the population mean phenotype post-burn-in. The position of the optimum is defined as:

Where is the vector of phenotype means, is the per-locus, per-generation mutation rate; , is the number of mutational steps to reach the optimum, and is the number of generations of burn-in. For our purposes, 8.045x10-6, 100, and . This distance was close to the original phenotypes, meaning most of the simulation (approximately 98000 generations of the simulation) investigated the maintenance of variation at a fitness optimum.

The fitness of an individual in the population was defined as:

Where s is the selection coefficient, represents the gradient of the selection curve, n is the number of traits, and xn is the phenotype for trait n. To ensure a theoretical minimum and maximum fitness, s was fixed at 0.9, ensuring minimum fitness was , and maximum fitness was 1. This results in individuals at the optimum being at most ten times as fit as those infinitely far from the optimum. The model-specific maximum fitness difference depends on, which adjusts the realized fitness gradient via the curvature of the fitness function.

## Model Parameterization

Five parameters were shared between models, with a sixth for testing selection (Table 1). These were sampled using a Latin hypercube sampling design, with 1024 parameter combinations testing the null model, and 256 for the selection model (Figure S1). These samples were generated using the R packages ‘DoE.Wrapper’ and ‘LHS’, using the maximin algorithm (Melo *et al.* 2015; R Developmental Core Team 2019). Each model was repeated 100 times, using 100 seed values fed to SLiM. These seeds were randomly sampled from a uniform distribution of the total range of unsigned 32 bit integers (1 to 232 – 1) (R Developmental Core Team 2019). The array of parameter combinations and replicates was processed across 1152 cores on the University of Queensland’s Tinaroo high performance computing (HPC) system, using embedded Nimrod scripts to feed parameter/seed combinations to individual SLiM processes.

## Analysis

Despite not all data conforming to normality, no data was transformed owing to the large sample sizes. Previous work into the robustness of t-tests, and F-tests have shown that departures from normality can usually still provide reliable estimates, provided the number of observations is large enough that coefficient estimates are approximately normally distributed due to the central limit theorem (Lumley *et al.* 2002). This was verified with diagnostic tools in the R package “jtools” (Long 2020). In terms of regression analysis, heteroscedasticity can still remain a problem, even with large sample sizes. To account for this, I used Eicker-Huber-White (EHW) robust standard errors in my linear regression models via the ‘estimatr’ package in R (Eicker 1967; Huber 1967; White 1980; Blair 2020).

For analysis, the interaction between and mutation rate was treated as a ‘model’ parameter, indicating whether the simulation approximated House-of-Cards allelic effects, or Gaussian effects. An additional model type, ‘Null’, summarized the models with no selection and any mutation rate. Remaining models with intermediate selection strengths and deleterious mutation rates were not considered for analysis, although that remains an exciting prospect for the future. Across all analyses, responses were compared at the final generation of the simulation (100,000). Trait variances and covariances were pooled and averaged to form a ‘mega-trait’ average variance and covariance, since traits were functionally identical. Trait variances and covariances were compared with multiple regression models using EHW standard errors.

In addition, I computed the population mean Euclidean distance from the optimum for each replicate and model:

Where pi and qi are the population mean and optimum value, respectively, for trait *i*. I compared distances with EHW-error multiple regression.

I also collected the mutational effects of segregating alleles at the end of the simulation. With this, I compared mean distributions of allelic effect sizes according to additive effect size, recombination rate, and selection strength with multivariate multiple regression. Responses included mean allelic effect, variance, and kurtosis of the distribution. I adjusted for heteroskedasticity with EHW robust standard errors. Multiple regressions were calculated across 50 replicates owing to RAM limitations.

# Results

## Tracking population dynamics over time

To determine the dynamics of the model under selection, we plotted variance and distance to the optimum over time across selection strengths. By generation 100,000, models have not yet reached mutation-selection-drift equilibrium, as variance continues to increase, however trajectories approach stability. Mean variance was consistently greatest over time under a Gaussian model, with House-of-Cards models maintaining variance lower than Null and Gaussian models (Figure 3A). Covariance acted similarly: under Gaussian allelic effects, covariance was greatest, and vice versa for House-of-Cards models (Figure 3B). Mean trait variance remains stable after generation 50,000 across all selection strengths. Covariance reaches an equilibrium with more sizeable fluctuations (Figure 3B). Knowing that by generation 100,000 we are at mutation-selection-drift equilibrium, we can investigate whether specific models have been more successful in allowing populations to reach the optimum.

## Patterns of adaptation with Continuum of Alleles models

Knowing that by generation 100,000 populations had reached mutation-selection-drift equilibrium, we determined the likelihood of populations to reach the optimum given their CoA model approximation (Fig. 4, Table 2). All populations were significantly different (χ22 = 9602.1, p < 0.0001). Gaussian models strayed further from the optimum than House-of-Cards models on average, however average Gaussian models seemed to stray further than null models from the optimum (Fig. 4). However, both Gaussian and House-of-Cards models showed a small proportion of populations that reached very small distances from the optimum, with a visible division between adapted and maladapted populations (Fig. 4). Adapted populations encompassed 0 to 16 units from the optimum, before a ‘dead space’ from this point separated these populations from more maladapted models. Null models did not show this divide between adapted and maladapted populations (Fig. 4). To understand how these populations were able to reach close distances to the optimum, the effects of genetic architecture and the CoA model assumption on distance to the optimum (Fig. 5), mean trait variance (Fig. 6), and mean trait covariance (Fig. 7) were compared.

, I compared the effects of model type, pleiotropy rate, recombination, and additive effect size on mean trait variance with a multiple regression (F14, 108385 = 25590, p < 0.0001, Adjusted R2 = 0.7681). Mean trait variance scaled quadratically, so variance was transformed by square root. Additive effect size contributed strongly to the square root of variance (Figure 3A). A unit increase in additive effect size resulted in an increase of 3.079 ± 0.089 units of (t108385 = 218.673, p < 0.0001). A change from null to a Gaussian model resulted in a decrease of 3.129 ± 0.183 units of (t108385 = --17.089, p < 0.0001). A change from null to a House-of-Cards model reduced by 1.773 ± 0.148 units (t108385 = -12.002, p < 0.0001). Recombination had no effect, and pleiotropy increased by 8.472 ± 0.219

However, these main effects were masked by a strong interaction: the effect of deleterious mutation rate on mean trait variance decreased with increasing additive effect size (β3 = -174.2782 ± 0.4452; t127996 = -391.5, p < 0.0001). Low deleterious mutation rates enabled large increases in mean variance with increasing additive effect size, however this increase was largely constrained under high deleterious mutation rates (Figure 4). These changes to trait variance have strong predictions for adaptation under stabilising selection, specifically in the (Zhang 2012) adherence of trait means to a trait optimum.

## Adherence to a multi-trait optimum with increasing background selection and additive effect size

It is commonly theorised that genetic variability is strongly linked to the adaptability of populations under stabilising selection (Zhang 2012; Walsh and Lynch 2018). To measure this, I calculated Euclidean distances of populations () from the optimum at generation 100,000, and the probability of a given model to reach the optimum, . Deleterious mutation rate and additive effect size, along with their interaction were included in a linear model (F3, 127996 = 122193.3, p < 0.0001, Adjusted R2 = 0.7412; Figure 3). Again, pleiotropy rate, recombination rate, and selection strength (along with their pairwise interactions) explained <1% of variation and were excised from the linear model. Increasing deleterious mutation rate by 10% decreased distance to the optimum by 23.305 ± 0.088 units (t127996= -252.5, p < 0.0001), whilst additive effect size by 1 unit increased the distance to the optimum by 47.874 ± 0.089 units (t127966 = 536.37, p < 0.0001). Again, a significant interaction was observed (Figure 5). Increasing additive effect size under high rates of deleterious mutation resulted in smaller increases in distance to the optimum than under low rates of deleterious mutation (β3 = -36.860 ± 0.296; t127996 = -124.4, p < 0.0001). The probability of reaching the optimum reflected this, with the probability of reaching the optimum increasing with deleterious mutation rate under low effect sizes, but remaining constant at 0 with effect sizes greater than 3 (Figure 6). The probability of reaching the optimum increased linearly under strong selection pressure, however more quadratic trends were visible at lower selection strengths (Figure 6). To understand these patterns, the alleles underpinning trait variation and adaptation needed to be quantified.

## Distributions of segregating alleles under background selection and growing additive effect size

I compared rare allele frequency (RAF) with increasing additive effect size and deleterious mutation rate. The resulting linear model found significant differences between additive effect size, deleterious mutation rate, pleiotropy rate, stabilizing selection presence/absence and interactions between these four parameters (F15, 63937 = 1174, p < 0.0001, Adjusted R2 = 0.2784).Increasing deleterious mutation rates by 10% decreased RAF by 1.158 ± 0.609, however this difference was marginally insignificant effect (t63937 = -1.903, p = 0.057). Under selection, this decrease became highly significant, decreasing deleterious mutation rate’s effect on RAF by 9.381 ± 0.924 (t63937 = -10.148, p < 0.0001). Increasing additive effect size showed a small increase in the number of rare alleles under no selection (2.288 ± 0.6658 rare alleles per unit increase in additive effect size; t63937 = 3.437, p = 0.0006). Under stabilising selection, this effect was reduced by 5.113 ± 0.894 rare alleles (t63937 = -5.721, p < 0.0001). Under null conditions, the RAF reduction due to increasing deleterious mutation rate decreases by a further 3.020 ± 0.893 for a unit increase in additive effect size (t63937 = -3.388, p = 0.0007). Hence, increasing deleterious mutation rate reduces RAF to a greater extent under higher additive effect sizes. Under selection, this effect was reversed; the RAF reduction due to deleterious mutation is alleviated by 12.437 ± 1.314 units for a unit increase in additive effect size (t63937 = 9.464, p < 0.0001). This implies that deleterious mutation rate reduces RAF to a greater extent under lower additive effect sizes when under stabilising selection. The effects of additive effect size and deleterious mutation rate were highly visible in terms of the distributions of segregating alleles (Figure 7). The total numbers of all mutations decreased with increasing selective pressures (either by the presence of stabilising selection in Figure 7B or increasing deleterious mutation rates).

# Discussion

Surprising result: deleterious mutation reduces distance to optimum under maintenance, particularly under large size effects; still anchored in quant gen theory, even though pop gen predicts the opposite; pop gen – Ne reduced with BS, decreased variation expected, worse selection, more drift etc.

We found that increasing rates of deleterious mutation resulted in populations being more able to maintain their position around the optimum, overcoming some of the difficulties of fending with large-effect alleles that may pull populations away from the optimum (Figures 3, 5). Although it may at first seem counter-intuitive that stronger background selection increases the ability of populations to maintain their position at an optimum (Figure 5, 6), the effect can be explained with existing quantitative genetics expectations. To understand this, we must first explore the population genetics expectations of the effects of background selection on adaptation, and distinguish the difference in expectations between a population approaching the optimum and maintaining its position once it has arrived there.

It is well understood in population genetics that background selection reduces effective population size, reducing the effectiveness of selection and increasing the strength of genetic drift (Charlesworth *et al.* 1997; Houle 1998). As deleterious mutations are removed from the population, close-by linked QTLs are also removed (Charlesworth and Charlesworth 2010). The effect of this is decreased genetic diversity. In population genetics studies this is usually expressed in terms of FST or , whereas in quantitative genetics the analog is additive genetic variance (Falconer 1996; Charlesworth *et al.* 1997). Reductions in VA with increasing background selection were observed in this study, supporting this expectation (Figure 3A, 4). The expected effect of this on adaptation is quite clear when considering the initial approach towards the optimum: in quantitative genetics models, genetic variability is expected to increase the trait space that populations are able to explore, improving their ability to travel towards an optimum (Fisher 1930; Charlesworth and Charlesworth 2010; Aguirre *et al.* 2014). Indeed, these theoretical expectations have been found in natural populations: for example, Pujol and Pannell (2008) showed that populations of annual mercury, *Mercualis annua,* were able to respond to selection for pollen production when standing genetic variation was higher. Similarly, studies into the adaptation of red flour beetle (*Tribolium castaneum*) populations to new niches found high standing variation decreased the likelihood of extinction, and increased rates of niche expansion (Agashe and Bolnick 2010; Agashe *et al.* 2011). However, these expectations do not describe what we found in the current study: the most well-adapted populations consistently have higher rates of deleterious mutation, and hence lower standing genetic variance. The key to this lies in the expectations of the *maintenance* of variation and fitness around an optimum rather than the *approach* towards said optimum. The expectations surrounding this temporal space is considerably less extensive than that of the adaptive walk.

While reduced standing variation is expected to increase the time a population takes to reach an optimum (or perhaps prevent populations from reaching it at all), once a population has reached its optimum or stabilizes around its ‘local optimum’, the closest position it can maintain given the selected traits’ genetic architectures, mutation rates, and the population size – where does the population go?

In theoretical quantitative genetics, much debate is had over which particular models best describe the maintenance of variation in the presence of stabilizing selection over time. Selection is able to retain variation, particularly in large populations where drift is weak, and scenarios where balancing selection creates a non-linear fitness landscape, however the extent of this differs depending on many factors, including selection strength, genetic architectures, epistatic and dominant interactions, and the strength of selection relative to mutation (Walsh and Lynch 2018). Understanding the relative strength of selection to mutation has led to two distinct approximations of expected distributions of allelic effects. When mutation is much stronger than selection, Kimura (**1965a**) and Fleming’s (**1979**) Gaussian approximation holds true, whereas when the opposite occurs, Turelli’s (**1984**) house of cards approximation is more accurate. This distinction between models is arbitrarily granular, mostly for analytical viability. Computational methods allow for a continuous exploration of this space of models.

Figure 3: decrease in var with deleterious mutation is analogous to effects of lower Ne, but on a per locus level rather than genome wide. Hence, gives a proxy of the assumptions of CoA models with N -> Inf

Loss of fitness due to variation around optimum: expected to be 1/4Ne without any background selection (will vary with Ne due to effect on local Ne ) – Lande 1976

# Snippets

Underpinning this model is the continuum of alleles model of allelic effects, suggesting large numbers of alleles at many loci forming a continuous distribution of effect sizes, usually Normal in shape (Lande).

Pleiotropy fundamentally alters the signatures of HCA vs Gaussian approximation in COA so they approach each other - other parameters may as well?

Most effort in understanding stabilizing selection has focused on assuming either a Gaussian (as in this paper) or quadratic fitness function

Pleiotropy also had strong effects, due to contributing more than one trait value per mutation. Increasing pleiotropy rate by 10% increased RAF by 59.366 ± 2.531 alleles under no selection (t63937 = 23.458, p < 0.0001). Increasing deleterious mutation with pleiotropy rate significantly reduced this effect, with a 10% increase in pleiotropy rate and deleterious mutation rate simultaneously leading to a total loss of 22.555 ± 5.994 alleles (t63937 = -17.795, p < 0.0001). Under stabilising selection, a simultaneous 10% increase in pleiotropy rate and deleterious mutation rate led to an increase of 23.553 ± 8.567 alleles (t63937 = 19.193, p < 0.0001).

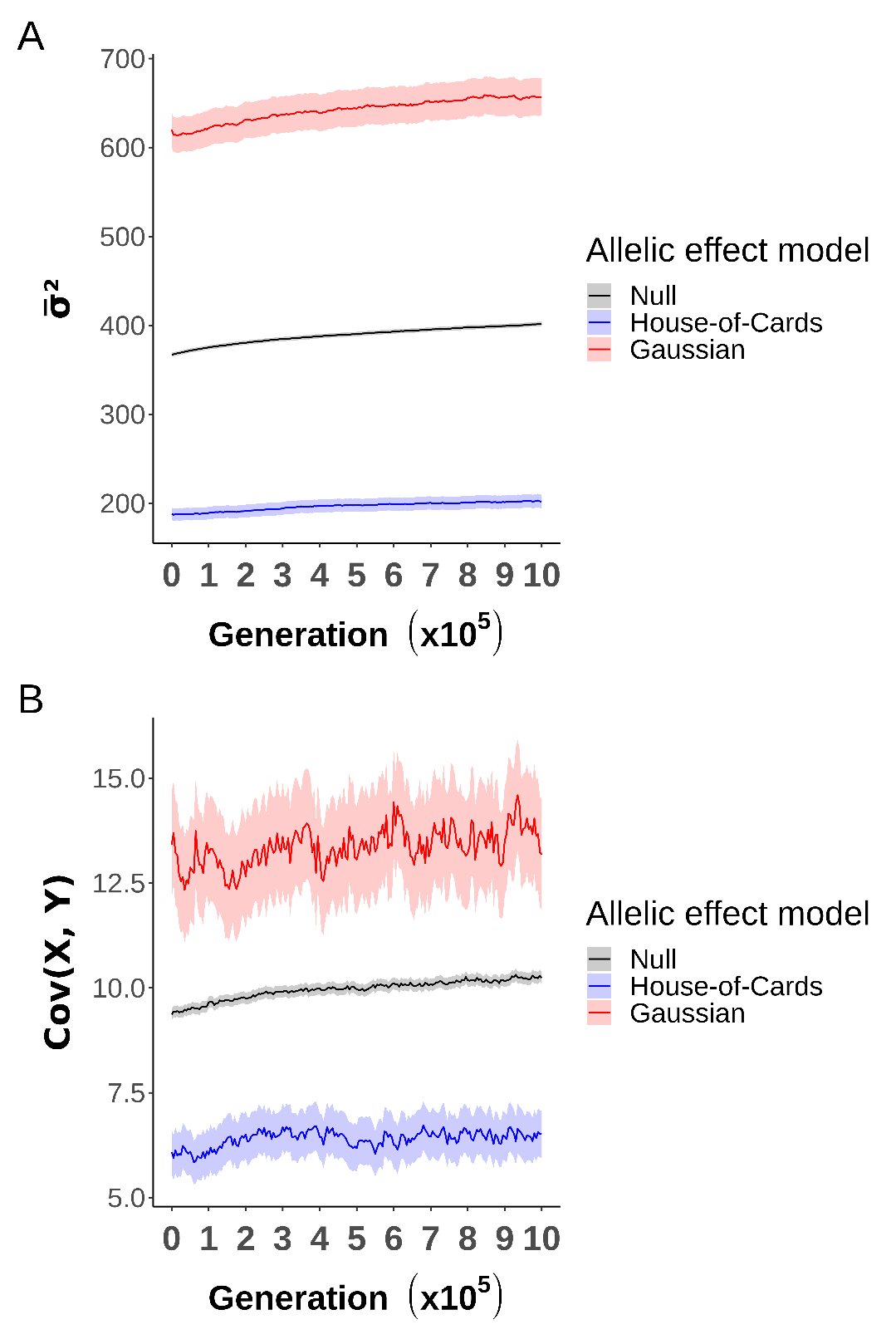


Figure 3 – Mean trait variance (A) and mean between-trait covariance (B) over 100,000 generations of stabilizing selection of different strengths (). 256 total models were sampled across the spectrum of selection strengths () with an additional 1024 models sampling the null space of parameters ().

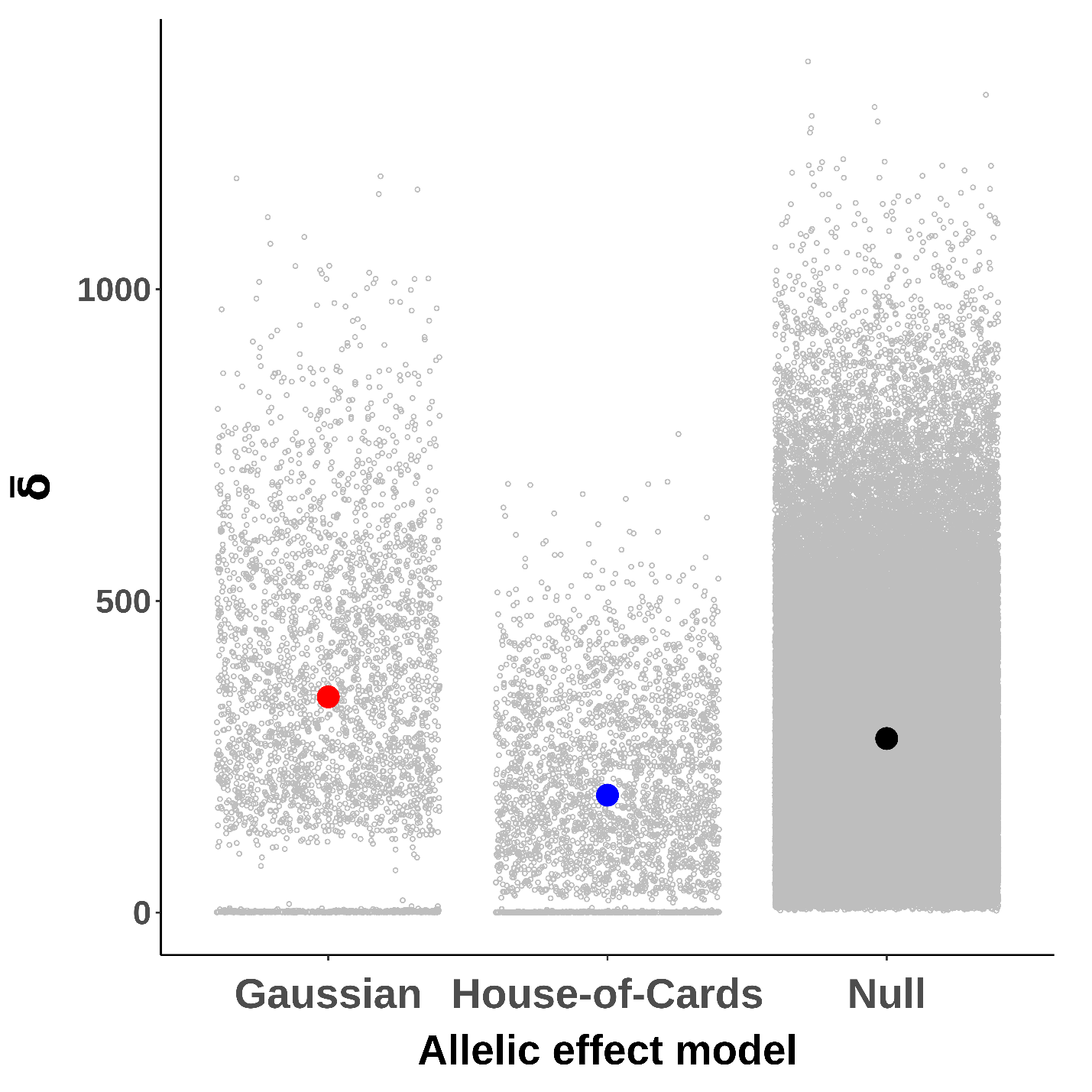


Figure 4: Spread of Euclidean distances from the optimum over models. Grey circles represent populations, filled circles represent means. In Gaussian and House-of-Cards models, the bottom populations close to 0 distance represent adapted populations. Whilst others further away are maladapted.

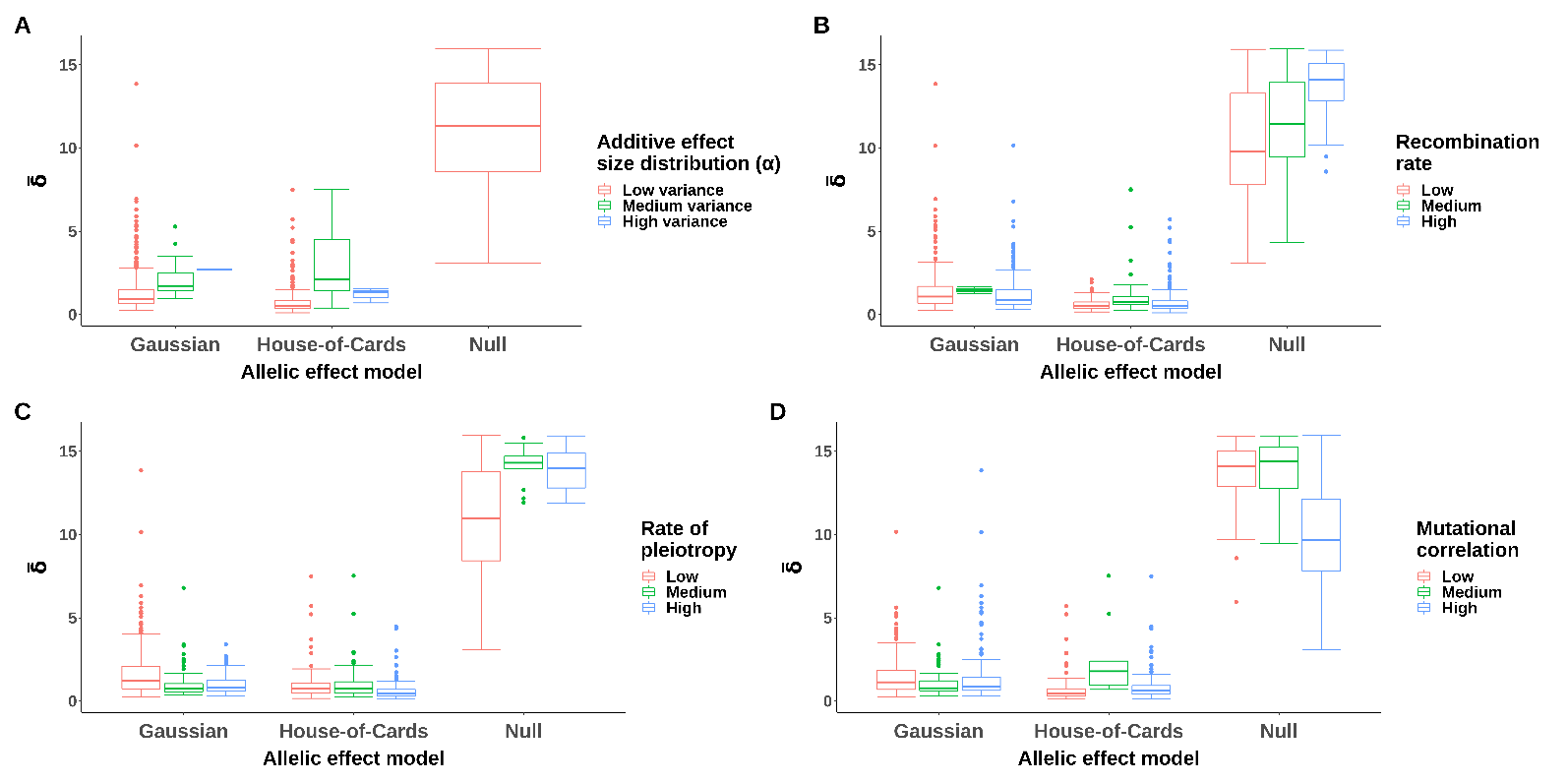


Figure 5: Euclidean distances from the optimum () among adapted populations with increasing additive effect size (A), per-locus recombination rate (B), pleiotropy (C), and mutational correlations (D). Note that there were no adapted populations with medium or high additive effect size distributions, as shown in (A).

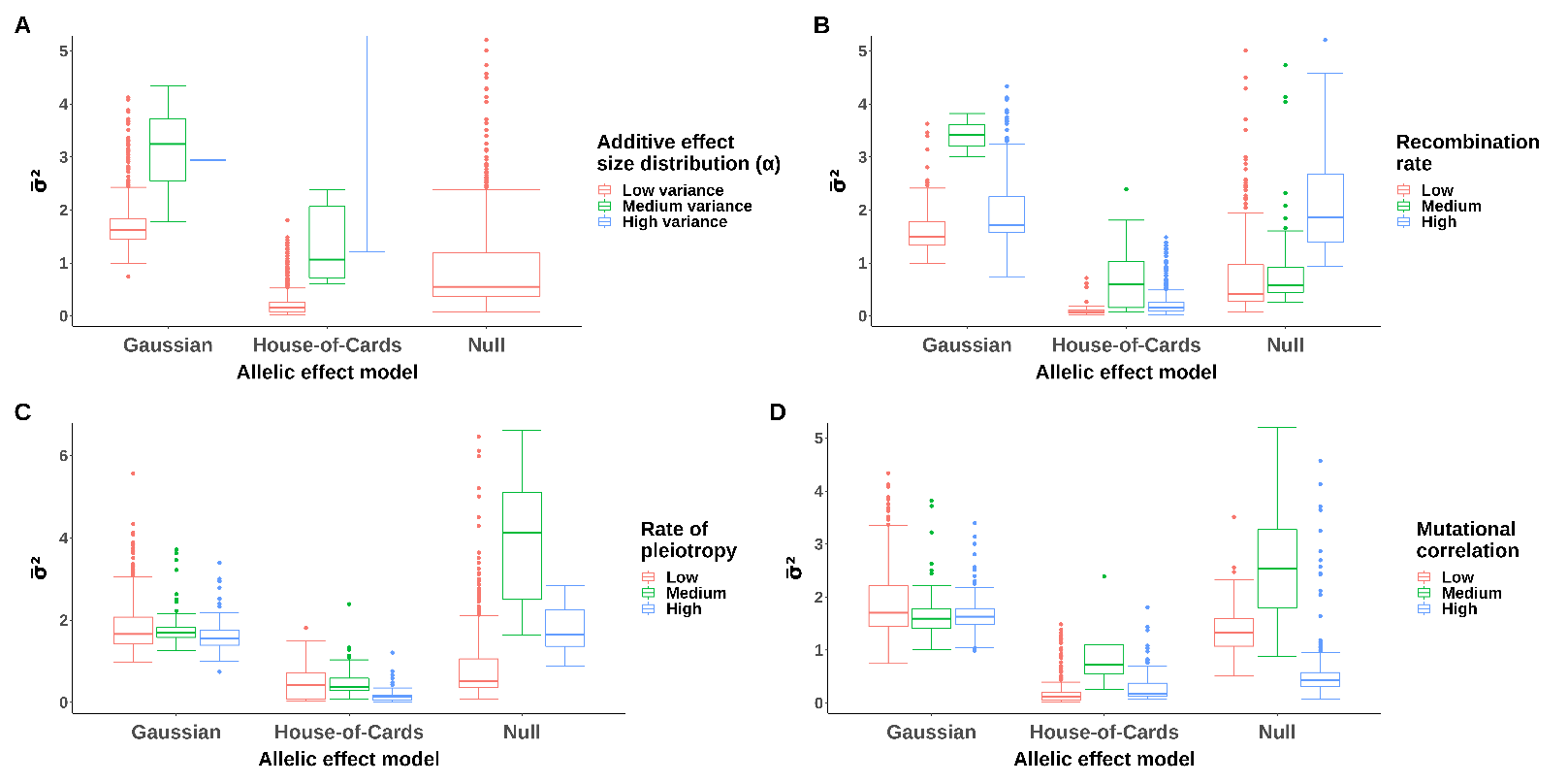


Figure 6: Mean trait variance () among adapted populations with increasing additive effect size (A), per-locus recombination rate (B), pleiotropy (C), and mutational correlations (D). Figures represent 94% of data points. For full data, refer to figure SX.

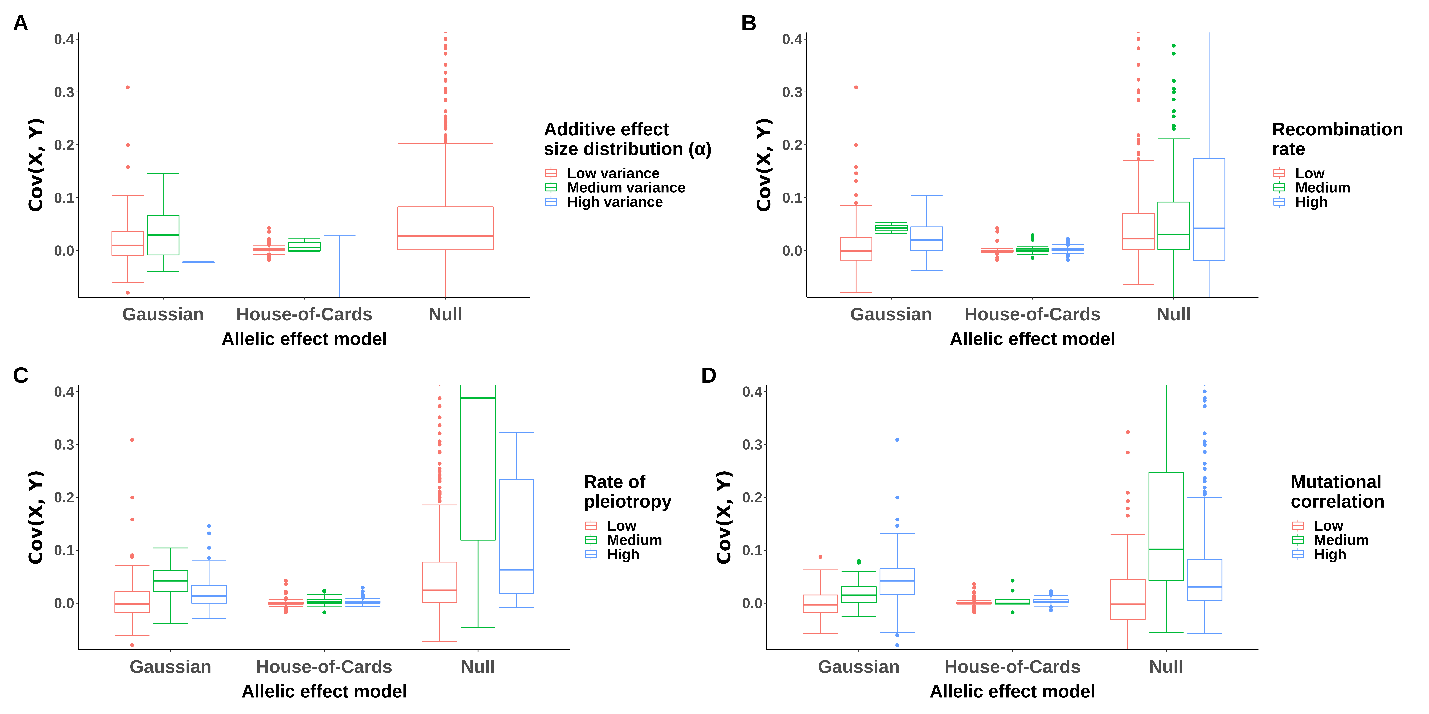


Figure 7 Mean trait covariance among adapted populations with increasing additive effect size (A), per-locus recombination rate (B), pleiotropy (C), and mutational correlations (D). Figures represent 98% of data points. For full data, refer to figure SX.

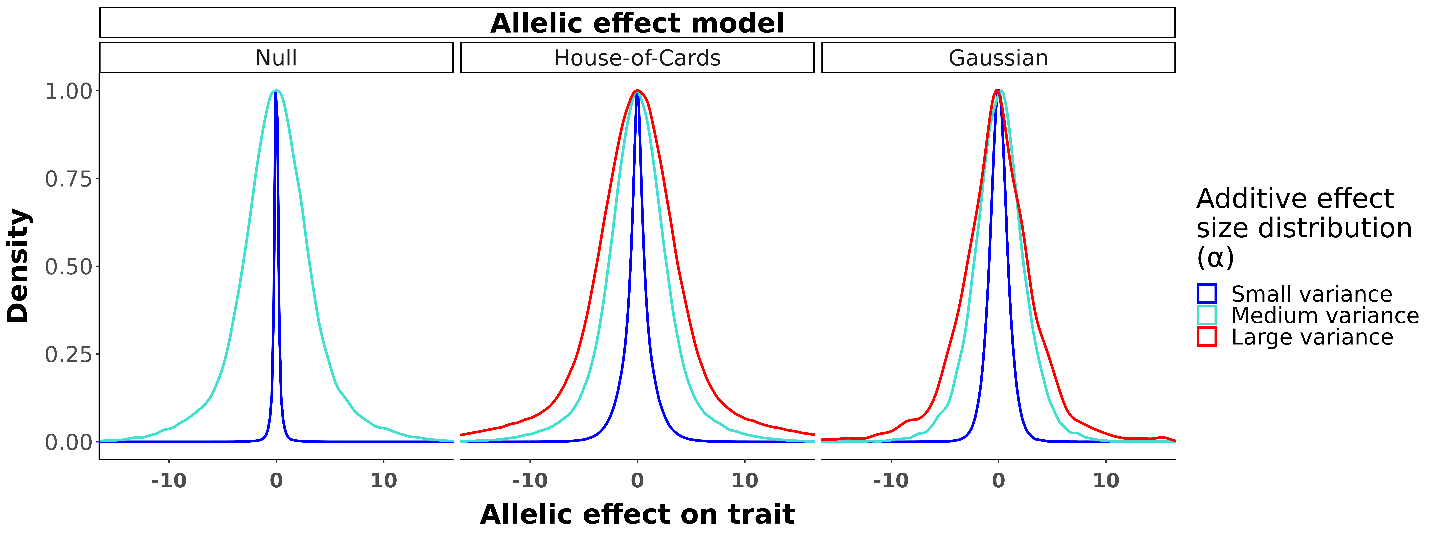


Figure 7: Density estimates of mutational effect sizes for adapted populations at generation 100,000 under different Continuum of Alleles models, with additive effect size distribution. 256 of the 1024 null models were randomly sampled to calculate the densities of null models.

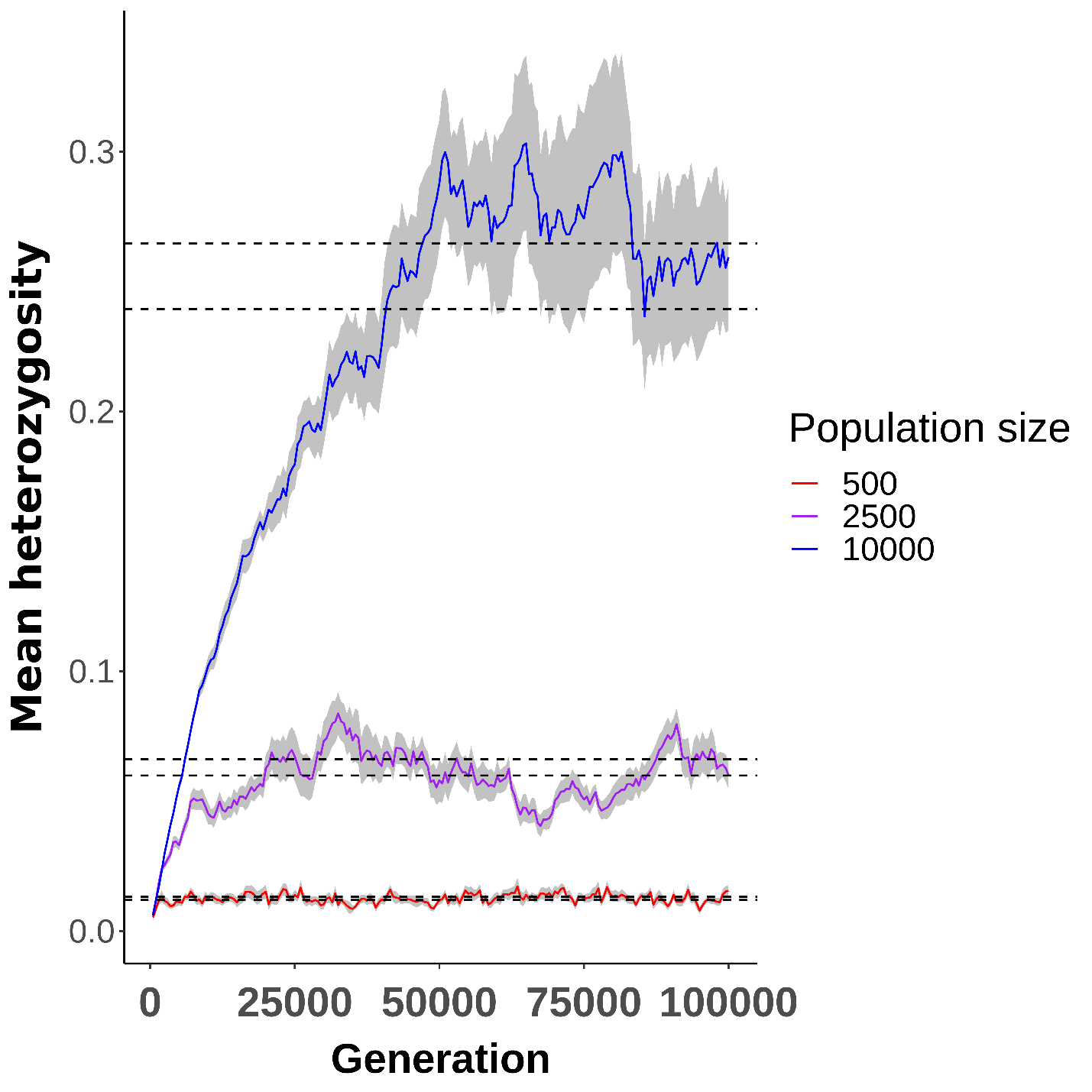


Figure S1: Mean population heterozygosity over time. Lines represent mean trajectories of 20 replicates, with ribbons representing standard errors. Dotted lines represent expected heterozygosities ± 5%, given by .

Table 2: Contingency table populations that reached the optimum (adapted) or failed to reach the optimum (maladapted). Model indicates the Continuum of Alleles assumption used to define relative strengths of mutation and selection. Outer figures are marginal counts.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Model | | | |  |
| Outcome |  | Gaussian | House-of-Cards | Null |  |
| Adapted | 472 | 467 | 545 | 1484 |
| Maladapted | 2628 | 2433 | 101855 | 106916 |
|  | 3100 | 2900 | 102400 | 108400 |

Table 1: Model parameters for both null and stabilizing selection models. The range of values is based on literature, but values are adjusted to be practical for the time of the experiment.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | Symbol | Range | Description | Source(s) |
| Genome wide recombination rate | r | 0 to 1.241x10-4 per locus | The singular recombination rate used across the entire simulated genome. | Stapley et al. 2017 |
| Background selection rate | δ | 0 to 1 | The number of non-trait, deleterious mutations that occur relative to trait mutations. |  |
| Rate of universal pleiotropy | ϖ | 0 to 0.5 | The proportion of trait mutations that affect all traits rather than a single trait. While 100 loci control a trait independently by default, this may be changed by this parameter. However ratios of loci affecting each trait will remain constant, especially across multiple replicates. | Chesmore et al. 2017; |
| Mutational pleiotropic correlation | m | 0 to 0.5 | The mutational correlation between additive effects of pleiotropic mutations determines the similarity of trait effects between traits for the same pleiotropic mutation. |  |
| Additive effect size | λ | 0.1 to 10 | Additive effect size controls the variance of trait effect size around mean 0, so that N(0, λ). | Albert et al. 2008; |
| Selection strength (selection model only) |  | 10 to 10000 | The parameter that controls the curve of the fitness function (eq. 3), with higher values resulting in a smaller difference in fitness between trait-differing individuals. |  |

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