Dissecting fluctuating selection: A unified population and quantitative genetics framework

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Abstract

One of the longstanding debates in evolutionary biology is the effect of fluctuating selection on genetic changes in populations. However, the extent to which these periodic forces influence organisms at both genomic and phenotypic levels remains unclear. Despite the compelling evidence of fluctuating selection from recent studies, there is a disconnect between empirical and theoretical findings concerning the underlying mechanisms due to the limited evidence regarding the scale and processes that generate stable genome-wide oscillations. This study aims to elucidate the genetic and ecological factors driving fluctuating selection and to identify the parameters that produce consistent oscillatory patterns. We developed a modeling framework integrating quantitative and population genetics to simulate a population under various selection regimes. We applied spectral analysis to detect periodicity, indicating cyclical selective environments. Our simulations highlight the conditions sustaining oscillations in allele frequencies over time. Spectral analysis successfully identifies the periodic patterns from allele frequency, even under highly complex selection regimes. Not only does our study clarify the conditions that yield long-term oscillatory behaviors, but these parameters are also relatively easy to predict from natural populations, providing a possibility of empirically testing these models.

Keywords: Fluctuating selection, oscillating allele frequency, quantitative genetics, population genetics, spectral analysis, evolution

Significance statement

As genomic data is becoming increasingly available for different species across time, one observation are patterns where alleles oscillate in a seasonal pattern, which has been interpreted as a signature of fluctuating selection. However, the field lacks theoretical models that predict these persistent oscillations in allele frequencies caused by fluctuating selection. We develop such a

theoretical model, defining the conditions under which persistent, strong oscillations in allele frequencies are predicted to occur because of fluctuating selection. In addition, we develop a novel method to detect patterns of fluctuating selection from genomic data using spectral analysis. Our model considers key parameters that are measurable in real populations, which is an added advantage to test them empirically. Our research paves the way for field biologists to test our predictions and brings us closer to reliably forecasting how populations will evolve in environments that are frequently changing.

Introduction

Understanding the dynamic nature of evolution in populations is at the core of evolutionary biology. The direction and intensity of selection can vary significantly through time (Grant & Grant 2002; Bell 2010; Campbell-Staton et al. 2017; Endler 2020). Various factors can lead to these fluctuations, perhaps the most notable of these being seasonal variability. In addition, as climate change imposes unprecedented alterations in conditions across the globe, fluctuations in selection pressure are predicted to intensify (Gienapp et al. 2014). Thus, the ability to predict how a population will evolve in response to dynamic environmental conditions has implications for the future of biodiversity. However, while there is widespread appreciation for the relevance of fluctuating selection for populations (Bergland et al. 2014; Yair & Coop 2022; Van Buskirk & Smith 2021; Pfenninger & Foucault 2022; Thomas E Reed et al. 2011; Bitter et al. 2024; Nunez et al. 2024), we still lack a clear understanding of the potential impact of fluctuating selection on genome-wide allele frequency dynamics, and what the genomic signature of fluctuating selection will be under different conditions.

Many empirical studies have shown that strong selective pressures can produce rapid phenotypic and genomic changes across diverse species, a phenomenon that has been vigorously documented

not only in domesticated plants and animals (Trut et al. 2009; Doebley et al. 2006) but also in wild populations exposed to well-defined selective pressures (Campbell-Staton et al. 2017; Waldvogel et al. 2018; Grant & Grant 2002) and through laboratory experiments (Burke et al. 2010; Tenaillon et al. 2016; Bersaglieri et al. 2004). Furthermore, the direction and intensity of selection have been shown to fluctuate over time (Bell 2010; Campbell-Staton et al. 2017; Roberts Kingman et al. 2021; Abdul-Rahman et al. 2021; Kelly 2022; Gossmann et al. 2014; Grant & Grant 2002) due to various factors, including seasonal temperature variability, boom and bust cycles of predator populations, and other biotic and abiotic agents (Waldvogel et al. 2018; Rusuwa et al. 2022; McAdam et al. 2019; Van Buskirk & Smith 2021; Louthan & Kay 2011). In natural populations, a recent observation is very rapid changes in allele frequencies, with some oscillating back and forth corresponding with the seasonal cycle, (e.g., (Behrman et al. 2018; Machado et al. 2021; Pfenninger & Foucault 2022; Rudman et al. 2022)), with the explanation for the pattern being fluctuating seasonal selection. For example, Behrman et al. 2018 suggested that seasonal changes in bacterial populations infecting fruit flies, *Drosophila melanogaster (D. melanogaster)* cause seasonal cycling of allele frequencies in immunity-related genes. In addition, Pfenninger & Foucault (2022), studied fluctuating environments using *Chironomus riparius* and found similar results with those reported from the previous studies of *D. melanogaster* (Behrman et al. 2018; Bitter et al. 2024; Machado et al. 2021; Rudman et al. 2022) about the genomic and phenotypic changes brought by the seasonal environment on natural populations.

Despite the many empirical examples identifying recurrently oscillating allele frequencies and attributing the cause to fluctuating selection, population genetic models that include fluctuating selection coefficients generally find only a narrow range of parameter space leading to stable oscillations in allele frequencies (Hoekstra et al. 1985; Wittmann et al. 2017; Bertram & Masel

2019). This disconnect between theory and empirical results has led to disagreement and uncertainty in whether the observed empirical patterns of oscillating allele frequencies are a genomic signature of fluctuating selection or an experimental artifact, or some other mechanism, such as short-term changes from recent selection and demographic alterations (Bertram & Masel 2019; Glaser-Schmitt et al. 2021; Lynch et al. 2024). Previous theoretical models of fluctuating selection have typically fallen broadly into two classes: 1) population genetic models that focus on predicting allele frequency trajectories, often focusing on a single or very few loci, and modeling fluctuating selection coefficients directly on loci; and 2) quantitative genetic models that focus on predicting phenotypic trajectories and typically assume a polygenic (often infinitesimal) genetic architecture defined by emergent genetic properties (i.e. heritabilities and genetic correlations) and often ignored the dynamics of individual loci. Past computational limitations of tracking loci genome-wide motivated the contrast in these two approaches, but while these limits have been diminishing rapidly over time, most models still fall largely into one of these two frameworks without fully bridging these approaches, a gap in the field that has been noted by others (e.g., Barghi *et al.* 2020). Many previous quantitative genetic models of fluctuating selection have produced robust predictions for resulting phenotypic evolution (Gillespie 1973, 1977), the evolution of phenotypic plasticity and bet-hedging (Roff 1997), and the maintenance of genetic variation (Bürger & Ghnelfarb 1999; Ellner & Hairston Jnr 1994)**.** While most previous population genetic approaches to fluctuating selection focused on allele frequency dynamics have found only very limited conditions that will lead to stable oscillations in allele frequencies, recently, some models have considered more complex scenarios to define the parameters under which allele frequency oscillations are possible. For example, Wittmann et al. found the maintenance of polymorphism on hundreds of loci under a segregating lift mechanism, in which heterozygotes

achieve higher geometric fitness across seasons (Wittmann et al. 2017). Furthermore, the extension of these models indicates that additional parameters, such as the reversal of dominance, population demography, and mechanisms like dormancy, might as well explain the perceived temporal oscillating polymorphisms(Bertram & Masel 2019; Glaser-Schmitt et al. 2021), even though validation is still required. An important detail of most population genetic approaches is that they assign a specific selection coefficient to each locus under consideration, with the selection coefficient remaining constant within each seasonal period. However, in nature, selection acts on the phenotype and genome dynamics can be quite different when selection is modeled at the phenotypic level with fluctuating optima, rather than with a fluctuating selection coefficient acting directly at specific loci. In particular, under a fluctuating optima model, the selection pressure acting at loci will decrease as the population approaches the new optimum. Thus, we might expect very different patterns of genome dynamics in a model integrating quantitative genetic and population genetic approaches in exploring the genomic signature of fluctuating selection in different conditions.

Here, we develop a general modeling framework integrating population genetic and quantitative genetic approaches, implemented in the powerful and flexible simulation software SLiM (Haller & Messer 2023). As in other quantitative genetic models, we parameterize the model by assigning a trait heritability and defining specific trait optima and fitness functions based on phenotypic values. Like population genetic models, we specifically consider individual loci genome-wide, tracking frequency changes over time due to the forces of genetic drift and selection. We sought to identify:

1) The parameter space in which fluctuating phenotypic optima lead to a clear genomic signature of persistent oscillating allele frequencies

2) The circumstances in which the genomic signature of fluctuating selection can be inferred from allele frequency and phenotypic data

Acquiring knowledge about the above objectives will not only help us understand evolutionary dynamics, but it will also help in implementing accurate predictive models of evolution, especially currently, where species are experiencing novel environmental shifts due to climate change.

Methods

We used SLiM V4.2.2 (Haller & Messer 2023) to simulate a set of Wright-Fisher models including a null model, a new constant optimum model, and a set of models with fluctuating optima. In all models, the population size was constant at 10,000 individuals and run for 2000 generations, and we assumed sexual reproduction with an equal sex ratio, random mating, no new mutations, and a recombination rate of 10^{-8}, which is a commonly used value in other SLiM models (Haller & Messer 2023), reflecting the average recombination rate for many mammals (Dumont & Payseur 2008). An overall schematic of our modeling approach, as well as the different models considered, is in Figure 1.

Genomic Characteristics & Generating the Initial Population

We modeled a phenotype with a known set of causative quantitative trait loci (QTL). The number of QTL contributing to the phenotype was set as L, with parameter values of 1, 10, 70, 100, or 300. We set a genome size to be approximately 1.2MB for an autosomal chromosome, with QTL spaced equidistantly across the genome. For each QTL, the effect of the locus on the phenotype was drawn from exponential distribution with a rate parameter $\lambda = 1$, which assumes most loci have minor effects on the phenotype and a few have a large effect size (Barton et al. 2017). The initial allele frequency also varied among the causative loci. In the initial population, by drawing from a

uniform distribution ranging from 0 to 1, we assigned a probability that an individual carries a given allele at the QTL. A draw from a binomial distribution determined whether a given individual harbored the allele at that locus. From this set of QTL, we assumed additivity and calculated a phenotype for each individual based on the initial heritability (h^2) of the phenotype. In all of our models, we considered initial heritability (h^2) parameter values of 0.1, 0.5, and 0.8. To generate the phenotype, we first calculated the genetic effect (G_j) for the *j*th individual as $G_j = \sum_{i=1}^{L} a_i e_i$, where a_i is the allele call at the *i*th locus, e_i is the effect size at the *i*th locus, and L is the number of QTL. To determine the environmental effect (E_j) for each individual, we first calculated the expected environmental variance from the heritability parameter (h^2) by rearranging the classic equation, $h^2 = \frac{V_A}{(V_A+V_E)}$ to $V_E = \frac{V_A}{h^2} - V_A$, where V_A is the additive genetic variance and V_E is the environmental variance (Sella & Barton 2019; Hayward & Sella 2022). Based on the distributions we used to generate the genetic effect, the expected additive genetic variance is $V_A = \frac{2}{3}L$, thus we used this value for all simulations to set the environmental variance. We then obtained an environmental effect (E_j) for each individual by drawing random values from a normal distribution with a mean of zero and standard deviation of $\sqrt{V_E}$. Thus, for the *j*th individual, the raw phenotype value was $P_j = G_j + E_j$. We did not include a term for genotype by environment interaction in this model, meaning it is not possible for phenotypic plasticity to evolve. Our method of generating effect sizes and a model of additivity means that models with more causative loci will produce phenotypes with higher numerical values. To ease comparison across models and maintain values on the same scale, we scaled all phenotypes by using the expected mean and standard deviation for the population phenotype. For our model parameters above, the expected phenotypic mean is: $\mu_P = L$, and the expected phenotypic standard deviation is $sd_p = \sqrt{\frac{VA}{h^2}}$. Thus, the scaled phenotype

is to $Z_j = \frac{P_j - \mu_p}{sd_p}$, with an expected adjusted mean of 0 and standard deviation of 1 to keep the phenotypes on a similar scale regardless of the number of contributing loci. The structure described above is summarized in Figure 1A.

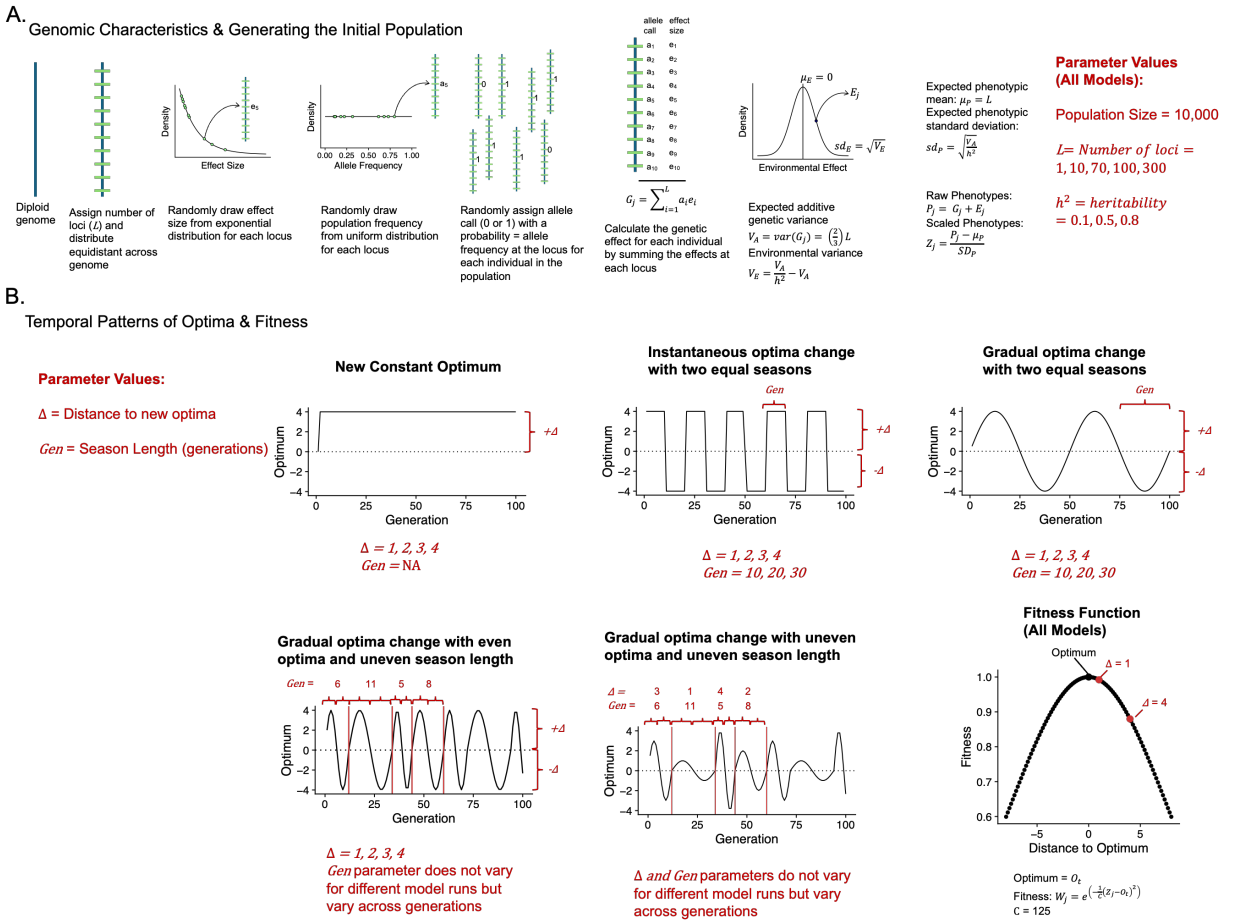

***Figure 1**. Schematic of the model simulations in SLiM with the model parameters defined. A. The genomic characteristics and process of generating the initial population allele frequencies and phenotypes. B. Overview of the models we considered excluding the null model showing the different patterns of optima over time and the fitness function used in all models.*

Temporal Patterns of Optima and Fitness

We simulated six different types of models that differed in the temporal pattern of the optima over time including a null model, a new constant optimum model, and four different models in which

the optima fluctuate over time. These models and the fitness function are summarized in Figure 1B. As a null model, we performed simulations with the same genomic characteristics described above but with individuals assigned a random fitness value drawn from a uniform distribution ranging from 0.1 to 1. For all other models, an individual's fitness was dependent on the distance between an individual's phenotype and the optimum at a given timepoint as follows: $W_j = e^{\left(-\frac{1}{C}(Z_j - O_t)^2\right)}$, where W_j is the *j*th individual's fitness, Z_j is the *j*th individual's scaled phenotype value, O_t is the optimum at time *t,* and *C* is a constant that influences the steepness of the fitness surface. When the optimum shifts, the strength of selection experienced in the population can both be altered by altering how far the optimum moves and by altering *C.* Because it is not necessary to change both these factors to change selection strength, we chose to keep *C* constant throughout all simulations at *C = 125* and only adjusted the distance the optimum shifts as a parameter.

(i) Constant new optimum

In the model where there is a single new constant optimum, the optimum is $O_t = \mu_z + \Delta\sigma_z$, where μ_z is the mean scaled phenotype in the initial population, $\sigma_z$is the standard deviation of the scaled phenotype in the initial population, and Δ is the distance to the new optima. We considered parameter values of 1, 2, 3, and 4 for the Δ parameter, which determined how far away the new optimum was from the initial population mean in units of standard deviations. In this constant model, the optimum shifted immediately at the start of the simulation and was constant for the entire simulation.

(ii) Two-season models with fluctuating optima

In our simplest fluctuating optima model, we simulated an optimum that shifted instantaneously between two values, each lasting a season length (*Gen)* in generations. The two optima were set

in the same way as the constant model, based on the initial population mean as follows: $O_t = \mu_z \pm \Delta\sigma_z$. The optimum switches between the (+) and (-) values, each for a period of *Gen* generations. We considered the following *Gen* parameter values: 10, 20, and 30. In nature, shifts between seasons often occur gradually (Gregory 2009; Oz et al. 2014). Thus, we also considered a two-season model (referred to a simple gradual model) where the shift in the two optima occurred gradually with the optimum at time *t* defined as: $O_t = \mu_z + \Delta\sigma_z * sin\left(2\pi * \frac{t}{Gen}\right)$.

Models with complex patterns of optima and season lengths

The above two season models kept the distance to the optima (Δ) and the season length (*Gen*) consistent across the entire simulation to serve as simple, general models. Actual patterns of fluctuating selection in nature are expected to more complex and variable over time. Thus, we simulated two models with additional complexity. These models included a situation in which the season length differed across four time periods (gradual optima change with even optima and uneven season length - referred to as complex gradual I), and a situation in which both the distance to the optima and the season length differed across four time periods (gradual optima change with uneven optima and uneven season length - referred to as complex gradual II). For both models, the optimum at time *t* is defined as: $O_t = \mu_z + \Delta_t\sigma_z * sin\left(2\pi * \frac{t}{Gen_t}\right)$. The difference here is that Δ_t and Gen_t vary across time. In the model of gradual optima change with even optima and uneven season length, Δ_t remains constant throughout the simulation and we consider the same parameter values of either 1, 2, 3, or 4. The Gen_tvalues follow a pattern of four time periods that then repeat of 12, 22, 10, 16. Within each of these four time periods, there is a single sinusoidal cycle, for example, the 12 generation period consists of 6 generations of a high optimum and six of a low optimum. In the model of gradual optima change with uneven optima and uneven season length,

the Gen_t parameter is set in the exact same way but the optimum also shifts in each of the four time periods in the following order: 3, 1, 4, 2. These models help understand complex evolutionary scenarios in which a population may experience a gradual change in optima with multiple sub-seasons, each resulting in a different number of generations and corresponding selection pressure, a typical situation for multivoltine organisms that exhibit different generation numbers over the seasons (Bjørnstad et al. 2016; Mendonça, Jr. & Romanowski 2012; Harvey et al. 2023; Subedi et al. 2023; Buckley et al. 2017).

Identifying signals of fluctuating selection from allele frequencies and phenotypes

We used ggplot2 (Wickham 2016) to visualize changes in allele frequency and the population mean phenotype over time. Furthermore, spectral analysis as a mathematical tool that decomposes a time-domain signal into its frequency-domain representation, it reveals how variance in a time series is distributed across different frequencies (Jenkins 1965; Shumway & Stoffer 2017). Although it may not identify the underlying biological background, spectral analysis can detect periodic components and their strength in a well sampled timeseries. Consequently, we used spectral analysis to decompose the allele frequency signal and identify seasonality (selection length), which enabled us to detect fluctuating selection in our dataset assuming the cyclic selection. Specifically, we first averaged the allele frequencies across all loci to obtain a single mean frequency per generation. We then organized these mean values into time-series, with each generation corresponding to a time point, to illustrate changes in allele frequency over time. Finally, we estimated the spectral density of each time series using the spectrum function from base R (R Core Team 2022) and applied a smoothing span of 2 to reduce noise and reveal the dominant periodic components. This approach enabled us to detect and characterize cyclical patterns in allele frequencies across generations.

Results

Our main focus in this project was comparing genome dynamics in different models of the temporal pattern of the optima across seasons. We compared a model with no relationship between the phenotype and fitness as a null model, a model with a single shift to a new constant optimum, and four models of fluctuating optima across time: (1) instantaneous optima change with two equal seasons, (2) gradual optima change with two equal seasons (simple gradual), (3) gradual optima change with four uneven seasons and even optima (complex gradual I), and (4) gradual optima change with four uneven seasons and uneven optima(complex gradual II). In all models we varied the parameters for heritability ($h^{2)}$ and the number of causative loci (L). In three of the four fluctuating optima models, we also examined the effect of the parameter for the distance to the optimum (Δ), which determines the strength of the selective event of a changed optimum. Finally, in the two models with two equal seasons, we varied the season length (Gen) as a parameter. Below, we summarize the major results, emphasizing the effects of different parameters and differences between the models. A full description of all results for all models is given in the supplementary information.

Higher heritability, stronger selection, and longer season length produce greater evolutionary changes across all models

As has been observed often in evolutionary models previously (Walsh & Lynch 2018), we observed larger changes in allele frequencies when the heritability was higher, the shift in the optimum was larger, and/or the season length and thus selection period was longer. This pattern is clear in the polygenic (100 causative loci) model of instantaneous optima change with two seasons, where one can see that seasonal oscillations in both the phenotype and the allele frequencies across the genome showed greater change when comparing low heritability to high heritability, a small

266 shift in optimum to a larger one, and a short season length to a longer one (Figure 2A & 2B). These
267 overall effects were consistent across all models that included selection (Supplementary
268 Information), showing that the population tracked the change in optima more closely in parameter
269 combinations with high heritability, stronger selection, and longer selection periods, as expected.

270 We performed spectral analysis to identify when the genome-wide allele frequency patterns in the
271 population showed periodicity (also termed recurrent seasonal shifts). In our fluctuating selection
272 models, spectral analysis confirmed the effects of heritability, selection strength, and season length
273 by showing more pronounced peaks under these same parameter values (Figure 2C;
274 Supplementary Information), indicating a stronger signal of periodicity for these parameter
275 combinations.

276 **Clear fluctuations in allele frequencies persist long-term in fluctuating selection models in**
277 **most parameter combinations**

278 Many previous population genetic models have modeled fluctuating selection by altering the
279 selection coefficient at specific loci between seasons and keeping this selection coefficient
280 constant within each seasonal cycle and have found that oscillations in allele frequencies do not
281 persist long-term across most of the parameter space. In contrast to this result, we find that our
282 shifting optima models of fluctuating selection typically lead to persistent oscillations in allele
283 frequencies and phenotypes over at least 2,000 generations. We see no evidence for an overall
284 diminishment of these oscillations in either the allele frequency patterns or the phenotypic pattern
285 across time (Figure 2; Supplementary Information). This result is consistent for most parameter
286 combinations in all of our fluctuating selection models (Supplementary Information). The two
287 exceptions to this overall pattern either 1) when the parameter combination does not lead to
288 discernable seasonal oscillations across the entire time period, or 2) when the phenotype is

289 determined by few loci and these go to fixation, thus preventing future oscillation. We detail the
290 parameter space in which we observe these two cases in the sections below.

291 While in many parameter combinations the seasonal oscillation of allele frequencies is obvious
292 visually (e.g. Figure 2A, bottom right plot), even in parameter combinations where these
293 oscillations are more subtle, spectral analysis is often able to detect the recurrent periodicity. This
294 ability is clear in the example of the polygenic model of instantaneous optima change with two
295 seasons in the combination of low heritability ($h^2 = 0.1$), weaker selection strength ($\Delta = 1$), and
296 shorter selection length (Gen = 10) where the oscillations in allele frequencies are not visually
297 obvious (Figure 2A) but spectral analysis detects a clear peak at the correct periodicity of 20
298 generations for a full seasonal cycle of 10 generations in each of the two seasons (Figure 2C). This
299 same ability of spectral analysis to correctly identify periodicity even for parameter combinations
300 when individual allele frequency oscillations are subtle occurs for most of our fluctuating selection
301 models (Supplemental Information section 1.2). Although spectral analysis does successfully
302 detect periodicity in parameter combinations with more subtle allele frequency shifts, we note
303 there is more variability in spectral density in these parameter combinations (see Figure 2.C;
304 Supplemental information).

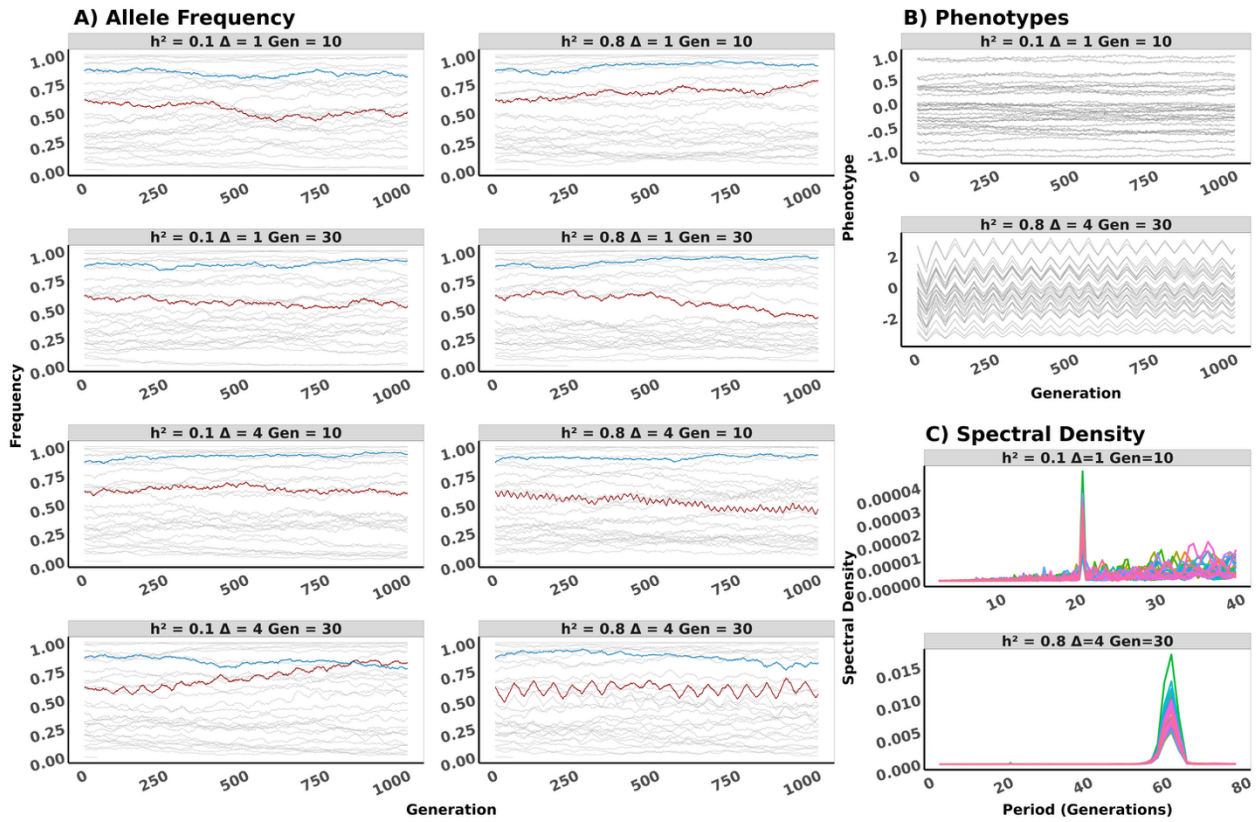

Figure 2. *Evolutionary dynamics for a population with polygenic trait (loci = 100) experiencing an instantaneous fluctuating selection.* ***A****. represents allele frequency dynamics and shows parameter combinations from a single replicate for 1000 generations. Each line in the plot represents the frequency trajectory of a locus among 30 loci randomly sampled from 100 loci, and the highlighted lines indicate loci with different initial frequencies and effect sizes(dark-red position having highest effect with blue having the smallest effect).* ***B.*** *Distribution of population mean phenotype dynamics representing 30 replicates over 1000 generations.* ***C.*** *The spectral density from allele frequency for all 2000 generations; each colored line represents a single replicate. The peak in the spectral plots marks a complete cycle of season length. The variables are heritability (h^2), selection strength (Δ: magnitude of the shift in the optimum), and the season length in terms of number of generations (Gen).*

Genetic architecture influences the rate of fixation of alleles

We also examined how the number of loci contributing to the trait in instantaneous selection model affects the observed evolutionary dynamics. Generally, the patterns described above for a

310 polygenic model extend to models with fewer causative loci, although fewer positions affecting
311 the trait for a given heritability tend to produce more pronounced oscillations in allele frequencies
312 and phenotypes (Figure 3A & 3B). The differences among the genetic architectures shown in
313 Figure 3 are driven by the fact that the heritability of the trait is held constant in each case. Thus,
314 for a given heritability, having fewer causative loci means that each of those loci will contribute a
315 larger share to the percentage of genetic variation for the trait and thus have a larger genetic effect.
316 Therefore, the observation that individual loci show greater fluctuations when there are fewer loci
317 is driven by this effect, rather than it being a feature of the genetic architecture itself. We observe
318 similar oscillations in the phenotype for different numbers of causative loci, though in the case of
319 a single locus, we do see cases where the phenotype becomes constant when one allele becomes
320 fixed, which does not occur when more than one locus affects the trait (Figure 3B).

321 Spectral analysis successfully identifies periodicity regardless of the number of causative loci. For
322 a given heritability, models with fewer causative loci often show distinct peaks with high spectral
323 densities, while polygenic traits typically have lower spectral densities (Figure 3C & Supplemental
324 information 1.2). Nevertheless, the greater variation in spectral peaks across replicates in single-
325 locus traits may demonstrate the susceptibility to genetic drift and high fixation rate. As a result,
326 even though the shifts are more subtle when there are more loci sharing the effect, the analysis
327 across all of them gives a well-defined signal. Ultimately, despite the differences, spectral analysis
328 reliably detects seasonality across all genetic architectures, particularly when considering
329 aggregate behavior across loci.

330 Finally, in addition to the described means of differentiating behaviors per genomic architecture,
331 we calculated the percentage of fixed loci in our simulations. The fixation rates are percentages
332 that were calculated as the ratio of the total number of fixed loci to the total number of loci from

all replicates, multiplied by 100. The results show that when relatively few loci affect the trait, the proportion of fixed alleles is substantially higher than in polygenic models (Figure 4). In polygenic traits, increasing the number of causative loci does not notably alter fixation rates, and other parameters (e.g., heritability or selection duration) have little impact on this outcome (Figure 4). When there are few causative loci and they become fixed, obviously continued oscillations in the phenotype and in allele frequencies cease. Thus, this increased rate of fixation when few loci influence the trait highlight a key parameter showing when we fail to see persistent seasonal oscillations in allele frequencies.

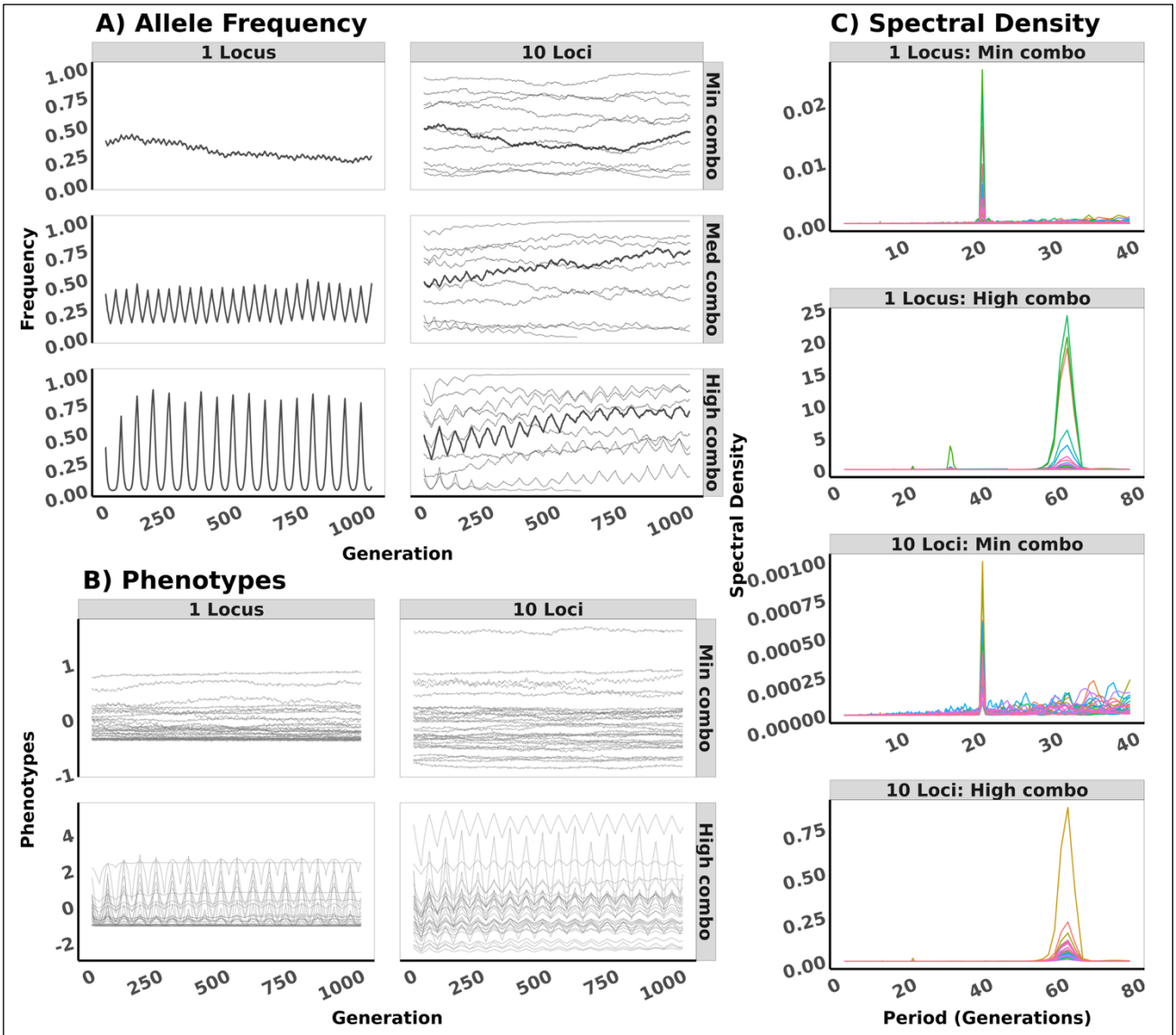

Figure 3. *Comparison of genetic architectures (1 locus and 10 loci traits) under instantaneous fluctuating selection.* ***A.*** *represents allele frequency dynamics for a single replicate for small (Min combo: h^2 = 0.1, Δ = 1, Gen = 10), medium (Med combo: h^2 = 0.5, Δ = 2, Gen = 20), and large (High combo: h^2 = 0.8, Δ = 4, Gen = 30) parameter combinations over 1000 generations. Each line represents the frequency trajectory of a locus, with a highlight of the dynamics in a single locus.* ***B.*** *Shows distribution of population means phenotype dynamics for 30 replicates over 1000 generations for both small and high parameter combinations in each architecture.* ***C.*** *Displays spectral density of allele frequency over 2000 generations, where each colored line represents a single replicate for both small and large parameter combinations for each architecture. The large peak in the spectral plot marks a complete cycle of the season length.*

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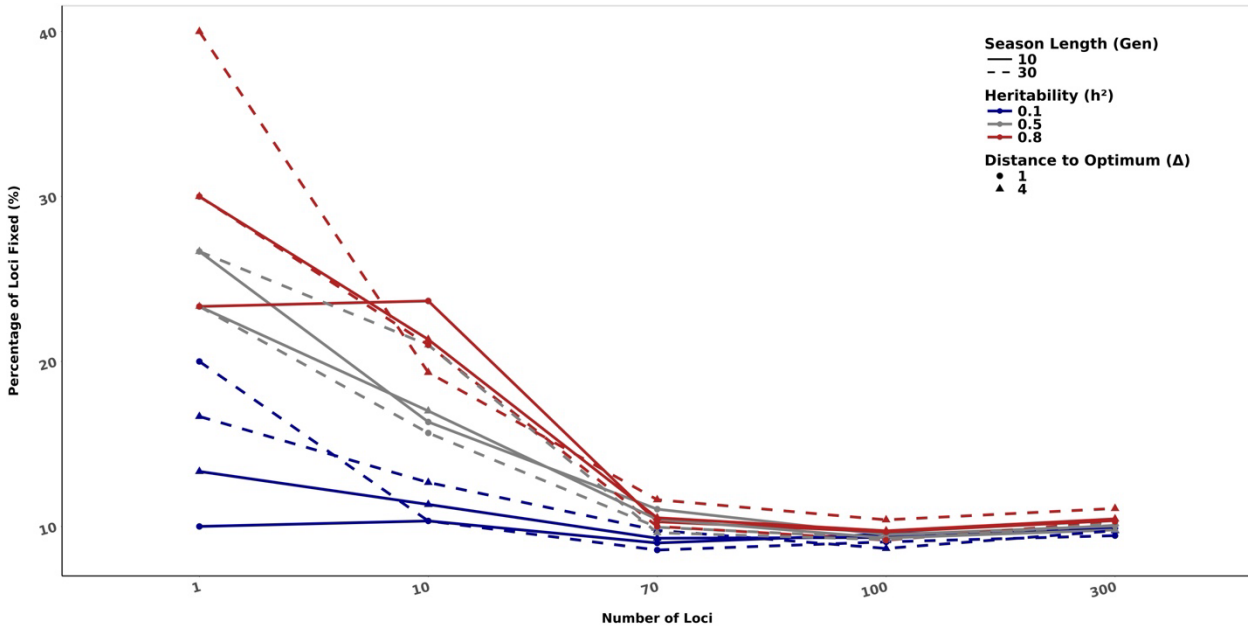

Figure 4. *Percentage of fixed loci across different genetic architectures based on parameter interactions from instantaneous selection model. The single locus trait exhibits the highest percentage of fixed loci among the 30 replicates, followed by the 10 loci model, while 70 loci or more shows a consistent fixation rate.*

More complex seasonal patterns are more difficult to detect

Above, we emphasized results from our most straightforward model, the instantaneous optima change with two seasons model. However, we also explored more complex and closer to realistic scenarios including a model of gradual optima change with two equal seasons and models of gradual optima change with uneven season lengths where each season consisted of two equal sub-seasons with even or uneven optima. These gradual-change models introduce selection more slowly, with smooth transitions between seasonal optima; hence, they may reflect natural environments where conditions do not shift abruptly. As the temporal pattern of change in the optima becomes more complex, it becomes more difficult to visually observe seasonal oscillations in allele frequences for a given parameter combination (Figure 5). Our most complex model is the

354 gradual optima change with uneven season length models because it involves different season
355 length (12, 22, 10, and 16 generations) in a single cycle, and it was further subdivided into two
356 variants 1) One with a Δ value that varies across models but not generation and 2) another that Δ
357 remains the same across models, but changes depending on the season length (see Figure 1). This
358 setup reflects scenarios with an asymmetric season length throughout the year or across life stages,
359 complicating evolutionary dynamics and blurring the distinction between allele frequency changes
360 driven by selection and by drift. In these more complex models, we see similar effects of
361 heritability, selection strength, and the number of causative loci as we described above
362 (Supplemental information 2.1 – 4.1).

363 Despite more subtle seasonal allele frequency shifts, spectral analysis can identify periodicity
364 effectively for most parameter combinations (Supplemental information 3.2 & 4.2). The limits to
365 detecting periodicity via spectral analysis become clear in the highly complex gradual optima
366 change with uneven season length model in parameter combinations with low heritability and/or
367 weak selection (Supplemental information, figures 3.2.1 & 3.2.2 upper left corner). These
368 parameter combinations are some of the few in which clear spectral peaks are difficult to detect
369 for any of our fluctuating selection models. While the complex model with varying *Δ* values and
370 season lengths may produce a peak under certain conditions, for instance low heritability, this peak
371 reflects mainly the selection strength during that period (Supplemental information section 4.2).
372 Consequently, it emphasizes how selection strength influences the ability to detect such signal
373 from genomic data. Once again, we observe that for a given heritability, while models where fewer
374 loci contribute to the heritability provide more readily observable patterns in allele frequencies,
375 spectral analysis across many loci produces more consistent results (Figure 6). Thus, in polygenic
376 models, one is more likely to reliably detect fluctuating selection genome-wide, though it may be

less discernable when examining individual loci in isolation. The results emphasize that genetic architecture and fluctuating selection pattern complexity significantly influence how populations respond to fluctuating environments. .

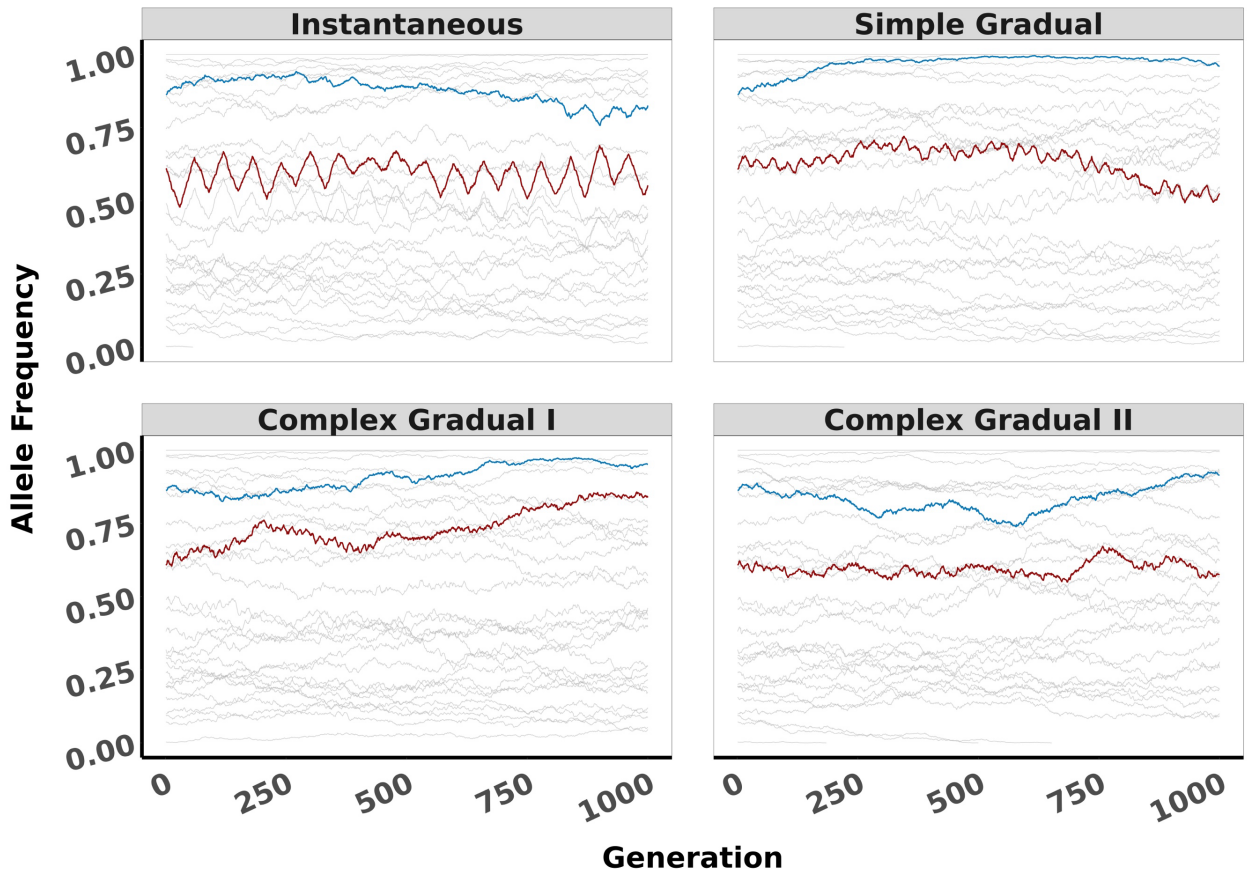

Figure 5*: Allele frequencies from 30 sampled loci out 100 to compare all fluctuating selections models with instantaneous and gradual selections. The instantaneous model shows clearer seasonal oscillations, followed by the gradual two-season, and finally gradual four unequal-season models. For two equal season models the heritability is h^2 = 0.8, with Δ=4, and Gen = 30. For the four uneven season lengths models with different distance to optima, Δ, values were set to 3, 1, 4, and 2 for generations 12, 22, 10, and 16, respectively. In the version of even the optima, the value is Δ=4 for all seasons. The highlighted lines indicate loci with different initial frequency and effect sizes(dark-red position having highest effect while blue has the smallest effect), where loci with higher effect and intermediate starting frequencies exhibit stronger oscillations.*

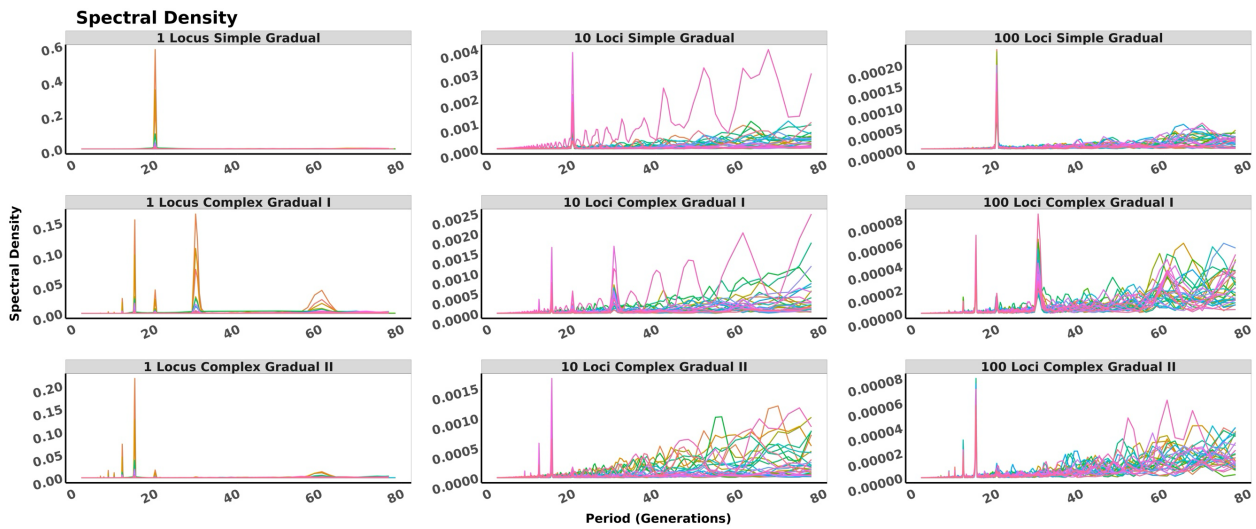

Figure 6: *Spectral analysis across 30 replicates for monogenic(left), oligogenic(middle), and polygenic(right) traits, with each colored is one replicate. For the simple gradual model, the parameters are* $h^2 = 0.5$, $\Delta = 2$, *and Gen = 20. Thus, the dominant spectral peaks occur at 40, consistent with a full seasonal cycle. Although the oligogenic model has more noise, the complex gradual model 1 (uneven season lengths and even distance to optima* Δ*) exhibit four distinct peaks alighed with the four-season lengths, plus a faded long period peak at 60 which signal the recurrence across multiple cycles. In complex gradual II (uneven season lengths and uneven* Δ*), the spectrum is noisier than other selection regimes, and it is challenging to observe all peaks corresponding to the number of considered seasons mainly because some seasons have a small selection pressure and the dynamics in those seasons are masked by the presence of seasons experiencing stronger selections.*

Difference between fluctuating selection models to null and constant selection models

Comparing fluctuating optima models with null and new constant optimum models is indispensable to fully understanding how fluctuating selection affects allele frequencies and phenotypes. Under both null and constant scenarios, neither allele frequencies (Figure 7) nor phenotype trajectories display clear seasonal oscillations, as confirmed by spectral density analyses (see supplemental file for more details: Sections 5 and 6 for null and constant selections, respectively).

In null models, there are random fluctuations with no discernible pattern mainly because allele frequencies change solely via genetic drift. That is, all the genetic architectures show similar allele

390 frequency dynamics, and loci with terminal initial frequency fix (Supplemental information, figure
391 5.1). By contrast, constant models exert steady selective pressures, leading to predictable shifts in
392 allele frequencies and phenotypes until they plateau, either when certain alleles fix, are lost, or
393 when the population reaches its optimum. The plateauing behavior is particularly pronounced in
394 polygenic models (Supplemental information, sections 6.1 and 6.2 for allele frequencies and
395 phenotypes, respectively, under constant selection). Monogenic traits under strong selection often
396 go to fixation more quickly, while polygenic and oligogenic traits tend to remain within specific
397 frequency ranges over many generations. Such behavior does not appear under null model, where
398 frequencies drift randomly. Despite these distinctions, spectral analyses of null and constant
399 selection models reveal no evident periodicity in either regime (Figure 7 lower panel. see also
400 supplemental information, section 5.3 and 6.3 for null and constant selections, respectively).
401 Consequently, it is difficult to pinpoint out the effects of individual parameters via spectral analysis
402 in these two models.

403 In contrast, fluctuating selection models, both instantaneous and gradual, introduce seasonally or
404 temporally varying selective pressures that can drive noticeable oscillations in allele frequencies
405 and phenotypes. These oscillations are especially marked in monogenic and oligogenic traits, as
406 well as in polygenic traits with high heritability under strong selection. However, when selection
407 intensities or heritability are low, the behavior of polygenic traits under fluctuating selection may
408 appear similar to that under null or constant selection (Figure 7). Insufficient selection pressure or
409 limited heritability prevents large frequency shifts and cause some alleles to remain in stable
410 ranges (mimicking constant selection) or to drift randomly (mimicking null model). As selection
411 intensity and heritability increase, however, the oscillatory patterns become more pronounced,

clearly setting fluctuating selection apart from either purely directional (constant) or random (null) processes.

The gradual two-season model often exhibits easily detectable seasonal oscillations in allele frequencies, much like the instantaneous model. In more complex scenarios, such as the four unequal season model, these oscillations may be harder to distinguish from null model, particularly for polygenic traits (Figure 7). At lower parameter values, the peaks in spectral analyses may be weak, resembling drift. Nonetheless, increasing certain parameters can amplify the oscillatory signal, making it possible to differentiate fluctuating selection from null model in some cases.

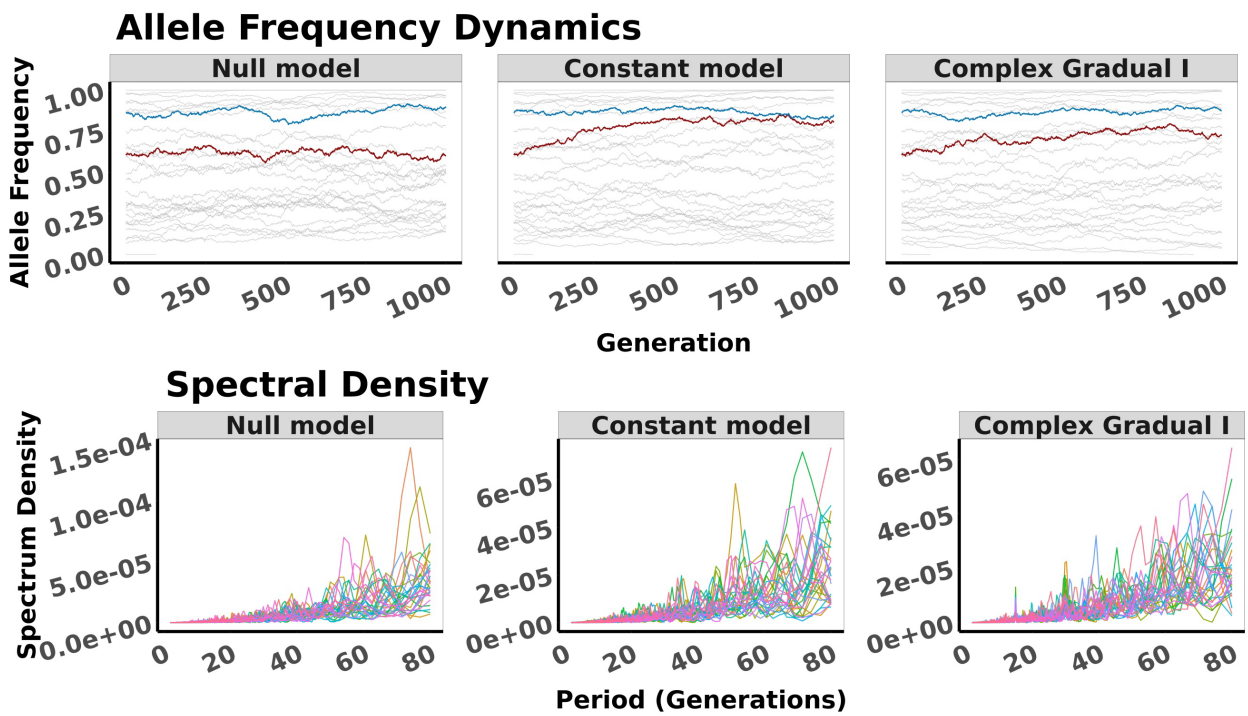

***Figure** 7: Comparison of polygenic allele frequency trajectories (L = 100 loci) and corresponding spectral densities (each line representing a single replicate) under lower parameter combinations ($\Delta = 1$ & $h^2 = 0.1$) among null, constant, and gradual uneven seasons and even Δ value. For allele frequency panel, only 30 loci of 100 are shown; the highlighted lines indicate loci with different initial frequency and effect sizes(dark-red position having highest effect with blue having the smallest effect). Not only that the allele frequency dynamics look similar, but also the spectral densities have many variations which can hinder the ability to distinguish models.*

Discussion

Parameters leading to persistent allele frequency oscillations

A topic of recent debate has been the conditions under which fluctuating selection will lead to stable oscillations that persist across time and whether the recently observed empirical results (Bergland et al. 2014) are genuinely due to fluctuating environmental conditions. To isolate the role of fluctuating selection in generating oscillatory polymorphisms, we model fluctuating selection under simplifying assumptions (e.g., constant population size, no migration, and no mutation). This allows us to evaluate whether fluctuating selection alone is enough to maintain oscillation. Also, it serves as a starting point to introducing more complex models with additional forces to test their interactions and the parameters considered in here. Previous models have produced mixed results, with some showing restrictive parameter spaces leading to long-term oscillations (Ellner & Hairston Jnr 1994; Glaser-Schmitt et al. 2021) and others suggest numerous loci may remain polymorphic under certain seasonal dominance assumptions (Wittmann et al. 2017) and protection from selection (Bertram & Masel 2019). However, it remains challenging to empirically verify those conditions, partly because dominance relationships and other relevant parameters, for instance, degree of protection, are often difficult to quantify in natural populations, as noted by the authors. In contrast, our study shifts focus away from dominance assumptions and emphasizes on parameters that are more readily estimated in natural populations (heritability, selection strength, season length, and the number of loci affecting trait). Although the study assumes known candidate loci, which can be challenging, their identification is becoming increasingly feasible with the advancement in sequencing technology, evolve and resequence experiments, and genome-wide association studies. Therefore, our study shows that oscillatory allele frequencies dynamics can persist for a long-term across many positions even under weak

selective pressure, particularly when selection acts instantaneously. However, the magnitude of these oscillations, scales directly with selection strength; thus, it is the primary determinant of how pronounced the cyclical patterns are, and the combination of selection strength with other parameters leads to numerous positions with long-term oscillations.

When both heritability and selection intensity were high, the population exhibited pronounced oscillations, a finding consistent with classical quantitative genetic theory (Bijma 2011; Barton & Turelli 1989; Hill & Mackay 2004). Moreover, with intermediate to high selection pressure and heritability, we can visually see those fluctuations at high amplitude, contradicting the claim that not all positions will experience strong selection (Nuzhdin & Turner 2013). Under these conditions, we observed marked fluctuations and, at times, near-fixation of alleles, consistent with other reports suggesting that increased selection intensity may lead to allele fixation (Wilson et al. 2014; Stephan 2019; Chevin 2019; Wientjes et al. 2022, 2023; Franssen et al. 2017). However, complete fixation is often prevented because the environment fluctuates, thereby maintaining numerous alleles at intermediate frequencies. Although some alleles can exhibit long-term oscillation, some of them may eventually stabilize or fix, while some others the previously stable alleles can sometimes begin to oscillate. Therefore, as scenario worth to explore in the future, we suspect that with recurrent mutation, new arising variant may also change oscillatory dynamics, as a result, even if oscillations at particular loci may fade, the oscillatory behavior at population level can persist. Furthermore, longer seasons grant sufficient time for selection to shift allele frequencies, as seen in the evolutionary experiment study by (Burke et al. 2010) and (Turner et al. 2011), and mean phenotypes toward the new optimum, accentuating oscillations. Conversely, smaller season lengths can diminish these effects because the environment changes again before the population fully adapts, as seen in classic field studies such as Grant and Grant's finch research

467 (Grant & Grant 2002) and theoretical predictions (Kopp & Hermisson 2009). Also, the fact that
468 we cannot observe the oscillation directly from allele frequencies does not mean that the
469 fluctuating selection is not happening and is involved in maintaining polymorphism (Lynch et al.
470 2024). Our results illustrate that high season length amplifies the visible shifts in allele frequencies,
471 especially under high selection pressure, thereby producing more pronounced cyclical patterns.
472 Oscillations are very challenging to observe for individual loci in polygenic traits with small
473 parameter combinations, however, spectral analysis readily recovers the spectral peak, especially
474 in the instantaneous model and the two gradual season models. Therefore, the identification of
475 oscillatory behavior will be predicated on the parameter combination and the complexity of the
476 selection regimes. That is, trait's heritability, size of season length and the selection strength will
477 determine the level of oscillation among alleles.

478 **Genomic architecture effect on oscillation and fixation**

479 Previous theoretical models investigating the effects of fluctuating selection on genome dynamics
480 often used the approach of selection acting directly on the causative loci, generally demonstrating
481 that polymorphism could be maintained under specific conditions, notably if heterozygote fitness
482 exceeded that of homozygotes (Haldane & Jayakar 1963; Bürger Reinhard & Gimelfarb 2002).
483 They also indicated that single-locus models could lead to fixation over extended periods of
484 fluctuating selection, thus limiting long-term polymorphism (Turelli & Barton 2004; Bürger &
485 Ghnelfarb 1999; Bürger Reinhard & Gimelfarb 2002; Gillespie 1973). In contrast to those models
486 that focused on a single locus selection coefficient, our study employs a phenotype-based selection
487 approach (Lande 2007, 2009), where changes in environmental conditions shift the optimal
488 phenotype and shifts in selection on the causative loci are emergent. The results support temporary
489 genetic diversity by showing that monogenic models exhibit larger fluctuations, mainly because a

single genetic locus drives the entire phenotypic shift for a given heritability. In some cases, these fluctuations persist until fixation occurs, while in others they endure for an extended period. Although monogenic models tend to show a high rate of fixation, alleles do not always fix, and the degree of fixation depends on the specific parameter combination (Figure 4).

Extending our analysis from single-locus models to oligogenic and polygenic frameworks reveals that selection acts simultaneously across multiple loci, leading to oscillations in allele frequencies and phenotypes under appropriate conditions. In contrast to single-locus models, where parameter changes strongly influence allele fixation, polygenic models tend to mask selection effects at individual loci, with the cumulative impact spreading across a large genomic architecture (Höllinger et al. 2023; Bertram 2021; Barghi et al. 2020; Sibly & Curnow 2023). Therefore, that diffused selection effect can explain the need for intense selection on highly heritable polygenic traits to sustain observable oscillations in allele frequencies across many loci. In addition, our current results indicate that alleles with intermediate initial frequencies fluctuate more than others. This pattern reflects the effect of fluctuating selection where allele's selective advantage changes between seasons (Hedrick 1976; Wittmann et al. 2017). Unlike models that rely on specific and difficult to measure dominance relationship, our approach takes into consideration of key parameters that are quantifiable in nature; therefore, not only our framework provides a compelling explanation of the identified fluctuations, but it offers more practical tool for studying these dynamics in empirical systems.

Fluctuations in complex selection regimes

Our study contrasts two principal types of fluctuating selection models: (1) instantaneous (where the environment switches sharply between two states) and (2) gradual (where the environment transitions more smoothly through two equal or four uneven season length). The observed

similarities in instantaneous and simple gradual models likely arise from having even season lengths and magnitude of the shift in the optimum. Although the simulated more complex models do not correspond to a specific biological scenario, they rather serve as one example of more complex patterns over time, of which there are many varied examples in nature (Park 2019; Hernández-Carrasco et al. 2025). A good analogy is the effect of El Niño on the southern oscillation index where the oscillation in the index is associated with the variation in fish recruitment in the Pacific Ocean. However, these oscillations do not happen every year and occur in addition to the regular annual seasonal cycle (Shumway & Stoffer 2017), a scenario that can be experienced by a population under various evolutionary forces. When there are four uneven season lengths with/without same magnitude of the shift in the optimum, the population struggles to adapt; thus, the complex oscillatory dynamics. Nevertheless, gradual models better represent complex natural environments where multiple seasons may have different generation turnover. These more complex scenarios, especially those with four uneven season lengths, create subtle patterns that can resemble null or constant selection when parameters (e.g., selection strength, heritability) are low (de Vladar & Barton 2014; Chevin et al. 2022; Wittmann et al. 2017). Indeed, a particularly long or short season under these gradual models can either strengthen or weaken selection signals, respectively, making detection more difficult (Cvijović et al. 2015; Abdul-Rahman et al. 2021; West & Mobilia 2020) for the latter.

We employed spectral analysis to tackle the challenge of identifying subtle oscillatory signals. This approach successfully discerned cyclical patterns in allele frequency across most parameter combinations, particularly in simpler models (i.e., the instantaneous and two equal seasons models). However, spectral analysis struggled to detect periodicity when parameter values were low (e.g., low heritability or weak selection) or when the model included multiple complex

environments (as in the Complex gradual I and 2). These difficulties mirror empirical findings (Bitter et al. 2024) and may be explained by the short duration of each season, which hinders the population's ability to adapt to new conditions. A similar challenge in identifying seasonality was observed in the statistical analysis of experimental data from Bergland et al. (2014), who reported seasonal allele-frequency oscillations in thousands of SNPs. However, a subsequent reanalysis (Buffalo & Coop 2020) failed to replicate this result, likely due to the complex selection pressures experienced by the population, the timing of sample collection (i.e., the generation intervals used by Bergland et al. in their 2014 data set), or the analysis assumptions as described by (Nunez et al. 2024). These results highlight and define the limits for detecting fluctuating selection from allele frequency data under complex scenarios.

Ideally, sequencing multiple sequential generations for a long time would help identify seasonality from genomic data using the currently developed statistical tools. However, its feasibility is almost impossible due to the associated cost and labor. Although Phillips et al. 2020 (Phillips et al. 2020) did not examine fluctuating selection, they argued that taking more samples over time can dramatically improve our ability to understand the complexity into evolutionary dynamics. Therefore, researchers studying populations under complex fluctuating conditions should also aim to estimate the optimal sampling points required to capture such dynamics. Furthermore, new computational methods, including machine learning and generative models, may reduce empirical demands or detect cyclical selection signals even in sparser datasets (Greener et al. 2021).

Applicability of spectral analysis in evolution studies to identify seasonal selection and cyclic allele frequencies

In this study, we employ spectral analysis with the Fast Fourier Transform (FFT) to characterize oscillations in allele frequencies, under the simplified assumptions that fluctuating selection is the

559 dominant force shaping allele-frequency and phenotypic dynamics. This assumption allows us to
560 treat the signal as stationary, although in nature, signals are often nonstationary due to
561 environmental variability and demographic fluctuations. Moreover, natural data are expected to
562 contain substantial noise (Lotterhos et al. 2017), which can obscure or distort periodic signals and
563 cause shifts in amplitude or bandwidth.

564 While FFT provides a tractable first step, alternative methods such as wavelet transforms or the S-
565 transform may offer greater robustness in detecting oscillations under nonstationary conditions or
566 asymmetric selection regimes (Khan & Pierre 2019; Shumway & Stoffer 2017; Arnab et al. 2023).
567 Our results show that fluctuating selection can indeed generate long-term oscillations in allele
568 frequencies under controlled, symmetric models, reinforcing its plausibility as a detectable force
569 in natural systems. Thus, spectral methods provide a promising framework to distinguish signals
570 of fluctuating selection, mainly when it dominates other evolutionary forces or when the combined
571 action of multiple seasonal forces produces cyclic patterns.

572 Although we did not apply our approach directly to empirical data, our framework establishes a
573 foundation for refining spectral methods to detect fluctuating selection, a field that is far less
574 developed than approaches for positive/directional and other forms of selection (Hancock & Di
575 Rienzo 2008; Haasl & Payseur 2016; Qin et al. 2022). Consequently, future work will need to
576 incorporate confounding processes such as fluctuating population sizes, migration, and
577 overlapping selection pressures to test the robustness of spectral analysis in realistic scenarios.
578 Nonetheless, our complex model that includes multiple sub-seasons demonstrates that, under
579 appropriate conditions, spectral analysis can reliably identify oscillatory signatures of fluctuating
580 selection.

581

Limitations and future directions

Our simulations assume non-overlapping generations, constant population sizes, no new mutations, and fixed recombination rates, all of which may limit the extent to which these results can generalize. In addition, our models did not allow for any genotype by environment interaction at any loci. Previous quantitative genetic models of fluctuating selection have frequently identified the conditions under which fluctuating selection is expected to lead to the evolution of phenotypic plasticity driven by genotype by environment interactions (Via & Lande 1985; Lande 2014; Oostra et al. 2018). Our models did not allow for the evolution of plasticity in this way, removing a major potential way for populations to adapt to fluctuating selection pressures. Thus, our results shed light on whether it is ever possible for fluctuating selection to drive recurrent, stable, allele frequency oscillations in a population, given these simplifying assumptions. Future models incorporating additional factors, including allowing for mutation, genotype by environment interactions, and incorporating dynamic population sizes are necessary to capture the complexity of natural populations (Gloss & Whiteman 2016; Barghi et al. 2019; Agashe et al. 2023; Holstad et al. 2024). While the current study offers a foundation for understanding how traits evolve and persist under dynamic natural conditions by revealing how seasonal and environmental changes modulate selective pressures over time, researchers should also test the observations through evolve-and-resequence experiments and refine methods for parameter estimation from time-series genomic data.

Concluding remarks

This study highlights the intricate interplay among heritability, genomic architecture, selection intensity, and season length in shaping oscillatory allele-frequency dynamics under fluctuating environments. High heritability and strong selection produce pronounced and persistent frequency

oscillations, and these effects become more evident when selection acts over longer seasons. Meanwhile, the broad genomic architecture of polygenic traits can mask individual locus fluctuations, yet substantial oscillations still emerge when selection is sufficiently strong. Spectral analysis is valuable for detecting cyclical patterns, but its effectiveness diminishes in highly complex or weakly selective environments. Therefore, improved methods are needed to identify seasonality from very complex models.

Overall, our results underscore the importance of the discussed ecological and genetic parameters in understanding the evolutionary fate of populations under fluctuating selection. Accurately modeling additional parameters and empirically testing these dynamics will be key to predicting evolutionary outcomes and identifying conditions that promote sustained genetic diversity as environmental variability increases.

Reference:

Abdul-Rahman F, Tranchina D, Gresham D. 2021. Fluctuating environments maintain genetic diversity through neutral fitness effects and balancing selection. Mol Biol Evol. 38:4362–4375. doi: 10.1093/molbev/msab173.

Agashe D, Sane M, Singhal S. 2023. Revisiting the Role of Genetic Variation in Adaptation. Am Nat. 202:486–502. doi: 10.1086/726012.

Arnab SP, Amin MR, DeGiorgio M. 2023. Uncovering Footprints of Natural Selection Through Spectral Analysis of Genomic Summary Statistics Kim, Y, editor. Mol Biol Evol. 40. doi: 10.1093/molbev/msad157.

Barghi N et al. 2019. Genetic redundancy fuels polygenic adaptation in Drosophila. PLoS Biol. 17. doi: 10.1371/journal.pbio.3000128.

Barghi N, Hermisson J, Schlötterer C. 2020. Polygenic adaptation: a unifying framework to understand positive selection. Nature Reviews Genetics 2020 21:12. 21:769–781. doi: 10.1038/s41576-020-0250-z.

Barton NH, Etheridge AM, Véber A. 2017. The infinitesimal model: Definition, derivation, and implications. Theor Popul Biol. 118:50–73. doi: 10.1016/j.tpb.2017.06.001.

Barton NH, Turelli M. 1989. Evolutionary quantitative genetics: How little do we know? Annu Rev Genet. 23:337–370. doi: 10.1146/annurev.ge.23.120189.002005.

Behrman EL et al. 2018. Rapid seasonal evolution in innate immunity of wild Drosophila melanogaster. Proceedings of the Royal Society B: Biological Sciences. 285. doi: 10.1098/rspb.2017.2599.

Bell G. 2010. Fluctuating selection: the perpetual renewal of adaptation in variable environments. Philosophical Transactions of the Royal Society B: Biological Sciences. 365:87–97. doi: 10.1098/rstb.2009.0150.

Bergland AO, Behrman EL, ’brien O, Schmidt KR, Petrov PS. 2014. Genomic Evidence of Rapid and Stable Adaptive Oscillations over Seasonal Time Scales in Drosophila. PLoS Genet. 10:1004775. doi: 10.1371/journal.pgen.1004775.

Bersaglieri T et al. 2004. Genetic signatures of strong recent positive selection at the lactase gene. Am. J. Hum. Genet. 74:1111–1120. doi: 10.1086/421051.

Bertram J. 2021. Allele frequency divergence reveals ubiquitous influence of positive selection in Drosophila Buerkle, A, editor. PLoS Genet. 17:e1009833. doi: 10.1371/journal.pgen.1009833.

Bertram J, Masel J. 2019. Different mechanisms drive the maintenance of polymorphism at loci subject to strong versus weak fluctuating selection. Evolution (N Y). 73:883–896. doi: 10.1111/evo.13719.

Bijma P. 2011. A general definition of the heritable variation that determines the potential of a population to respond to selection. Genetics. 189:1347–1359. doi: 10.1534/genetics.111.130617.

Bitter MC et al. 2024. Continuously fluctuating selection reveals fine granularity of adaptation. Nature 2024 634:8033. 634:389–396. doi: 10.1038/s41586-024-07834-x.

Bjørnstad ON, Nelson WA, Tobin PC. 2016. Developmental synchrony in multivoltine insects: generation separation versus smearing. Popul Ecol. 58:479–491. doi: 10.1007/s10144-016-0564-z.

Buckley LB, Arakaki AJ, Cannistra AF, Kharouba HM, Kingsolver JG. 2017. Insect development, thermal plasticity and fitness implications in changing, seasonal environments. Integr Comp Biol. 57:988–998. doi: 10.1093/icb/icx032.

Buffalo V, Coop G. 2020. Estimating the genome-wide contribution of selection to temporal allele frequency change. Proc Natl Acad Sci U S A. 117:20672–20680. doi: 10.1073/PNAS.1919039117/SUPPL_FILE/PNAS.1919039117.SAPP.PDF.

Bürger R, Ghnelfarb A. 1999. Genetic Variation Maintained in Multilocus Models of Additive Quantitative Traits Under Stabilizing Selection. Genetics. 152:807–820. doi: 10.1093/GENETICS/152.2.807.

Bürger Reinhard, Gimelfarb A. 2002. Fluctuating environments and the role of mutation in maintaining quantitative genetic variation. Genet Res. 80:31–46. doi: 10.1017/S0016672302005682.

Burke MK et al. 2010. Genome-wide analysis of a long-term evolution experiment with Drosophila. Nature. 467:587–590. doi: 10.1038/nature09352.

Van Buskirk J, Smith DC. 2021. Ecological causes of fluctuating natural selection on habitat choice in an amphibian. Evolution (N Y). 75:1862–1877. doi: 10.1111/evo.14282.

Campbell-Staton SC et al. 2017. Winter storms drive rapid phenotypic, regulatory, and genomic shifts in the green anole lizard. Science (1979). 357:495–498. doi: 10.1126/science.aam5512.

Chevin LM. 2019. Selective sweep at a QTL in a randomly fluctuating environment. Genetics. 213:987–1005. doi: 10.1534/genetics.119.302680.

Chevin LM, Gompert Z, Nosil P. 2022. Frequency dependence and the predictability of evolution in a changing environment. Evol Lett. 6:21–33. doi: 10.1002/EVL3.266.

Cvijović I, Good BH, Jerison ER, Desai MM. 2015. Fate of a mutation in a fluctuating environment. Proceedings of the National Academy of Sciences. 112:E5021–E5028. doi: 10.1073/pnas.1505406112.

682 Doebley JF, Gaut BS, Smith BD. 2006. The Molecular Genetics of Crop Domestication. Cell.
683 127:1309–1321. doi: 10.1016/j.cell.2006.12.006.
684 Dumont BL, Payseur BA. 2008. Evolution of the gnomic rate of recombination in mammals.
685 Evolution (N Y). 62:276–294. doi: 10.1111/J.1558-5646.2007.00278.X.
686 Ellner S, Hairston Jnr NG. 1994. Role of overlapping generations in maintaining genetic variation
687 in a fluctuating environment. Am Nat. 143:403–417. doi: 10.1086/285610.
688 Endler JA. 2020. *Natural Selection in the Wild. (MPB-21), Volume 21*. Princeton University Press
689 doi: 10.2307/j.ctvx5w9v9.
690 Franssen SU, Kofler R, Schlötterer C. 2017. Uncovering the genetic signature of quantitative trait
691 evolution with replicated time series data. Heredity (Edinb). 118:42–51. doi: 10.1038/hdy.2016.98.
692 Gienapp P, Reed TE, Visser ME. 2014. Why climate change will invariably alter selection
693 pressures on phenology. Proceedings of the Royal Society B: Biological Sciences. 281:20141611.
694 doi: 10.1098/rspb.2014.1611.
695 Gillespie J. 1973. Polymorphism in random environments. Theor Popul Biol. 4:193–195. doi:
696 10.1016/0040-5809(73)90028-2.
697 Gillespie JH. 1977. Natural Selection for Variances in Offspring Numbers: A New Evolutionary
698 Principle. Source: The American Naturalist. 111:1010–1014.
699 Glaser-Schmitt A, Wittmann MJ, Ramnarine TJS, Parsch J. 2021. Sexual Antagonism, Temporally
700 Fluctuating Selection, and Variable Dominance Affect a Regulatory Polymorphism in *Drosophila*
701 *melanogaster* Larracuente, A, editor. Mol Biol Evol. 38:4891–4907. doi:
702 10.1093/molbev/msab215.
703 Gloss AD, Whiteman NK. 2016. Balancing Selection: Walking a Tightrope. Current Biology.
704 26:R73–R76. doi: 10.1016/j.cub.2015.11.023.

Gossmann TI, Waxman D, Eyre-Walker A. 2014. Fluctuating selection models and Mcdonald-Kreitman type analyses. PLoS One. 9. doi: 10.1371/journal.pone.0084540.

Grant PR, Grant BR. 2002. Unpredictable evolution in a 30-year study of Darwin's finches. Science (1979). 296:707–711. doi: 10.1126/science.1070315.

Greener JG, Kandathil SM, Moffat L, Jones DT. 2021. A guide to machine learning for biologists. Nature Reviews Molecular Cell Biology 2021 23:1. 23:40–55. doi: 10.1038/s41580-021-00407-0.

Gregory TR. 2009. Understanding Natural Selection: Essential Concepts and Common Misconceptions. Evolution: Education and Outreach. 2:156–175. doi: 10.1007/s12052-009-0128-1.

Haasl RJ, Payseur BA. 2016. Fifteen years of genomewide scans for selection: trends, lessons and unaddressed genetic sources of complication. Mol Ecol. 25:5–23. doi: 10.1111/MEC.13339.

Haldane JBS, Jayakar SD. 1963. Polymorphism due to selection of varying direction. J Genet. 58:237–242. doi: 10.1007/BF02986143.

Haller BC, Messer PW. 2023. SLiM 4: Multispecies Eco-Evolutionary Modeling. American Naturalist. 201. doi: 10.1086/723601.

Hancock AM, Di Rienzo A. 2008. Detecting the Genetic Signature of Natural Selection in Human Populations: Models, Methods, and Data. Annu Rev Anthropol. 37:197. doi: 10.1146/ANNUREV.ANTHRO.37.081407.085141.

Harvey JA et al. 2023. Scientists' warning on climate change and insects. Ecol Monogr. 93. doi: 10.1002/ecm.1553.

Hayward LK, Sella G. 2022. Polygenic adaptation after a sudden change in environment. Elife. 11. doi: 10.7554/eLife.66697.

Hedrick PW. 1976. Genetic variation in a heterogeneous environment. II. Temporal heterogeneity and directional selection. Genetics. 84:145–157. doi: 10.1093/GENETICS/84.1.145.

Hill WG, Mackay TFC. 2004. D. S. Falconer and Introduction to Quantitative Genetics. Genetics. 167:1529–1536. doi: 10.1093/genetics/167.4.1529.

Hoekstra RF, Bijlsma R, Dolman AJ. 1985. Polymorphism from environmental heterogeneity: models are only robust if the heterozygote is close in fitness to the favoured homozygote in each environment. Genet Res (Camb). 45:299–314. doi: 10.1017/S001667230002228X.

Höllinger I, Wölfl B, Hermisson J. 2023. A theory of oligogenic adaptation of a quantitative trait Jain, K, editor. Genetics. 225. doi: 10.1093/genetics/iyad139.

Holstad A et al. 2024. Evolvability predicts macroevolution under fluctuating selection. Science (1979). 384:688–693. doi: 10.1126/science.adi8722.

Jenkins GM. 1965. A Survey of Spectral Analysis. Appl Stat. 14:2. doi: 10.2307/2985352.

Kelly JK. 2022. The genomic scale of fluctuating selection in a natural plant population. Evol Lett. 6:506–521. doi: 10.1002/evl3.308.

Khan MA, Pierre JW. 2019. Detection of Periodic Forced Oscillations in Power Systems Using Multitaper Approach. IEEE Transactions on Power Systems. 34:1086–1094. doi: 10.1109/TPWRS.2018.2870838.

Kopp M, Hermisson J. 2009. The Genetic Basis of Phenotypic Adaptation II: The Distribution of Adaptive Substitutions in the Moving Optimum Model. Genetics. 183:1453–1476. doi: 10.1534/GENETICS.109.106195.

Lande R. 2009. Adaptation to an extraordinary environment by evolution of phenotypic plasticity and genetic assimilation. J Evol Biol. 22:1435–1446. doi: 10.1111/J.1420-9101.2009.01754.X.

Lande R. 2014. Evolution of phenotypic plasticity and environmental tolerance of a labile quantitative character in a fluctuating environment. J Evol Biol. 27:866–875. doi: 10.1111/JEB.12360.

Lande R. 2007. Expected relative fitness and the adaptive topography of fluctuating selection. Evolution (N Y). 61:1835–1846. doi: 10.1111/J.1558-5646.2007.00170.X.

Lotterhos KE et al. 2017. Composite measures of selection can improve the signal-to-noise ratio in genome scans Kelley, J, editor. Methods Ecol Evol. 8:717–727. doi: 10.1111/2041-210X.12774.

Louthan AM, Kay KM. 2011. Comparing the adaptive landscape across trait types: larger QTL effect size in traits under biotic selection. BMC Evol Biol. 11:60. doi: 10.1186/1471-2148-11-60.

Lynch M, Wei W, Ye Z, Pfrender M. 2024. The genome-wide signature of short-term temporal selection. Proceedings of the National Academy of Sciences. 121:e2307107121. doi: 10.1073/pnas.2307107121.

Machado HE et al. 2021. Broad geographic sampling reveals the shared basis and environmental correlates of seasonal adaptation in Drosophila. Elife. 10. doi: 10.7554/eLife.67577.

McAdam AG, Boutin S, Dantzer B, Lane JE. 2019. Seed Masting Causes Fluctuations in Optimum Litter Size and Lag Load in a Seed Predator. Am Nat. 194:574–589. doi: 10.1086/703743.

Mendonça, Jr. M de S, Romanowski HP. 2012. Population ecology of the multivoltine Neotropical gall midge Eugeniamyia dispar (Diptera, Cecidomyiidae). Iheringia Ser Zool. 102:170–176. doi: 10.1590/S0073-47212012000200009.

Nunez JCB et al. 2024. A cosmopolitan inversion facilitates seasonal adaptation in overwintering Drosophila. Genetics. 226. doi: 10.1093/genetics/iyad207.

Nuzhdin S V, Turner TL. 2013. Promises and limitations of hitchhiking mapping. Curr Opin Genet Dev. 23:694–699. doi: 10.1016/j.gde.2013.10.002.

Oostra V, Saastamoinen M, Zwaan BJ, Wheat CW. 2018. Strong phenotypic plasticity limits potential for evolutionary responses to climate change. Nature Communications 2018 9:1. 9:1–11. doi: 10.1038/s41467-018-03384-9.

Oz T et al. 2014. Strength of Selection Pressure Is an Important Parameter Contributing to the Complexity of Antibiotic Resistance Evolution. Mol Biol Evol. 31:2387–2401. doi: 10.1093/molbev/msu191.

Pfenninger M, Foucault Q. 2022. Population Genomic Time Series Data of a Natural Population Suggests Adaptive Tracking of Fluctuating Environmental Changes. Integr Comp Biol. 62:1812–1826. doi: 10.1093/icb/icac098.

Phillips MA, Kutch IC, Long AD, Burke MK. 2020. Increased time sampling in an evolve-and-resequence experiment with outcrossing Saccharomyces cerevisiae reveals multiple paths of adaptive change. Mol Ecol. 29:4898–4912. doi: 10.1111/MEC.15687.

Qin X, Chiang CWK, Gaggiotti OE. 2022. Deciphering signatures of natural selection via deep learning. Brief Bioinform. 23:1–10. doi: 10.1093/BIB/BBAC354.

R Core Team. 2022. R: A language and environment for statistical computing. https://www.r-project.org/ (Accessed February 14, 2025).

Roberts Kingman GA et al. 2021. Predicting future from past: The genomic basis of recurrent and rapid stickleback evolution. Sci Adv. 7:5285–5303. doi: 10.1126/sciadv.abg5285.

Roff DA. 1997. Phenotypic Plasticity and Reaction Norms. Evolutionary Quantitative Genetics. 196–240. doi: 10.1007/978-1-4615-4080-9_6.

Rudman SM et al. 2022. Direct observation of adaptive tracking on ecological time scales in Drosophila. Science (1979). 375. doi: 10.1126/science.abj7484.

Rusuwa BB, Chung H, Allen SL, Frentiu FD, Chenoweth SF. 2022. Natural variation at a single gene generates sexual antagonism across fitness components in Drosophila. Current Biology. 32:3161-3169.e7. doi: 10.1016/j.cub.2022.05.038.

Sella G, Barton NH. 2019. Thinking About the Evolution of Complex Traits in the Era of Genome-Wide Association Studies. Annu Rev Genomics Hum Genet. 20:461–493. doi: 10.1146/annurev-genom-083115-022316.

Shumway RH, Stoffer DS. 2017. *Time Series Analysis and Its Applications*. Springer International Publishing: Cham doi: 10.1007/978-3-319-52452-8.

Sibly RM, Curnow RN. 2023. Allele frequencies and selection coefficients in locally adapted populations. J Theor Biol. 565:111463. doi: 10.1016/j.jtbi.2023.111463.

Stephan W. 2019. Selective Sweeps. Genetics. 211:5–13. doi: 10.1534/genetics.118.301319.

Subedi B, Poudel A, Aryal S. 2023. The impact of climate change on insect pest biology and ecology: Implications for pest management strategies, crop production, and food security. J Agric Food Res. 14:100733. doi: 10.1016/j.jafr.2023.100733.

Tenaillon O et al. 2016. Tempo and mode of genome evolution in a 50,000-generation experiment. Nature. 536:165–170. doi: 10.1038/nature18959.

Thomas E Reed, Daniel E Schindler, Robin S Waples. 2011. Interacting Effects of Phenotypic Plasticity and Evolution on Population Persistence in a Changing Climate. Conservation Biology. 25:56–63. doi: 10.1111/j.1523-1739.2010.01552.x.

Trut L, Oskina I, Kharlamova A. 2009. Animal evolution during domestication: the domesticated fox as a model. BioEssays. 31:349–360. doi: 10.1002/bies.200800070.

Turelli M, Barton NH. 2004. Polygenic Variation Maintained by Balancing Selection: Pleiotropy, Sex-Dependent Allelic Effects and $G \times E$ Interactions. Genetics. 166:1053–1079. doi: 10.1093/genetics/166.2.1053.

Turner TL, Stewart AD, Fields AT, Rice WR, Tarone AM. 2011. Population-Based Resequencing of Experimentally Evolved Populations Reveals the Genetic Basis of Body Size Variation in Drosophila melanogaster Gibson, G, editor. PLoS Genet. 7:e1001336. doi: 10.1371/journal.pgen.1001336.

Via S, Lande R. 1985. GENOTYPE-ENVIRONMENT INTERACTION AND THE EVOLUTION OF PHENOTYPIC PLASTICITY. Evolution (N Y). 39:505–522. doi: 10.1111/j.1558-5646.1985.tb00391.x.

de Vladar HP, Barton N. 2014. Stability and Response of Polygenic Traits to Stabilizing Selection and Mutation. Genetics. 197:749–767. doi: 10.1534/genetics.113.159111.

Waldvogel A et al. 2018. The genomic footprint of climate adaptation in *Chironomus riparius*. Mol Ecol. 27:1439–1456. doi: 10.1111/mec.14543.

Walsh B, Lynch M. 2018. *Evolution and Selection of Quantitative Traits*. Oxford University Press doi: 10.1093/oso/9780198830870.001.0001.

West R, Mobilia M. 2020. Fixation properties of rock-paper-scissors games in fluctuating populations. J Theor Biol. 491:110135. doi: 10.1016/j.jtbi.2019.110135.

Wickham H. 2016. ggplot2. doi: 10.1007/978-3-319-24277-4.

Wientjes YCJ et al. 2022. The long-term effects of genomic selection: 1. Response to selection, additive genetic variance, and genetic architecture. Genetics Selection Evolution. 54:19. doi: 10.1186/s12711-022-00709-7.

Wientjes YCJ et al. 2023. The long-term effects of genomic selection: 2. Changes in allele frequencies of causal loci and new mutations. Genetics. 225. doi: 10.1093/GENETICS/IYAD141.

Wilson BA, Petrov DA, Messer PW. 2014. Soft Selective Sweeps in Complex Demographic Scenarios. Genetics. 198:669–684. doi: 10.1534/genetics.114.165571.

Wittmann MJ, Bergland AO, Feldman MW, Schmidt PS, Petrov DA. 2017. Seasonally fluctuating selection can maintain polymorphism at many loci via segregation lift. Proceedings of the National Academy of Sciences. 114:E9932–E9941. doi: 10.1073/pnas.1702994114.

Yair S, Coop G. 2022. Population differentiation of polygenic score predictions under stabilizing selection. Philosophical Transactions of the Royal Society B: Biological Sciences. 377. doi: 10.1098/rstb.2020.0416.