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(Epi)mutation rates and the evolution of composite trait architectures

Bastien Polizzi, Vincent Calvez, Sylvain Charlat, Etienne Rajon*

December 23, 2022

Abstract

Mutation rates vary widely along genomes and across inheritance systems. This suggests that complex traits – resulting from the contributions of multiple determinants – might be composite in terms of the underlying mutation rates. Here we investigate through mathematical modeling whether such a heterogeneity may drive changes in a trait’s architecture, especially in fluctuating environments where phenotypic instability can be beneficial. We first identify a convexity principle, related to the shape of the trait’s fitness function, setting conditions under which composite architectures should be adaptive or, conversely and more commonly, should be selected against. Simulations reveal, however, that applying this principle to realistic evolving populations requires taking into account pervasive epistatic interactions that take place in the system. Indeed, the fate of a mutation affecting the architecture depends on the (epi)genetic background, itself depending upon the current architecture in the population. We tackle this problem by borrowing the adaptive dynamics framework from evolutionary ecology – where it is routinely used to deal with such resident/mutant dependencies – and find that the principle excluding composite architectures generally prevails. Yet, the predicted evolutionary trajectories will typically depend on the initial architecture, possibly resulting in historical contingencies. Finally, by relaxing the large population size assumption, we unexpectedly find that not only the strength of selection on a trait’s architecture, but also its direction, depend on population size, revealing a new occurrence of the recently coined phenomenon of ‘sign inversion’.

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1 Introduction

2 Complex traits, those resulting from the combined contributions of multiple determinants, may in prin-
3 ciple be subject to composite mutation rates. For example, genes contributing to the same trait may
4 mutate at rates spanning orders of magnitude because their genomic environments differ, or simply their
5 lengths (Rando and Verstrepen 2007; Hodgkinson and Eyre-Walker 2011; Oman, Alam, and Ness 2022).
6 The possibility of heritable yet non-genetic contributions introduces even more pronounced heterogeneity
7 in mutation rates *sensu lato*, that is, in the rates of random change, whatever the inheritance mechanism
8 (Rando and Verstrepen 2007; Danchin 2013). Indeed, non-genetic inheritance systems, as multiple as
9 they may be, share the property of being less stable than DNA sequences (Johannes et al. 2009; Rechavi,
10 Minevich, and Hobert 2011; Denkena, Johannes, and Colomé-Tatché 2021; Dodson and Rine 2015; Graaf
11 et al. 2015). Here we investigate whether such an heterogeneity in mutation rates may drive the evolution
12 of a trait’s architecture: just as mutation rates can be adaptively tuned by the degree of environmen-
13 tal stability (Ishii et al. 1989; Johnson 1999; Andre and Godelle 2006), can trait architectures evolve
14 toward optimally mixed contributions of determinants differing in their rates of mutations? Or, on the
15 contrary, are non-composite mutation rates generally selected for, which should lead to simplified traits
16 architectures, homogeneous in terms of the underlying mutation rates?

17 We address these questions through mathematical modeling, assuming that selection acts on a single
18 trait in an environment oscillating between two states. We further assume that the relative contribu-
19 tions of two (or more) determinants to the trait, differing only in their respective mutation rates, are
20 controlled by one evolving parameter, and we study its evolution. In our analysis, the mutation rates
21 differ by orders of magnitude, such that they can be referred to as ‘fast’ and ‘slow’ in the case of two
22 determinants. We start with the analytical treatment of an idealized situation where only the absolute
23 growth rate of a mutant determines its fate, and find the architectures that maximize this fitness proxy.
24 We thereby identify a general mathematical principle setting boundaries to the conditions where complex
25 architectures, and thus composite mutation rates, may be optimal. According to this principle, whatever
26 the degree of environmental instability, non-composite mutation rates are favored as long as individuals of
27 intermediate phenotypic value do not perform better across different environments than the average of the
28 extreme phenotypes. In other words, if the fitness function of the trait is convex, favoring specialists over
29 generalists, the fitness function of the trait architecture is also convex such that non-mixed contributions
30 are selectively favored. However, we also show that, as long as the degree of environmental instability

31 is not too high, non-composite mutation rates remain optimal even if the fitness function of the trait is
32 concave.

33 Absolute growth rates, however, ignore a potentially important aspect of the evolutionary dynamics
34 at play in this system: a mutation necessarily occurs in an (epi)genetic background whose state (i) may
35 depend on the strategy in place, and (ii) may critically affect the mutant’s fate. We address this issue by
36 using the adaptive dynamics framework, initially built to deal with ecological interactions by accounting
37 explicitly for context-dependencies in a mutant’s invasion success (Metz, Nisbet, and Geritz 1992; Geritz
38 et al. 1998). This approach generally confirms the above outlined convexity argument, but also reveals that
39 pervasive epistatic interactions render the system reluctant to change, because determinants contributing
40 little to the trait tend to accumulate cryptic variation that becomes deleterious if the trait architecture
41 is changed. This reveals that historical contingencies may prove important in the evolution of genetic
42 architectures.

43 Finally, we use simulations to relax the assumption of a large population size and thus investigate the
44 consequences of genetic drift on the evolution of a trait’s architecture. In doing so, we reveal a counter-
45 intuitive pattern whereby reducing population size below a threshold changes not only the efficiency but
46 also the direction of selection. We relate this finding to a recently described phenomenon, coined ‘sign-
47 inversion’, that generally takes place whenever some source of variability produces selective pressures
48 differing in their direction, average duration, and strength (Raynes, Wylie, et al. 2018; Raynes, Burch,
49 and Weinreich 2021). In such situations, weak but stable selection in one direction is dominant in large
50 populations, while strong but occasional selection in the other direction becomes the main player in small
51 populations. In our case, sudden environmental changes strongly select for a large contribution of the
52 fastest determinant whereas environment stasis selects for a reduced input of mutations and therefore
53 a high contribution of the slowest determinant. Yet, the latter selection pressure is typically weak and
54 long-lasting, thereby acting efficiently in large populations only, resulting in a trait’s architecture that is
55 contingent on population size.

56 2 Models and tools

57 2.1 Qualitative summary of the model

58 **Trait architecture.** The model considers $I \geq 2$ determinants with distinct mutation rates that con-
59 tribute to a phenotypic trait, varying continuously from 0 to 1. Each determinant is characterized by

60 (i) its (epi)genotype, taking a binary value ($X_i = 0$ or $X_i = 1$), (ii) its mutation rate ($\mu_i > 0$) at which
61 the (epi)genotype switches randomly from X_i to $1 - X_i$, and (iii) its relative contribution to the trait
62 ($\alpha_i \in [0, 1]$). The contributions sum to one, that is $\sum_i \alpha_i = 1$. The resulting trait for a given individual
63 is the weighted sum of its determinant values: $\Phi_X(\alpha) = \sum_i \alpha_i X_i$ (simply denoted as Φ if unambiguous).

64 In the following, the vector of contributions $\alpha = (\alpha_i)_{1 \leq i \leq I}$ of a single individual is referred to as its
65 *trait architecture*. In the simulations, we assume that the values of α are subject to mutational changes,
66 at the slowest rate $\min \mu_i$. Mutated α values are drawn in a Gaussian law centered on the parental value
67 with variance 0.1, and constrained to satisfy $\sum_i \alpha_i = 1$.

68 **Notations in the case of two determinants (fast versus slow).** The main part of our study
69 is devoted to the case of two determinants, below referred to as ‘fast’ and ‘slow’, in reference to their
70 contrasted mutation rates μ_F and μ_S ($\mu_F \gg \mu_S$). In this particular case, we can denote the respective
71 contributions of the fast and slow inheritance systems as α_F and $\alpha_S = 1 - \alpha_F$. The (epi)genotype values
72 are then denoted X_F and X_S , both in $\{0, 1\}$.

73 **Evolutionary dynamics.** We use a birth and death model, continuous in time, so that generations
74 are overlapping. The fecundity rate is assumed to be homogeneous. Up to changing units of time, it is
75 set to 1. Selection acts on the rate of mortality, namely $s|\Phi - \Phi^*(t)|^\gamma$, where the strength of selection is
76 controlled by parameter s , Φ^* is the environment-dependent optimal phenotype, and the exponent $\gamma \geq 0$
77 is the shape parameter of the fitness function (see Figure 1). We distinguish three cases on the basis of
78 γ values: $\gamma = 1$ is our reference case, and corresponds to a linear relationship between trait and fitness;
79 $\gamma < 1$ corresponds to a convex relationship resulting in a higher average fitness of *specialists* (Φ close to
80 extremal values 0 or 1); in contrast $\gamma > 1$ results in a concave relationship favoring *generalists* (Φ close
81 to $\frac{1}{2}$).

82 We assume that population size is regulated by an additional density-dependent contribution to the
83 mortality rate $\frac{N(t)}{K}$, where $N(t)$ is the instantaneous population size, and K denotes the carrying capacity.

84 **Environmental variation.** We assume that the environment fluctuates between two possible states
85 \mathcal{A}/\mathcal{B} associated with different optimal phenotypes $\Phi_A^* = 0$ and $\Phi_B^* = 1$. We consider periodic changes of
86 period T , with a symmetrical alternance between \mathcal{A} and \mathcal{B} . It is relevant to distinguish three regimes of
87 environmental variation in relation with mutation rates. First, the environment may be changing very
88 rarely, that is, even more slowly than the slowest determinant ($T(\min \mu_i) \gg 1$). Second, the environment

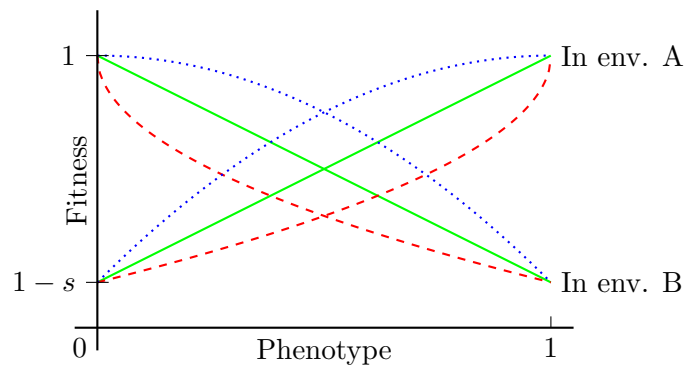


Figure 1: **Shape of the fitness function** $1 - s|\Phi - \Phi^*|^\gamma$, for $\gamma = 1$ (plain green, linear case), $\gamma = 1/2$ (dashed plain red, strictly convex case) and $\gamma = 2$ (dotted blue, strictly concave case).

89 may be changing very often, that is much faster than the least stable determinant ($T(\max \mu_i) \ll 1$). A
 90 third, intermediate regime, is one where the rate of environmental change is comparable to the range of
 91 mutation rates.

92 **Previous occurrence of the model.** The model is inspired by the study in (Rajon and Charlat
 93 2019) who restricted their model to the case of two determinants ($I = 2$), with respective contributions
 94 $\alpha_1 = 1 - \alpha$ and $\alpha_2 = \alpha$, and to $\gamma = 1$. In their interpretation, the number $\alpha \in [0, 1]$ measures the
 95 balance between genetic and epigenetic contributions to the trait value. The only difference lies in the
 96 mutation rate, being significantly larger for the epigenetic contribution. While not limiting our interest
 97 to epigenetic inheritance, we retain from this initial work the focus on the variability of the mutation
 98 rates μ_i 's and its consequences on the evolution of α . Separation of mutation timescales remains indeed
 99 the main component of our mathematical analysis.

100 2.2 A Lyapunov exponent approach in infinite populations

101 We begin our analysis by considering a monomorphic population for the trait architecture $\alpha = (\alpha_i)_{1 \leq i \leq I}$,
 102 taking its growth rate as a proxy for its fitness. To this end, we introduce the Lyapunov exponent $\lambda(\alpha)$,
 103 which is the overall growth rate of the population over a complete cycle of environmental fluctuations.
 104 The rate $\lambda(\alpha)$ is measured in the long run, that is, once the respective frequencies of the (epi)genotypes
 105 $(X_i)_{1 \leq i \leq I}$ have reached their periodic equilibrium distribution $f_g(t)$, where g denotes the (epi)genotype,
 106 taking value in $\{0, 1\}^{2^I}$. Technically, this equilibrium distribution is characterized by a periodic eigenvalue
 107 problem (Floquet spectral theory, see Appendix A), with the eigenvalue $\lambda(\alpha)$ defined by the following
 108 formula:

$$W(\boldsymbol{\alpha}) = \exp(\lambda(\boldsymbol{\alpha})) = \left(\text{eigenvalue} \left(\exp\left(\frac{T}{2}B\right) \exp\left(\frac{T}{2}A\right) \right) \right)^{\frac{1}{T}} \quad (1)$$

109 where A (resp. B) is the matrix describing the population dynamics in environment \mathcal{A} (resp. \mathcal{B}),
 110 which is defined by the various rates of mutation and mortality in the population. For instance, when
 111 $I = 2$, there are $2^2 = 4$ possible states in the population, namely $(0, 0)$, $(1, 0)$, $(0, 1)$, $(1, 1)$. In particular,
 112 the variation of the state $(0, 1)$ results from: (i) mutations from the states $(0, 0)$ and $(1, 1)$ at respective
 113 rates μ_2 and μ_1 , (ii) mutations to the states $(0, 0)$ and $(1, 1)$ at the same rates, (iii) birth-death dynamics
 114 specific to the state $(0, 1)$ at rate $1 - s\alpha_2^\gamma$.

115 The birth-death-mutation dynamics of the four states are then summarized in the following matrix

$$A = \begin{pmatrix} 1 - \mu_1 - \mu_2 & \mu_2 & \mu_1 & 0 \\ \mu_2 & 1 - \mu_1 - \mu_2 - s\alpha_2^\gamma & 0 & \mu_1 \\ \mu_1 & 0 & 1 - \mu_1 - \mu_2 - s\alpha_1^\gamma & \mu_2 \\ 0 & \mu_1 & \mu_2 & 1 - \mu_1 - \mu_2 - s \end{pmatrix}$$

116 Note that the matrix B is the same, up to a symmetrical change in the diagonal:

$$B = \begin{pmatrix} 1 - \mu_1 - \mu_2 - s & \mu_2 & \mu_1 & 0 \\ \mu_2 & 1 - \mu_1 - \mu_2 - s\alpha_1^\gamma & 0 & \mu_1 \\ \mu_1 & 0 & 1 - \mu_1 - \mu_2 - s\alpha_2^\gamma & \mu_2 \\ 0 & \mu_1 & \mu_2 & 1 - \mu_1 - \mu_2 \end{pmatrix}$$

117 2.3 Adaptive dynamics

118 The Lyapunov exponent approach described above ignores the influence that the state of the population
 119 in place (denoted the ‘resident’, with trait architecture $\boldsymbol{\alpha}_r$), may have on the population dynamics of
 120 a ‘mutant’ with a different architecture $\boldsymbol{\alpha}_m$. The adaptive dynamics framework allows to take these
 121 interactions into account by calculating the mutant’s growth rate at the time of invasion – also known as
 122 invasion fitness – assuming that its own influence on the resident’s population dynamics can be neglected
 123 at this initial stage.

124 In our model, the way the resident may exert an influence on the mutant’s fitness is through its impact
 125 on the equilibrium frequencies of the (epi)genotypes, hence providing a favorable or unfavorable context
 126 for a different genetic architecture. For example, in the two-determinants case, and assuming a stable

127 environment, if the resident population happens to be monomorphic for $\alpha_{F,r} = 1$ and thus $\alpha_{S,r} = 0$, then
 128 X_S reaches its neutral equilibrium distribution (1/2; 1/2). This means that a mutant with non zero $\alpha_{S,m}$
 129 will on average have lower fitness than the resident, even though the absolute growth rate, as measured
 130 by the Lyapunov exponent approach, would be highest for $\alpha_S = 1$.

131 To take such resident / mutant interdependence into account, we computed in the two-determinants
 132 case the invasion fitness in all possible pairs of mutant and resident architectures $(\alpha_{F,m}, \alpha_{F,r})$, with $\alpha_{F,m}$
 133 and $\alpha_{F,r}$ taken among 65 equally spread discrete values in the range $[0, 1]$. Since the environment state
 134 fluctuates cyclically, the equilibrium frequencies of the four combinations of possible (epi)genotype values
 135 (X_F, X_S) are periodic functions of time (see Section 2.2 and Appendix A). We thus calculated these
 136 frequencies at each of 64 timesteps equally spread over a period T . We then calculated, at each timestep
 137 and for each pair $(\alpha_{F,m}, \alpha_{F,r})$, the growth rate of the mutant. The instantaneous growth rate at time t
 138 of the mutant in a given genetic background can be calculated as:

$$W_{m,X_F,X_S}(t) = 1 - s |(1 - \alpha_{F,m})X_S + \alpha_{F,m}X_F - \Phi^*(t)|^\gamma, \quad (2)$$

139 with $\Phi^*(t)$ denoting the optimal phenotype at time t (either Φ_A^* or Φ_B^*). Assuming that the architecture
 140 is determined by a modifier locus linked with those controlling the determinants, each combination created
 141 at the time of a mutation has its own independent dynamics and long-term relative growth rate, which is
 142 not impacted by the change in frequencies in the population and can thus be calculated as the arithmetic
 143 mean of the $W_{m,X_F,X_S}(t)$ over the period.

144 The average invasion fitness of a mutant's architecture depends on its probability to appear in each
 145 background, represented by background frequencies in the following equation:

$$\begin{aligned} \overline{W}(m, r) = & f_{(0,0)}(t)W(m, 0, 0) + f_{(1,0)}(t)W(m, 1, 0) \\ & + f_{(0,1)}(t)W(m, 0, 1) + f_{(1,1)}(t)W(m, 1, 1) \end{aligned} \quad (3)$$

146 We represent the mutants' relative invasion fitnesses for our 65×65 pairs (α_m, α_r) in so-called Pairwise
 147 Invasibility Plots (PIP), from which we identify singular strategies and characterize their evolutionary
 148 stability (according to Geritz et al. 1998).

149 2.4 Simulations in infinite and finite populations

150 The numerical simulations for infinite populations are based on the discretisation of the continuous model
 151 described below. Although the model is valid for any number of inheritance systems, the numerical results
 152 are shown only for two inheritance systems in the case of infinite populations. Then, the population is
 153 divided in four groups according to their (epi)genotype: $g_{(0,0)}$, $g_{(1,0)}$, $g_{(0,1)}$ and $g_{(1,1)}$. Further, each
 154 subpopulation is indexed by individual architecture α_F (simply denoted α in the following lines). The
 155 density within each subpopulation is driven by

$$\begin{aligned} \partial_t g_X(t, \alpha) = & (1 - s|\Phi_X(\alpha) - \Phi^*(t)|^\gamma - \rho(t))g_X(t, \alpha) + (MG)_X(t, \alpha) \\ & - \mu_\alpha g_X(t, \alpha) + \mu_\alpha \int_0^1 \mathcal{K}(\alpha - y, \alpha)g_X(t, y)dy. \end{aligned} \quad (4)$$

156 In this equation:

- $1 - s|\Phi_X(\alpha) - \Phi^*(t)|^\gamma - \rho(t)$ is the percapita growth rate, including selection and density dependent saturation where $\rho(t)$ is the total population density :

$$\rho(t) = \int_0^1 (g_{(0,0)}(t, \alpha) + g_{(1,0)}(t, \alpha) + g_{(0,1)}(t, \alpha) + g_{(1,1)}(t, \alpha))d\alpha.$$

- $(MG)_X(t, \alpha)$ describes the (epi)genotype mutation dynamics through the matrix operation MG
 158 defined by

$$MG = \begin{pmatrix} -\mu_S - \mu_F & \mu_F & \mu_S & 0 \\ \mu_F & -\mu_S - \mu_F & 0 & \mu_S \\ \mu_S & 0 & -\mu_S - \mu_F & \mu_F \\ 0 & \mu_S & \mu_F & -\mu_S - \mu_F \end{pmatrix} \begin{pmatrix} g_{(0,0)} \\ g_{(1,0)} \\ g_{(0,1)} \\ g_{(1,1)} \end{pmatrix}$$

- $\mu_\alpha g_X(t, \alpha)$ represents the mutation toward other trait architecture where μ_α is the mutation rate
 160 on α ,
- $\mu_\alpha \int_0^1 \mathcal{K}(\alpha - y, \alpha)g_X(t, y)dy$ corresponds to the mutation from other trait architecture to the current
 161 one; in this term \mathcal{K} is the mutation kernel that is assumed to be a Gaussian distribution centered
 162 on the progenitors trait architecture, conditioned to take values in $[0, 1]$.
 163

164 The values of α are uniformly discretised in $[0, 1]$. The time discretisation is based on an explicit Runge-
165 Kutta (RK2) scheme to reduce computational time and improve accuracy. The integral terms are com-
166 puted according to standard quadrature methods.

167 The model (4) is non-linear due to the density-dependent saturation. Nevertheless, it can be recast
168 into a linear problem, and, in the periodic setting, the Lyapunov exponent $\lambda(\alpha)$ coincides with the
169 averaged density over one period $\frac{1}{T} \int_0^T \rho(t) dt$ in the case of a monomorphic population when mutations
170 are neglected, see Appendix A.

171 For finite populations, the stochastic birth and death process described in Section 2.1 is simulated
172 using a Monte-Carlo approach. We opted for a fixed time step discretisation to reduce computational
173 time. Contrary to the infinite population density model (Equation 4), the population remains finite and
174 fluctuates around the carrying capacity K . The generalization of the model to any number of inheritance
175 systems is straightforward, at no computational cost, and so the Monte-Carlo approach is suitable when
176 the number of inheritance systems is larger than three.

177 **3 Results and discussion**

178 The evolution of the trait architecture α may stem from two distinct effects: (i) its impact on the average
179 fitness across the two environments, regardless of the various mutation rates and (ii) its control of the
180 phenotypic contribution of inheritance systems with different mutation rates and thus presumably different
181 variational properties. Our focus is on the second effect, that is, on the implications of the mutation rates
182 on the trait architecture. We thus begin our analysis (Section 3.1) by setting $\gamma = 1$ such that the first
183 effect is removed. Indeed, the averaged fitness does not depend on the phenotype when $\gamma = 1$, that is,
184 in mathematical terms: $1 - \frac{s}{2}(|\Phi - \Phi_A^*|^1 + |\Phi - \Phi_B^*|^1) = 1 - \frac{s}{2}(|\Phi - 0|^1 + |\Phi - 1|^1) = 1 - \frac{s}{2}$ for all Φ .
185 In Section 3.2, we then investigate the sensitivity of our conclusions to changes in the shape of the trait
186 fitness function.

187 **3.1 Architectures evolve in response to the degree of environmental instability**

188 **3.1.1 Composite architectures are selected against when the fitness function is linear**

189 To assess which architecture (pure or composite) is optimal under various degrees of environmental in-
190 stability, we first simulated temporal dynamics in the simple case $I = 2$ (two inheritance systems, fast
191 and slow, with respective mutation rates μ_F and μ_S). In this particular case, we recall that respective

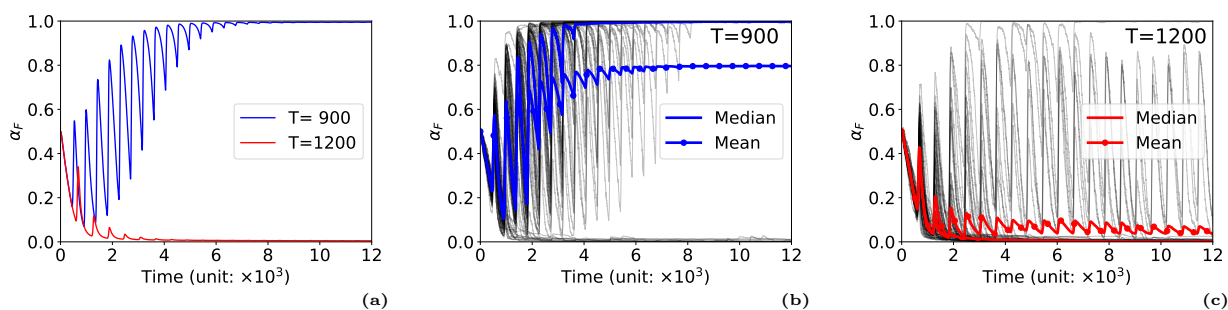


Figure 2: **Temporal dynamics of the trait architecture with polymorphic initial configuration.** (a) Simulation of the deterministic PDE model (Equation 4), corresponding to an infinite population size, with a polymorphic initial configuration where all α_F values have the same frequency. The mean α_F in the population is plotted over time for two values of the time period of environmental change T . We observed the selection towards $\alpha_F = 1$ for the smaller period $T = 900$ and the selection towards $\alpha_F = 0$ for the larger period $T = 1200$. (b-c) Monte-Carlo simulations associated with finite population sizes, respectively for $T = 900$ (b) and $T = 1200$ (c). The equilibrium population size is set to $K = 2^{16} \approx 65000$. The initial value of α_F is drawn uniformly within the population. Each black line represents the trajectory of the averaged value $\bar{\alpha}_F$ within the population over time. The colored lines represent the mean and median of 64 simulation replicates.

192 contributions of the fast and slow inheritance systems are denoted α_F and $\alpha_S = 1 - \alpha_F$. In this first set
 193 of simulations, the values of α_F are equidistributed within the population at initial time (polymorphic
 194 case). As illustrated in Figure 2, we only observed in the long run selection for one or the other of the two
 195 extreme, non-composite trait architectures ($\alpha_F = 0$ and, symmetrically, $\alpha_S = 1$, or $\alpha_F = 1$ and $\alpha_S = 0$),
 196 depending on the environmental cycle duration T .

197 Thus, in this setting, only the slow inheritance system should contribute to the trait ($\alpha_F = 0$) in
 198 scarcely changing environments (large T values); on the contrary, in unstable environments, only the fast
 199 inheritance system is expected to contribute ($\alpha_F = 1$). Interestingly, persistent intermediate values of
 200 α_F ($0 < \alpha_F < 1$) were never observed. This phenomenon can be illustrated by considering the relative
 201 fitnesses of different α_F as a function of T , as shown in Figure 3(a) where the intermediate value $\alpha_F = 0.5$
 202 never has maximal fitness (similar outcomes were observed for other intermediate values $0 < \alpha_F < 1$,
 203 not shown). Notably, at very high frequency of environmental change (small period T), fitness differences
 204 were found to be negligible.

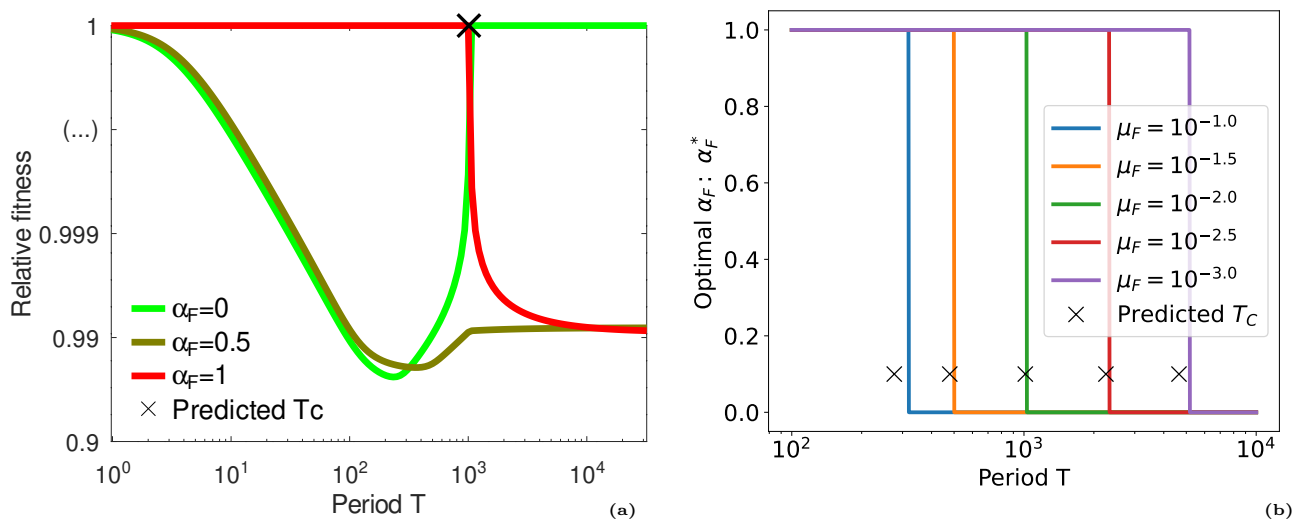


Figure 3: **The Lyapunov exponent is maximal for non-composite architectures.** (a) Relative fitness $\omega(\alpha) = \frac{W(\alpha)}{\max W}$ is represented as a function of the period T , for three different values of $\alpha_F = 0, 0.5, 1$. The maximal fitness is always attained at extremal values $\alpha_F = 0$ or $\alpha_F = 1$. The analytical value T_c of the transition between ‘unstable’ and ‘stable’ environments is reported by a cross-mark (Equation 5). (b) The optimal value ($\alpha_F^* = 0$ or $\alpha_F^* = 1$) is plotted as a function of the period T for different values of the fast mutation rate μ_F . Again, the switching time T_c is well approximated by the analytical expression (Equation 5) when μ_F is sufficiently distant from the values of s (10^{-1}) and μ_S (10^{-4}).

205 In fact, the counter-selection of intermediate α_F values (and symmetrically, of intermediate α_S values)
 206 turned out to be a theorem, whose statement is given below:

207 *Assume that the trait fitness function is linear ($\gamma = 1$), and $I \geq 2$. Then the Lyapunov*
 208 *exponent $\lambda(\alpha)$ is a convex function of the trait architecture α .*

209 This theorem is a consequence of the convexity properties of the spectral radius with respect to the
 210 diagonal coefficients (see *e.g.* Kingman 1961; Cohen 1981). A proof can be found in Appendix B for
 211 the sake of completeness. An immediate consequence of this theorem is that optimal values of the trait
 212 architecture are reached at some extremal point of the simplex set $\{\alpha = (\alpha_i) : (\forall i)\alpha_i \geq 0, \text{ and } \sum_i \alpha_i = 1\}$.
 213 Alternatively speaking, composite trait architectures should always be selected against when the selection
 214 function is linear.

215 Another implication of this theorem is the occurrence of sharp transitions, at specific threshold periods,
 216 corresponding to switches between optimal trait architectures α^* . In the case $I = 2$, there is one such
 217 switch at a critical value $T = T_c$, quantitatively separating unstable environments ($T < T_c$) where the
 218 Lyapunov exponent $\lambda(\alpha)$ is maximal at $\alpha_F = 1$ (full contribution of the fast inheritance system), from
 219 stable ones ($T > T_c$) where the Lyapunov exponent $\lambda(\alpha)$ is maximal at $\alpha_F = 0$ (full contribution of the
 220 slow inheritance medium), see Figure 3(b). The value of T_c can be computed analytically in the regime
 221 $\mu_S \ll \mu_F$, by seeking the value of T such that $\lambda(0) = \lambda(1)$. This was performed, and lead to the following

222 expression (after some further simplifications, see Appendix C for details):

$$\frac{T_c}{2} \approx \frac{1}{\mu_F} \log\left(\frac{\mu_F}{\mu_S}\right) \left(1 + \frac{\mu_F}{s}\right) \quad (5)$$

223 This approximation is valid in the regime $\mu_S \ll \mu_F \ll s$, that is, when the mutation rates are far
224 apart, and much below the maximal fitness defect s . It could be further simplified by neglecting $\frac{\mu_F}{s}$,
225 because selection is assumed to be strong enough so that it has limited influence on the threshold period
226 T_c .

227 As mentioned above, non-trivial outcomes are expected in the intermediate regime, when the rate
228 of environmental change falls in the range of mutation rates. Formula (5) makes this expectation more
229 precise as the switch occurs when the duration of one stasis (the half-period $\frac{T}{2}$) echoes the fast mutation
230 rate, up to a logarithmic correction. The latter correction is essential as it contains the ratio between
231 the two mutation rates (fast versus slow). Interestingly, although selection is obviously essential for this
232 process, its strength s only weakly influences the value of the switching period (no dependency at the
233 leading order in formula (5)). With more than two determinants (differing in their mutation rates), several
234 switching periods are expected, as exemplified in the case $I = 3$ (see Appendix D, Figure 7).

235 **3.1.2 Epistasis and contingency in the evolution of trait architectures**

236 A mutant genetic architecture may be more or less successful at invading particular (epi)genetic back-
237 grounds. For example, putting more weight on the fast inheritance system may be deleterious if this
238 system is not in the appropriate state in a certain environment (see Section 2). This creates an evolution-
239 ary interaction between a resident genetic architecture and the mutant architecture. Importantly, this is
240 ignored in the Lyapunov exponent approach, where the fitnesses of different architectures are compared
241 after each has reached its own (epi)genetic equilibrium frequencies. In contrast, this is well captured by
242 the adaptive dynamics framework. In this framework, the mutant invasion dynamics is approximated
243 through its growth rate at low frequency within a resident population under deterministic dynamics (infi-
244 nite population size approximation), that is when it is so rare that it does not itself impact the resident's
245 dynamics. This growth rate, calculated as detailed in Section 2, is represented in Figure 4(a) for
246 (65^2) pairs of mutant and resident strategies.

247 Based on this approach, we identified two types of singular strategies, as represented in Figure 4(a):
248 evolutionary repellors from which evolutionary trajectories tend to move away, and convergent stable
249 strategies (CSS) that represent possible long-term evolutionary attractors. Evolutionary trajectories

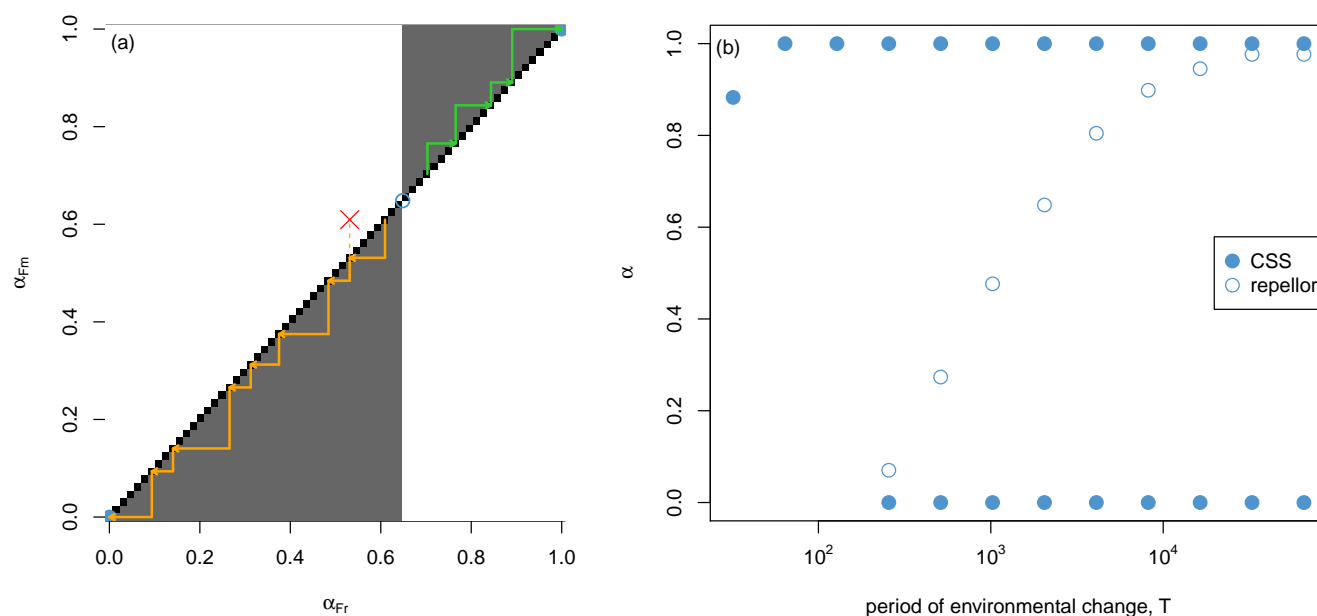


Figure 4: **Adaptive dynamics of trait architectures.** (a) A pairwise invasibility plot showing how evolutionary trajectories of the genetic architecture may depend on historical contingency. Black squares represent mutant/resident pairs where the relative growth rate of the mutant $\lambda(\alpha_{Fm}, \alpha_{Fr})$ is close to 1 ($\pm 10^{-9}$), while grey and white squares represent pairs where $\lambda(\alpha_{Fm}, \alpha_{Fr}) > 1$ and < 1 , respectively. A first example evolutionary trajectory is shown in orange: a mutant with a lower contribution of the ‘fast’ component α_{Fm} appears in a population with α_{Fr} close to 0.6. The mutant increases in frequency (*i.e.* it *invades*; grey square). It is expected to reach fixation (*i.e.* replace the resident) because the latter cannot invade back when it is rare (white square at the opposite coordinate, red cross). The evolutionary trajectory continues downwards until the architecture $\alpha_F = 0$ is fixed. Starting from a slightly different architecture ($\alpha_{Fr} \approx 0.7$, in green), the evolutionary trajectory goes in the opposite direction towards $\alpha_F = 1$, showing how the evolution of the genetic architecture may be contingent on the ancestral architecture of a population. Mutants increasing α_F in the orange trajectory or decreasing α_F in the blue one, not represented, may have appeared and failed to invade. The evolutionary repeller at $\alpha_F \approx 0.65$ is represented by an empty dot and the two CSS attractors at $\alpha_F = 0$ and 1 by plain dots. Parameter values: $\gamma = 1$, $T = 2048$, $s = 0.1$. (b) Singular strategies observed under a linear trade-off ($\gamma = 1$) and different frequencies of environmental change (x -axis in log scale). Singular strategies are either repellers (empty dots) or CSS attractors of the evolutionary dynamics (plain dots).

250 starting below or above the repeller will be markedly different. If the initial genotype has an architecture
 251 α_F below the repeller, *e.g.* $\alpha_F^{\text{repellor}} \approx 0.6$ in Figure 4(a), mutants with lower α_F will tend to invade and
 252 reach fixation. Because residents with higher α_F consistently fail to invade on average, these evolutionary
 253 dynamics will thus lead α_F downwards until $\alpha_F = 0$ is reached. The reverse occurs for starting points
 254 above the repeller. Thus, the existence of a repeller creates a contingency of the evolutionary dynamics
 255 on the initial genotype; whether, or rather how frequently it can be overcome by drift will depend on
 256 population features (but see Section 3.3) and the distribution of mutation effects on the trait’s architecture.
 257 But it should be noted that selection will consistently act against such crossing of the repeller, as shown
 258 by the large white areas in Figure 4(a) for which the probability of fixation is lower than that of a neutral
 259 mutant.

260 We next investigate how the types of singular strategies and their distribution change as a function of
 261 environmental instability, see Figure 4(b). When the environment is scarcely changing (up to $T \approx 256$),

262 two CSS attractors (at $\alpha_F = 0$ and $\alpha_F = 1$) and one repeller are present and only the position of the
263 repeller changes. In environments that change very rarely, the repeller is very close to $\alpha_F = 1$, such
264 that one may expect the evolution of architectures towards $\alpha_F = 0$, that is, with the lowest possible
265 contribution of the most unstable inheritance system. This conclusion is similar to that reached through
266 the Lyapunov exponent approach, and in line with the results of (Rajon and Charlat 2019). Under higher
267 environmental instability, the repeller moves to intermediate values of α_F such that the outcome will
268 depend on the initial genotype. This is again compatible with the results of (Rajon and Charlat 2019)
269 reporting an increase of the average α_F in similar contexts, especially since the initial (epi)genotypes were
270 uniformly distributed between 0 and 1 in their study. Decreasing further the period of environmental
271 change below a threshold of $T \approx 256$, only the CSS attractor at α_F equal or close to 1 remains.

272 The aforementioned conclusions derived from the adaptive dynamics were supported by Monte-Carlo
273 numerical simulations initialized with monomorphic populations, that is, where all individuals initially
274 have the same trait architecture: either $\alpha_F = 0.2$ as in Figure 5(a), or $\alpha_F = 0.8$ as in Figure 5(b). For
275 sufficiently large population size, $K = 4096$, we observed evolution towards one or the other of the two
276 extreme, non-composite trait architectures (blue trajectories), in agreement with results of Figure 4(a).
277 Individual trajectories are depicted respectively in Figure 5(e) and Figure 5(h), showing a clear selection of
278 the extreme values, with only few trajectories crossing the repeller in Figure 5(e), and none in Figure 5(h)
279 among 256 replicates. The other panels (smaller population sizes) will be discussed below in Section 3.3.

280 3.2 Sensitivity to the fitness function shape

281 3.2.1 Composite architectures are selected against when the fitness function is convex

282 The results of Section 3.1.1 can be extended to the case of a convex fitness function, in the sense of
283 Figure 1 ($\gamma < 1$). Indeed, the trait architecture fitness inherits convexity from the trait fitness function,
284 as stated in the following theorem.

285 *Assume that the trait fitness function is convex, and $I \geq 2$. Then, the Lyapunov exponent*
286 *$\lambda(\alpha)$ is a convex function of the trait architecture α .*

287 As a by-product of convexity, we deduce that, in the case $I = 2$, the critical time $T = T_c$ does
288 not depend on the shape parameter γ , provided that $\gamma \leq 1$ (convex selection), simply because it is
289 characterized by the Lyapunov exponents of the extreme trait architectures through the equality $\lambda(0) =$

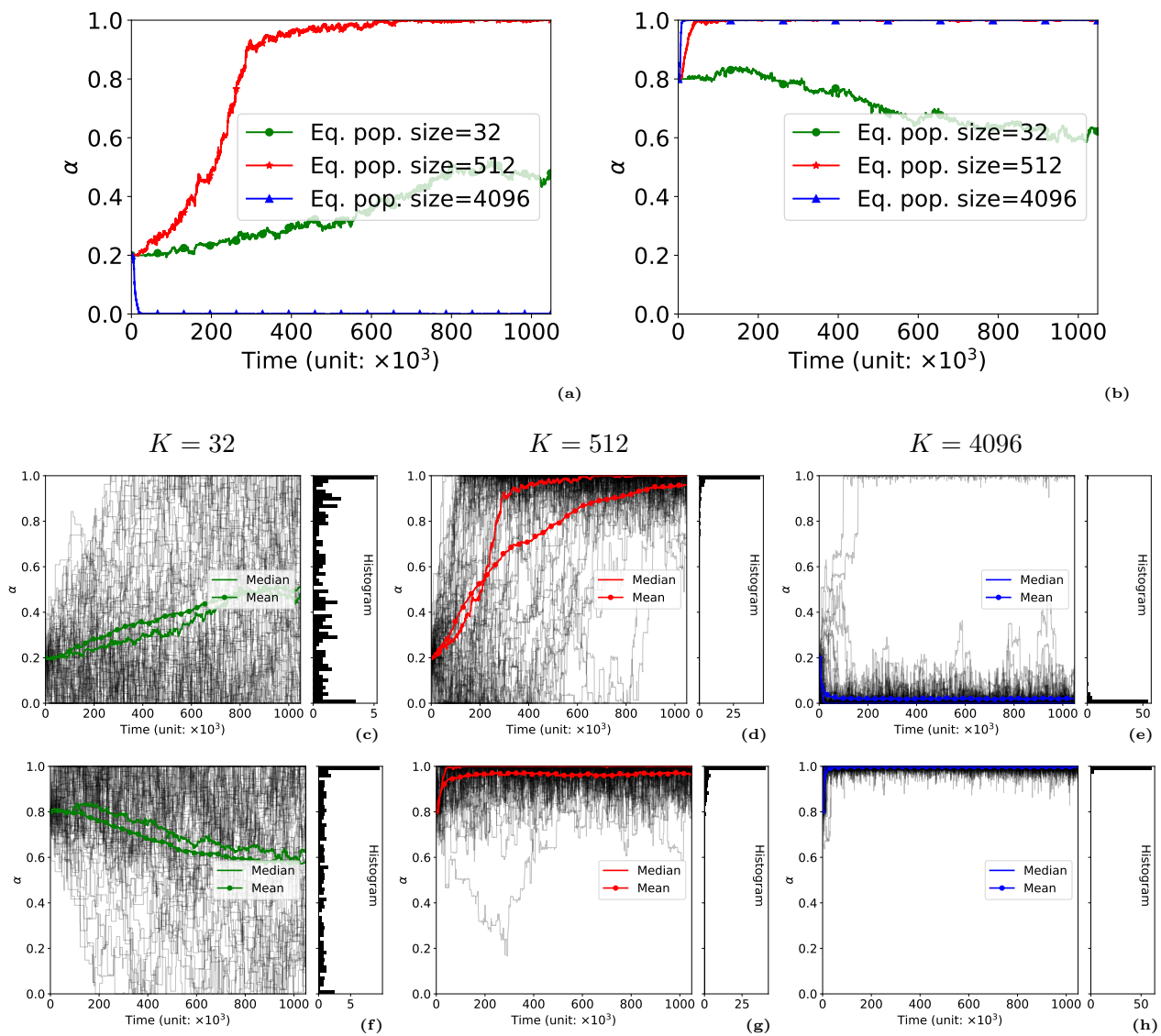


Figure 5: **Temporal dynamics of the trait architecture with monomorphic initial configuration.** (a-b) Median of the mean value $\overline{\alpha}_F$ over the population for 256 simulation replicates starting respectively from: $\alpha_F = 0.2$ (a), and $\alpha_F = 0.8$ (b), associated with various population size. The (epi)genotypes are initialized with the monomorphic equilibrium distribution, depending on the value of α_F . The figure legend indicates the typical population size for each of the three numerical experiments (resp. $K = 32, 512, 4096$). The case of small population size ($K = 32$) exhibits a pattern of neutral evolution, dominated by genetic drift. The cases of intermediate population size ($K = 512$) and large population size ($K = 4096$) exhibit the same trend when starting from $\alpha_F = 0.8$ (above the repeller value ≈ 0.65), but opposite trends when starting from $\alpha_F = 0.2$ (below the repeller value). (c-h) Sample of the simulation replicates ($N = 64$): trajectories of the mean value $\overline{\alpha}_F$ in each simulation out of the sample is plotted in dark line, and the final distribution is plotted as a side histogram. Values are as follows (typical population size K , and initial value of the monomorphic trait architecture α_F): $K = 32, \alpha_F = 0.2$ (c); $K = 512, \alpha_F = 0.2$ (d); $K = 4096; \alpha_F = 0.2$ (e); $K = 32, \alpha_F = 0.8$ (f); $K = 512, \alpha_F = 0.8$ (g); $K = 4096; \alpha_F = 0.8$ (h). Parameter values: period $T = 2048$, $s = 0.1$ (same as Figure 4).

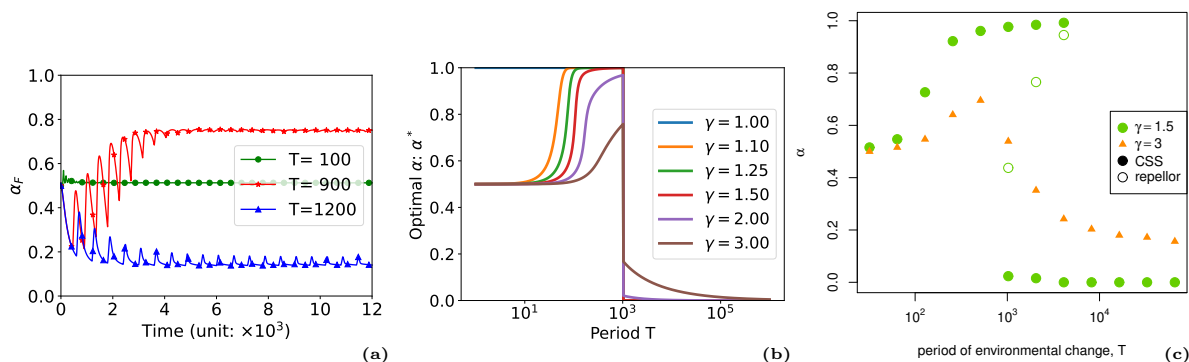


Figure 6: **Main outcomes for concave fitness functions.** (a) Temporal dynamics for the deterministic PDE models of infinite population size for three values of the time period $T = 100$, $T = 900$, and $T = 1200$, and $\gamma = 3$ (analogous to Figure 2(a)). The mean value of α_F in the population is plotted over time. In contrast with the linear case, we observed the selection for non-composite architectures, especially when the environment is very unstable ($T = 100$). (b) The optimal value α_F^* is represented as a function of the shape parameter $\gamma > 1$ (analogous to Figure 3(b)). In contrast with the linear case, non-composite architectures can result in a higher relative fitness ω , especially when the environment is very unstable, or when γ is large. (c) Singular strategies observed under a concave selection function ($\gamma > 1$) and different periods of environmental change). Singular strategies are either repellers (empty dots) or CSS attractors of the evolutionary dynamics (plain dots or triangles).

290 $\lambda(1)$. Since the intensity of selection does not depend on γ at the extremal architectures (either 1 or $1 - s$,
 291 and vice-versa), the balance $\lambda(0) = \lambda(1)$ does not involve the parameter γ .

292 It is important to notice that there is no corresponding statement regarding concavity, that is, the
 293 trait architecture fitness does not inherit concavity from the trait fitness function in general. For instance,
 294 the selection function in the case $\gamma = 1$ (Section 3.1.1) is both convex and concave because it is linear.
 295 However, the trait fitness architecture is strictly convex in this case. It is the transition between several
 296 (epi)genetic states by mutation, and the environmental variation which generates such strict convexity.

297 Since the convexity property is a strong feature, which holds true even in the case of a linear selection
 298 function, we expect that convexity of the Lyapunov exponent persists beyond the linear regime, even if the
 299 trait fitness function is not convex anymore, say slightly concave. Robustness of the previous conclusions
 300 with respect to the shape of the fitness function is the purpose of the next section.

301 3.2.2 Concave fitness functions may select for composite architectures

302 Contrary to convexity, concave fitness functions may result in positive selection for a balanced contribution
 303 of various determinants – that is $0 < \alpha_F < 1$ – compare Figure 6(a) with Figure 2(a). Thus, in order
 304 to assess the robustness of our main conclusions from Section 3.1.1, we investigated the optimal trait
 305 architecture maximizing the Lyapunov exponent $\lambda(\alpha)$ in the case of a concave selection function ($\gamma \geq 1$),
 306 see Figure 6(b). Interestingly, the concept of a critical switching value T_c still exists when composite

307 trait architectures are selected for, even for large values of γ . Fast inheritance systems have more weight
308 in the selected architecture ($\alpha_F^* > 0.5$) when $T < T_c$. In contrast, slow inheritance systems have more
309 weight in the selected architecture ($\alpha_F^* < 0.5$), when $T > T_c$. Moreover, the transition is sharp at $T = T_c$
310 (switch between a clear balance on the side of fast inheritance towards a clear balance on the opposite
311 side), a feature shared with the convex case, compare Figure 6(b) with Figure 3(b). Although we lack a
312 formula for the critical value T_c in the concave case, we see clearly that it does not depend on the shape
313 parameter (γ). Although this may appear surprising at first glance, it might be expected from the fact
314 that the critical value does not depend on the shape parameter (γ), nor on the intensity of selection (s)
315 at the leading order in the convex case, see Equation (5).

316 Notably, non-composite architectures can still be selected for, for moderate shape parameter ($\gamma \lesssim 1.5$)
317 and period T close enough to the switching period T_c . For large γ , the fastest inheritance system ($\alpha_F^* = 1$)
318 is never selected for, and the slowest one is selected for only in very stable environments ($T \gg T_c$).

319 Regarding the adaptive dynamics, the results in Figure 6(c) are consistent with the previous results.
320 When the selection function is moderately concave (here, $\gamma = 1.5$), and the environment changes in-
321 frequently ($T > 8192$), a single CSS attractor is present at α_F close to 0. For intermediate regimes of
322 environmental variation, a repeller and the two attractors at respectively low and high α_F are present,
323 similar to the case where $\gamma = 1$ (compare with Figure 6(b)). As environmental variations become more
324 frequent, at $T < 1024$ a single CSS remains and the expected selected architecture tends to intermediate
325 values of α_F , ending up at $\alpha_F = 0.5$ for very frequent changes. As concavity increases to $\gamma = 3$, the
326 transition between an architecture with a large contribution of the determinant with the lowest mutation
327 rate (low α_F) in scarcely varying environments to an architecture with a higher α_F no longer includes
328 a repeller, nor a very large contribution of the least stable determinant – *i.e.* α_F does not reach values
329 close to 1.

330 **3.3 Sensitivity to population size: a new case of sign inversion**

331 We used simulations to assess the predictions of the adaptive dynamics approach under more or less
332 effective selective regimes, that is, under various populations sizes. Simulations behave as expected when
333 the population size is sufficiently large ($K = 4096$), that is α_F goes to 0 when the population is initiated
334 with α_F below the repeller and to 1 otherwise. In very small populations, selection is overall inefficient
335 and α_F tends to become uniformly distributed, independently of its initial value ($K = 32$ in Figure 5).
336 This is also expected since genetic drift tends to dominate over selection in these conditions. But in

337 populations of intermediate sizes ($K = 512$ in Figure 5), simulations reveal a complex pattern. When
338 the initial value $\alpha_F = 0.8$ is above the repellor, it evolves toward 1, as expected. Yet, surprisingly, α_F
339 also evolves toward 1 when it is initiated *below* the repellor, at initial value $\alpha_F = 0.2$. In other words,
340 we found that not only the efficiency of selection, but also its direction, depends on the population size
341 (compare panels (d) and (e) of Figure 5, where the only parameter that differs is K).

342 We reached the following interpretation for this surprising pattern. The evolution of α_F in fluctu-
343 ating environments is dynamically driven by two opposite selective pressures: (1) upon shifts to a new
344 environment, high values of α_F are selected for, because these give more weight to the "fast" inheritance
345 system, that has a higher chance of being in a state that matches the new environment, or to reach this
346 state through an (epi)mutation; (2) during periods of environmental stasis, low values of α_F are selected
347 for, because these reduce the cost of frequent deleterious (epi)mutations. Depending on the frequency
348 of environmental change, one of these processes tends to dominate, provided that populations are large
349 enough. A plausible interpretation for the observed pattern (that is, for a deterministic evolution of α_F
350 toward high values in populations of "intermediate size") relies on noting that the strength and duration
351 of the selection associated with the two processes differ. As a result, one process, subject to stronger
352 selection than the other, may become effective in populations where the other is not. More specifically,
353 what we see here is in our view stemming for a strong (but infrequent) selection toward high α_F values
354 upon environmental change and a weak (but durable) selection toward low α_F values during periods of
355 environmental stasis. Both are effective in large populations, but weak and durable selection toward low
356 α_F dominates. In contrast, in populations of intermediate size, only the strong albeit infrequent selection
357 toward high α_F operates.

358 With this explanation in mind, we realized that other authors have recently shed light on a very similar
359 process that they coined 'sign inversion' (Raynes, Wylie, et al. 2018; Raynes, Burch, and Weinreich 2021).
360 This expression appropriately emphasizes the main point of the explanation: changes in population size
361 can not only make selection more or less efficient, but may also inverse its direction in systems where
362 two opposing pressures are at play and differ in their intensity and duration. In large populations, both
363 pressures are effective, but weak and long lasting selection may dominate; under a certain threshold
364 population size, only the strong but infrequent selection is effective. Following the discovery of this
365 process in a study focusing on the evolution of mutation rates, Raynes, Wylie, et al. 2018 have noted that
366 this process may be far more than anecdotal, because many traits can be subject to opposing selective
367 pressures, for example because of temporal variations in the environment. Our study provides one more

368 example of situations where this process would take place.

369 **4 Conclusion**

370 Our analysis was aimed at assessing the hypothesis that heterogeneity in the mutation rates of a trait's
371 determinants (of whatever nature) may affect the evolution of its architecture, that is, of the respective
372 contributions of the different determinants. Our main conclusion is that in a variety of conditions, in both
373 stable and unstable environments, non-composite architectures are effectively selected for, meaning that
374 trait values would tend to depend upon a single determinant, or several determinants characterized by
375 similar mutation rates. This sheds light on prior simulation results (Rajon and Charlat 2019) as we now
376 understand how the degree of environmental variation conditions which determinant, rather than which
377 mixture of determinants, takes part to the trait architecture. This focus on the mutational portfolio of
378 traits contributes to the general understanding of the evolution of a trait's architecture, as a complement
379 to the more common focus on the number of contributing genes, their epistatic and pleiotropic properties,
380 and the distribution of their respective effects.

381 Let us emphasize that a non-composite trait architecture may still be "complex" in the sense of
382 involving many determinants (*e.g.* Ungerer et al. 2002; Flint and Mackay 2009; Kemper, Visscher, and
383 Goddard 2012; Yengo et al. 2022). For example, Rajon and Plotkin 2013, in a model assuming a single
384 mutation rate, have shown that many genes should contribute to traits subject to a stabilizing selection
385 of mild intensity. In such a context, where the environment is kept stable, our model predicts that the
386 architecture should be non-composite. Overall, a complex yet non composite architecture would then be
387 expected, involving the most stable determinants.

388 The impact of environmental heterogeneity on the evolution of trait architecture has also been the
389 subject of previous studies. Yeaman and Whitlock 2011 have shown that spatial differences in traits
390 optima leads the evolution of recombination landscapes toward simplified architecture where clusters of
391 genes have large impact of the phenotype. Using yet another framework, the results of (Hansen et al.
392 2006) suggest that directional selection, producing an ever going requirement for adaptation should result
393 in an increase in mutational effects through changes in epistatic interactions, provided that mutations are
394 rare enough.

395 In our study, we focused on temporal environmental fluctuations on the evolution of the trait archi-
396 tecture. More specifically, we assumed that environmental changes reverse the direction of selection, with

397 fitness gains modeled as concave, linear, or strictly convex functions. These shapes were found critical:
398 only a concave fitness function resulted in composite architectures, provided that the degree of instability
399 overcomes a threshold. The same conclusion holds for a mixture of concave and convex fitness shapes,
400 like the typical case of a Gaussian function centered on a moving optimum, see Appendix D, Figure 8(a).
401 In such a case, the amplitude of the fluctuations may be critical because Gaussian functions are concave
402 close to the center, but convex at the border, as can be seen in Appendix D, Figure 8(b).

403 While the shape of fitness functions acting on the trait is a key parameter, it will only be relevant if
404 selection on the architecture is effective, which ultimately depends on its strength, in relation with popu-
405 lation size. We developed complementary approaches to investigate the strength of selection on the trait
406 architecture. The Lyapunov exponent approach revealed conditions where composite architecture are not
407 optimal, but it missed the notion that the evolution of trait architecture is driven by the background
408 variations, accumulated by different determinants through their distinct mutation rates and across envi-
409 ronmental fluctuations. The adaptive dynamics approach captured this effect, by assessing the average
410 strength of selection over an environmental fluctuation period. But Monte Carlo simulations in popula-
411 tions of finite size revealed a singular aspect of these dynamics, related to the effect of drift. Simulations
412 in large populations were in agreement with the adaptive dynamics predictions, and those in very small
413 populations were as expected driven by drift only. Yet, in populations of intermediate sizes, we found
414 that the trait architecture evolves deterministically in the opposite direction as in large populations. We
415 interpret this result as a new occurrence of ‘sign inversion’ (Raynes, Wylie, et al. 2018; Raynes, Burch, and
416 Weinreich 2021), stemming from the periodic alternation between long time windows of weak selection for
417 a heavy contribution of stable inheritance systems (inefficient in populations of intermediate sizes) and
418 short time windows of strong selection for a heavy contribution of unstable systems. This result further
419 complexifies our understanding of the evolution of genetic architectures, arguing in favor of a systematic
420 use of population genetics models and, as an aside, for further mathematical analyses that would clarify
421 and generalize the conditions for the occurrence of sign inversion.

422 References

423 Andre, J. B. and B. Godelle. “The evolution of mutation rate in finite asexual populations”. *Genetics* 172
424 (2006).

- 425 Clairambault, J., S. Gaubert, and T. Lepoutre. “Circadian rhythm and cell population growth”. *Mathe-*
426 *matical and Computer Modelling* 53 (2011).
- 427 Cohen, J. E. “Convexity of the dominant eigenvalue of an essentially nonnegative matrix”. *Proceedings of*
428 *the American Mathematical Society* 81 (1981).
- 429 Danchin, E. “Avatars of information: towards an inclusive evolutionary synthesis”. *Trends Ecol Evol* 28
430 (2013).
- 431 Denkena, J., F. Johannes, and M. Colomé-Tatché. “Region-level epimutation rates in *Arabidopsis thaliana*”.
432 *Heredity* 127 (2021).
- 433 Dodson, A. E. and J. Rine. “Heritable capture of heterochromatin dynamics in *Saccharomyces cerevisiae*”.
434 *eLife* 4 (2015).
- 435 Flint, J. and T. F. C. Mackay. “Genetic architecture of quantitative traits in mice, flies, and humans”.
436 *Genome Res.* 19 (2009).
- 437 Geritz, S., E. Kisdi, G. Meszéna, and J. Metz. “Evolutionarily singular strategies and the adaptive growth
438 and branching of the evolutionary tree”. *Evol Ecol* 12 (1998).
- 439 Graaf, A. van der, R. Wardenaar, D. A. Neumann, et al. “Rate, spectrum, and evolutionary dynamics of
440 spontaneous epimutations”. *Proceedings of the National Academy of Sciences* 112 (2015).
- 441 Hansen, T. F., J. M. Alvarez-Castro, A. J. R. Carter, and J. Hermis. “Evolution of Genetic Architecture
442 under Directional Selection”. *Evolution* 60 (2006).
- 443 Hodgkinson, A. and A. Eyre-Walker. “Variation in the mutation rate across mammalian genomes”. *Nature*
444 *Reviews Genetics* 12 (2011).
- 445 Ishii, K., H. Matsuda, Y. Iwasa, and A. Sasaki. “Evolutionarily stable mutation rate in a periodically
446 changing environment”. *Genetics* 121 (1989).
- 447 Johannes, F., E. Porcher, F. K. Teixeira, et al. “Assessing the impact of transgenerational epigenetic
448 variation on complex traits”. *PLoS Genet* 5 (2009).
- 449 Johnson, T. “Beneficial mutations, hitchhiking and the evolution of mutation rates in sexual populations”.
450 *Genetics* 151 (1999).
- 451 Kemper, K. E., P. M. Visscher, and M. E. Goddard. “Genetic architecture of body size in mammals”.
452 *Genome Biol.* 13 (2012).
- 453 Kingman, J. F. C. “A convexity property of positive matrices”. *The Quarterly Journal of Mathematics*
454 12 (1961).

- 455 Metz, J., R. Nisbet, and S. Geritz. “How should we define ‘fitness’ for general ecological scenarios?” *Trends*
456 *Ecol Evol* 7 (1992).
- 457 Oman, M., A. Alam, and R. W. Ness. “How Sequence Context-Dependent Mutability Drives Mutation
458 Rate Variation in the Genome”. *Genome Biology and Evolution* 14 (2022).
- 459 Rajon, E. and J. B. Plotkin. “The evolution of genetic architectures underlying quantitative traits”. *Proc.*
460 *R. Soc. Lond. B* (2013).
- 461 Rajon, E. and S. Charlat. “(In)exhaustible Suppliers for Evolution? Epistatic Selection Tunes the Adaptive
462 Potential of Nongenetic Inheritance”. *The American Naturalist* 194 (2019).
- 463 Rando, O. J. and K. J. Verstrepen. “Timescales of genetic and epigenetic inheritance”. *Cell* 128 (2007).
- 464 Raynes, Y., C. L. Burch, and D. M. Weinreich. *When good mutations go bad: how population size can*
465 *change the direction of natural selection*. preprint. *Evolutionary Biology*, 2021.
- 466 Raynes, Y., C. S. Wylie, P. D. Sniegowski, and D. M. Weinreich. “Sign of selection on mutation rate
467 modifiers depends on population size”. *Proceedings of the National Academy of Sciences* 115 (2018).
- 468 Rechavi, O., G. Minevich, and O. Hobert. “Transgenerational Inheritance of an Acquired Small RNA-
469 Based Antiviral Response in *C. elegans*”. *Cell* 147 (2011).
- 470 Ungerer, M. C., S. S. Halldorsdottir, J. L. Modliszewski, T. F. C. Mackay, and M. D. Purugganan.
471 “Quantitative trait loci for inflorescence development in *Arabidopsis thaliana*”. *Genetics* 160 (2002).
- 472 Yeaman, S. and M. C. Whitlock. “The genetic architecture of adaptation under migration-selection bal-
473 ance”. *Evolution* 65 (2011).
- 474 Yengo, L., S. Vedantam, E. Marouli, et al. “A saturated map of common genetic variants associated with
475 human height”. *Nature* (2022).

476 Appendices

477 A Model reduction for Lyapunov exponent computation

478 In this section, we aim to detail the links between the continuous model presented in Section 2.4 and
 479 formalized by Equation (4) and the Lyapunov exponent computation. Indeed, the dynamic is driven by
 480 the leading eigenvalues in a linear ordinary differential equation system. The presence of the integral
 481 term for the trait architecture mutation and the logistic growth rate to model the density dependent
 482 saturation make our model non-linear. However, in the case of a monomorphic population, when the
 483 trait architecture mutations are neglected, we demonstrate a correspondance with the Floquet spectral
 484 theory of periodic linear systems, such that the average of the density over one period, $\frac{1}{T} \int_0^T \rho(t) dt$, and
 485 the Lyapunov exponent defined in Equation (1), coincide.

486 Assume that mutations on the trait architecture α are negligible. For a given trait architecture α and
 487 group $X \in \{(0, 0), (1, 0), (0, 1), (1, 1)\}$ the equation (4) becomes

$$\partial_t g_X(t, \alpha) = (1 - s|\Phi_X(\alpha) - \Phi^*(t)|^\gamma - \rho(t))g_X(t, \alpha) + (MG)_X(t, \alpha). \quad (6)$$

488 Depending on the optimal phenotype Φ^* , the system gathering equations (6) writes

$$\begin{cases} \partial_t G(t, \alpha) = (A - \rho(t)\mathbf{I})G(t, \alpha), & \text{if } \Phi^*(t) = 0, \\ \partial_t G(t, \alpha) = (B - \rho(t)\mathbf{I})G(t, \alpha), & \text{if } \Phi^*(t) = 1. \end{cases} \quad (7)$$

489 Assume that both matrix A and B can be diagonalised. Thus, there exist a constant invertible matrix
 490 P_A (resp. P_B) and a diagonal matrix D_A (resp. D_B) such that $A = P_A D_A P_A^{-1}$ (resp. $B = P_B D_B P_B^{-1}$).
 491 So the systems (7) becomes

$$\begin{cases} \partial_t (P_A^{-1} G(t, \alpha)) = (D_A - \rho(t)\mathbf{I})P_A^{-1} G(t, \alpha), & \text{if } \Phi^*(t) = 0, \\ \partial_t (P_B^{-1} G(t, \alpha)) = (D_B - \rho(t)\mathbf{I})P_B^{-1} G(t, \alpha), & \text{if } \Phi^*(t) = 1. \end{cases} \quad (8)$$

492 With the notations $H_A(t, \alpha) = P_A^{-1}G(t, \alpha)$ and $H_B(t, \alpha) = P_B^{-1}G(t, \alpha)$ this systems writes

$$\begin{cases} \partial_t(H_A(t, \alpha)) = (D_A - \rho(t)\mathbf{I})H_A(t, \alpha), & \text{if } \Phi^*(t) = 0, \\ \partial_t(H_B(t, \alpha)) = (D_B - \rho(t)\mathbf{I})H_B(t, \alpha), & \text{if } \Phi^*(t) = 1. \end{cases} \quad (9)$$

493 **Relations between H components:** Let $H_{A,i}$ denotes the i^{th} components of H_A and $d_{A,i}$ the i^{th}
494 diagonal term of D_A . Assume that the $H_{A,i}$ never vanishes, then

$$\frac{\partial_t H_{A,i}(t, \alpha)}{H_{A,i}(t, \alpha)} - d_{A,i} = \rho(t). \quad (10)$$

495 Thus, for any pair (i, j)

$$\frac{\partial_t H_{A,i}(t, \alpha)}{H_{A,i}(t, \alpha)} - d_{A,i} = \frac{\partial_t H_{A,j}(t, \alpha)}{H_{A,j}(t, \alpha)} - d_{A,j} \quad (11)$$

$$\implies H_{A,i}(t, \alpha) = H_{A,j}(t, \alpha) \frac{H_{A,i}^0}{H_{A,j}^0} e^{(d_{A,i} - d_{A,j})(t - t_0)}. \quad (12)$$

496 with $H_A^0 = H_A(t_0, \alpha)$. Therefore, the relative dynamics of the components of the vector H depend on
497 the difference between the eigenvalues of A . By the same reasoning and using similar notations it also
498 comes

$$H_{B,i}(t, \alpha) = H_{B,j}(t, \alpha) \frac{H_{B,i}^0}{H_{B,j}^0} e^{(d_{B,i} - d_{B,j})(t - t_0)}. \quad (13)$$

499 **Solution characterization using total population size:** According to systems (9), as long as $\Phi^*(t)$
500 remains constant on the time interval $[t_0, t]$ with $t > t_0$ the solutions are

$$\begin{cases} H_A(t, \alpha) = \exp\left(D_A(t - t_0) - \int_{t_0}^t \rho(s) ds\right) H_A^0, & \text{if } \Phi^*(t) = 0, \\ H_B(t, \alpha) = \exp\left(D_B(t - t_0) - \int_{t_0}^t \rho(s) ds\right) H_B^0, & \text{if } \Phi^*(t) = 1 \end{cases} \quad (14)$$

501 with $H_A^0 = H_A(t_0, \alpha)$ and $H_B^0 = H_B(t_0, \alpha)$. Note that these formulas rely on $\int_{t_0}^t \rho(s) ds$ which is not
 502 explicitly known. Using the relation $G(t, \alpha) = P_A H_A(t, \alpha)$ and $G(t, \alpha) = P_B H_B(t, \alpha)$ it comes

$$\begin{cases} G(t, \alpha) = P_A \exp\left(D_A(t - t_0) - \int_{t_0}^t \rho(s) ds\right) P_A^{-1} G_0, & \text{if } \Phi^*(t) = 0, \\ G(t, \alpha) = P_B \exp\left(D_B(t - t_0) - \int_{t_0}^t \rho(s) ds\right) P_B^{-1} G_0, & \text{if } \Phi^*(t) = 1. \end{cases} \quad (15)$$

503 where $G_0 = (t_0, \alpha)$. These formulas simply into

$$\begin{cases} G(t, \alpha) = \exp\left(-\int_{t_0}^t \rho(s) ds\right) e^{A(t-t_0)} G_0, & \text{if } \Phi^*(t) = 0, \\ G(t, \alpha) = \exp\left(-\int_{t_0}^t \rho(s) ds\right) e^{B(t-t_0)} G_0, & \text{if } \Phi^*(t) = 1. \end{cases} \quad (16)$$

504 A.1 Groups dynamic in stable environment

505 Without loss of generality, let's consider the case of $\Phi^*(t) = 0$ and drop the subscript A to shorten
 506 notations. Using $G(t, \alpha) = P H(t, \alpha)$ one can deduce that the expression of G_i the i^{th} components of G is

$$G_i(t, \alpha) = \sum_{j=1}^n P_{i,j} H_j(t, \alpha) = \frac{H_\ell(t, \alpha)}{H_\ell^0} \sum_{j=1}^n P_{i,j} H_j^0 e^{(d_j - d_\ell)(t - t_0)}. \quad (17)$$

507 where ℓ is an arbitrary index to be fixed later. Thus, the total population size is

$$\rho(t) = \sum_{i=1}^n G_i(t, \alpha) = \frac{H_\ell(t, \alpha)}{H_\ell^0} \sum_{i=1}^n \sum_{j=1}^n P_{i,j} H_j^0 e^{(d_j - d_\ell)(t - t_0)}. \quad (18)$$

508 Therefore, the relative group size within the total population size is

$$\frac{G_i(t, \alpha)}{\rho(t)} = \frac{\sum_{j=1}^n P_{i,j} H_j^0 e^{(d_j - d_\ell)(t - t_0)}}{\sum_{i=1}^n \sum_{j=1}^n P_{i,j} H_j^0 e^{(d_j - d_\ell)(t - t_0)}} \quad (19)$$

$$= \frac{\sum_{j=1}^n P_{i,j} H_j^0 e^{d_j(t - t_0)}}{\sum_{i=1}^n \sum_{j=1}^n P_{i,j} H_j^0 e^{d_j(t - t_0)}} \quad (20)$$

509 Thus, the relative group size dynamic is fully determined by the eigenvalues of matrix A . Moreover,

510 this shows that the whole dynamic is driven by the A matrix leading eigenvalue:

$$\frac{G_i(t, \alpha)}{\rho(t)} \simeq \frac{P_{i,\ell} H_\ell^0 e^{d_\ell(t-t_0)}}{\sum_{i=1}^n P_{i,\ell} H_\ell^0 e^{d_\ell(t-t_0)}} = \frac{P_{i,\ell}}{\sum_{i=1}^n P_{i,\ell}} \quad (21)$$

511 assuming that d_ℓ is the leading eigenvalue. Note that $\frac{P_{i,\ell}}{\sum_{i=1}^n P_{i,\ell}}$ correspond to the normalised value of
 512 the i^{th} component of the eigenvector associated to d_ℓ . That is, the normalised eigenvector associated with
 513 the largest eigenvalue of A approximates the relative group sizes.

514 A.2 Groups dynamic in periodic environment

515 Let's consider a periodic environment of period T . Without loose of generality let assume that $\Phi^*(t) = 0$
 516 for $t \in [0, \frac{T}{2}]$ and $\Phi^*(t) = 1$ for $t \in [\frac{T}{2}, T]$. Thus, starting from $G_0 = G(0, \alpha)$ and using formulas (16) the
 517 solution at $t = T$ is

$$\begin{aligned} G(T, \alpha) &= \exp\left(-\int_{\frac{T}{2}}^T \rho(s) ds\right) e^{\frac{BT}{2}} \exp\left(-\int_0^{\frac{T}{2}} \rho(s) ds\right) e^{\frac{AT}{2}} G_0 \\ &= \exp\left(-\int_0^T \rho(s) ds\right) e^{\frac{BT}{2}} e^{\frac{AT}{2}} G_0 \end{aligned}$$

518 Assume that the solution becomes periodic, namely $G(T, \alpha) = G_0$ then the previous formula lead to

$$e^{\frac{BT}{2}} e^{\frac{AT}{2}} G_0 = \exp\left(\int_0^T \rho(s) ds\right) G_0.$$

519 So G_0 is the eigenvector associated to the leading eigenvalue $\exp\left(\int_0^T \rho(s) ds\right)$ of $e^{\frac{BT}{2}} e^{\frac{AT}{2}}$. Moreover,
 520 this demonstrates that the leading eigenvalue is real.

521 Up to renormalization, the eigenvector G_0 can be interpreted as the relative group sizes within the
 522 whole population. Indeed, the relative size of a group ℓ is simply $\frac{(G_0)_\ell}{\sum_i (G_0)_i}$.

523 B Proof of convexity

524 This section is devoted to the mathematical proof of our main convexity result, that is the convexity
525 of the Lyapunov exponent $\lambda(\alpha)$ in the case of a convex selection function ($\gamma \leq 1$). This result can be
526 recast in the framework of convexity of dominant eigenvalues of non-negativity matrices. To apply such
527 theory, one should be careful about the convex combination of coefficients during convex interpolation.
528 Indeed, the diagonal coefficients and the off-diagonal coefficients do not play the same role, for as they are
529 not subject to the same constraints (non-negativity constraints off the diagonal). More precisely, convex
530 combinations are arithmetical on the diagonal, but geometrical off the diagonal (see the θ -interpolation
531 below). The situation is facilitated in our model as the selection acts only on the diagonal terms via a
532 trait-dependent mortality rate. Nevertheless, we shall present a more general result to emphasize this
533 discrepancy between diagonal and off-diagonal coefficients.

534 We claim that the following Theorem encompasses our main convexity result:

535 *Let A, B two matrices with positive entries off the diagonal¹, that is $\forall(i, j) a_{ij} > 0, b_{ij} > 0$.*

536 *Let $\theta \in (0, 1)$. Consider the matrix C_θ defined by the following term-by-term interpolation:*

$$\begin{cases} c_{ii} = (1 - \theta)a_{ii} + \theta b_{ii} \\ c_{ij} = a_{ij}^{1-\theta} b_{ij}^\theta \quad (i \neq j) \end{cases}$$

537 *Then the dominant (Perron) eigenvalues $\lambda(A), \lambda(B), \lambda(C_\theta)$ satisfy the following convex in-*
538 *equality:*

$$\lambda(C_\theta) \leq (1 - \theta)\lambda(A) + \theta\lambda(B) \quad (22)$$

539 We make the following comments:

- 540 • This result is classically credited to (Kingman 1961).
- 541 • The result can be extended straightforwardly to irreducible matrices by a limiting argument.
- 542 • We are interested in the particular case where A and B differ only by their diagonal entries, that
543 is, $a_{ij} = b_{ij}$ if $i \neq j$. In this case, the interpolation $c_{ij} = a_{ij}^{1-\theta} b_{ij}^\theta$ is trivial, and the convex inequality

¹usually referred to as a Metzler matrix

544 (22) can be reformulated as: $\lambda((1 - \theta)A + \theta B) \leq (1 - \theta)\lambda(A) + \theta\lambda(B)$. Alternatively speaking, the
 545 dominant eigenvalue is convex with respect to its diagonal.

546 • In fact, the proof can be extended to the Floquet eigenvalues in the periodic setting, which is
 547 precisely our focus:

548 *Let $A(t), B(t)$ a pair of time-dependent, periodic, matrices with positive entries off the*
 549 *diagonal. Let $\theta \in (0, 1)$. Consider the matrix $C_\theta(t)$ defined pointwise as follows:*

$$\begin{cases} c_{ii}(t) = (1 - \theta)a_{ii}(t) + \theta b_{ii}(t) \\ c_{ij}(t) = a_{ij}^{1-\theta}(t)b_{ij}^\theta(t) & (i \neq j) \end{cases}$$

550 *Then the dominant (Floquet) eigenvalues $\lambda(A), \lambda(B), \lambda(C_\theta)$ satisfy the following convex*
 551 *inequality:*

$$\lambda(C_\theta) \leq (1 - \theta)\lambda(A) + \theta\lambda(B) \tag{23}$$

552 We present first the proof of the static case (Perron eigenvalues), then we extend the method to the
 553 time-periodic setting (Floquet eigenvalues).

554 Our approach is based on (Clairambault, Gaubert, and Lepoutre 2011), see also (Cohen 1981).

555 **The static case**

556 We need the following eigen-elements: X (resp. Y) the positive (right) eigenvector of A (resp. B), and Φ
 557 the positive (left) eigenvector of C . We have accordingly:

$$\begin{cases} AX = \lambda(A)X \\ BY = \lambda(B)Y \end{cases}, \quad \Phi^T C = \lambda(C)\Phi^T \tag{24}$$

558 We define Z by the pointwise interpolation: $z_i = x_i^{1-\theta}y_i^\theta$. Then, we evaluate the Collatz-Wielandt
 559 ratio:

$$\begin{aligned}
 \sum_j c_{ij} \frac{z_j}{z_i} &= (1 - \theta)a_{ii} + \theta b_{ii} + \sum_{j \neq i} a_{ij}^{1-\theta} b_{ij}^\theta \frac{x_j^{1-\theta} y_j^\theta}{x_i^{1-\theta} y_i^\theta} \\
 &\leq (1 - \theta)a_{ii} + \theta b_{ii} + (1 - \theta) \left(\sum_{j \neq i} a_{ij} \frac{x_j}{x_i} \right) + \theta \left(\sum_{j \neq i} b_{ij} \frac{y_j}{y_i} \right) \\
 &= (1 - \theta)\lambda(A) + \theta\lambda(B)
 \end{aligned}$$

560 where we have used the Hölder inequality in the second line, and the fact that X and Y are eigenvectors
 561 in the last line. We deduce that

$$CZ \leq ((1 - \theta)\lambda(A) + \theta\lambda(B))Z$$

562 Finally, multiplying by Φ^T , we find:

$$\lambda(C)\Phi^T Z \leq ((1 - \theta)\lambda(A) + \theta\lambda(B))\Phi^T Z, \quad (25)$$

563 hence, $\lambda(C) \leq (1 - \theta)\lambda(A) + \theta\lambda(B)$.

564 **The time-periodic case**

565 The proof is almost identical, but the fact that we have to consider time-periodic eigenvectors $X(t)$ (resp.
 566 $Y(t)$) and $\Phi(t)$ such that:

$$\begin{cases} -\dot{X}(t) + A(t)X(t) = \lambda(A)X(t) \\ -\dot{Y}(t) + B(t)Y(t) = \lambda(B)Y(t) \end{cases}, \quad \dot{\Phi}^T(t) + \Phi^T(t)C(t) = \lambda(C)\Phi^T(t) \quad (26)$$

567 We define again $Z(t)$ pointwise: $z_i(t) = x_i^{1-\theta}(t)y_i^\theta(t)$. Then, we evaluate the Collatz-Wielandt ratio:

$$\begin{aligned}
 -\frac{\dot{z}_i}{z_i} + \sum_j c_{ij} \frac{z_j}{z_i} &= -(1-\theta) \frac{\dot{x}_i}{x_i} - \theta \frac{\dot{y}_i}{y_i} + (1-\theta)a_{ii} + \theta b_{ii} + \sum_{j \neq i} a_{ij}^{1-\theta} b_{ij}^{\theta} \frac{x_j^{1-\theta} y_j^{\theta}}{x_i^{1-\theta} y_i^{\theta}} \\
 &\leq (1-\theta) \left(\lambda(A) - \sum_j a_{ij} \frac{x_j}{x_i} \right) + \theta \left(\lambda(B) - \sum_j b_{ij} \frac{y_j}{y_i} \right) \\
 &\quad + (1-\theta)a_{ii} + \theta b_{ii} + (1-\theta) \left(\sum_{j \neq i} a_{ij} \frac{x_j}{x_i} \right) + \theta \left(\sum_{j \neq i} b_{ij} \frac{y_j}{y_i} \right) \\
 &= (1-\theta)\lambda(A) + \theta\lambda(B)
 \end{aligned}$$

568 We deduce that

$$-\dot{Z}(t) + C(t)Z(t) \leq ((1-\theta)\lambda(A) + \theta\lambda(B))Z(t)$$

569 To conclude, we multiply by ϕ^T and integrate over one period:

$$-\int_0^T -\Phi^T(t)\dot{Z}(t) dt + \int_0^T \Phi^T(t)C(t)Z(t) dt \leq ((1-\theta)\lambda(A) + \theta\lambda(B)) \int_0^T \Phi^T(t)Z(t) dt$$

570 Integrating by parts the first term (using periodicity), we find

$$\begin{aligned}
 \int_0^T (\dot{\Phi}^T(t) + \Phi^T(t)C(t))Z(t) dt &\leq ((1-\theta)\lambda(A) + \theta\lambda(B)) \int_0^T \Phi^T(t)Z(t) dt \\
 \int_0^T \lambda(C)\Phi^T(t)Z(t) dt &\leq ((1-\theta)\lambda(A) + \theta\lambda(B)) \int_0^T \Phi^T(t)Z(t) dt
 \end{aligned}$$

571 Hence, $\lambda(C) \leq (1-\theta)\lambda(A) + \theta\lambda(B)$.

572 C Computation of the critical time T_c

573 This section presents the analytical computation of the critical time T_c of the transition between ‘unstable’
 574 and ‘stable’. According to our main results, see Section 3.1.1: *when the trait fitness function is linear*
 575 ($\gamma = 1$), *then the Lyapunov exponent $\lambda(\alpha)$ is a convex function of the trait architecture α* . Consequently,
 576 for the two determinant case the optimal trait architecture is either² $\alpha_F = 0$, or $\alpha_F = 1$ and the transition
 577 occurs when the Lyapunov exponents satisfy $\lambda(0) = \lambda(1)$. Thus, the critical time T_c can be computed
 578 by solving this equation. However, according to Equation (1), the Lyapunov exponent is the largest
 579 eigenvalue of a product of matrix exponential. Thus, its computation is very tedious so we relied on
 580 Maple (2022) to perform the preliminary steps of the calculation.

581 As mentioned above, the goal is to solve $\lambda(0) = \lambda(1)$ thus the first step consists in determining the
 582 Lyapunov exponent for $\alpha_F = 0$ and $\alpha_F = 1$. To shorten the notation, we abbreviate α_F to α . According
 583 to Maple, the eigenvalues of $\exp\left(\frac{AT}{2}\right) \exp\left(\frac{BT}{2}\right)$ when $\alpha = 0$ are

$$\Lambda(0) = \frac{\exp\left(\frac{T}{2}(2 - 2\mu_S - s) + \frac{\tau_S}{2}\right)}{4\mu_S^2 + s^2} \begin{pmatrix} 2\mu_S^2 e^{-\tau_S} + s^2 e^{-\frac{\tau_S}{2}} + 2\mu_S^2 + 2\xi_S \\ 2\mu_S^2 e^{-\tau_S} + s^2 e^{-\frac{\tau_S}{2}} + 2\mu_S^2 - 2\xi_S \\ \left(2\mu_S^2 e^{-\tau_S} + s^2 e^{-\frac{\tau_S}{2}} + 2\mu_S^2 + 2\xi_S\right) e^{-4\mu_F} \\ \left(2\mu_S^2 e^{-\tau_S} + s^2 e^{-\frac{\tau_S}{2}} + 2\mu_S^2 - 2\xi_S\right) e^{-4\mu_F} \end{pmatrix}$$

584 with

$$\begin{aligned} \tau_S &= T\sqrt{4\mu_S^2 + s^2}, \\ \xi_S &= \sqrt{\mu_S^2 \left(e^{-2\tau_S} \mu_S^2 - 2 e^{-\tau_S} \mu_S^2 - 2 e^{-\tau_S} s^2 + e^{-\frac{\tau_S}{2}} s^2 + e^{-\frac{3\tau_S}{2}} s^2 + \mu_S^2 \right)}. \end{aligned}$$

585 The mutation rate μ_F is strictly positive so $e^{-4\mu_F} < 1$ and thus the largest eigenvalue is either $\Lambda(0)_1$
 586 or $\Lambda(0)_2$. Besides, ξ_S simplifies into

$$\xi_S = \mu_S \left| e^{-\frac{\tau_S}{2}} - 1 \right| \sqrt{\left(e^{-\frac{\tau_S}{2}} + 1 \right)^2 \mu_S^2 + s^2 e^{-\frac{\tau_S}{2}}} > 0.$$

²We recall that in the two determinant case $\alpha = (\alpha_F, \alpha_S)$ with $\alpha_S = 1 - \alpha_F$.

587 Thus, when $\alpha = 0$ the largest eigenvalue is

$$\lambda(0)^T = \Lambda(0)_1 = \frac{\exp\left(\frac{T}{2}(2 - 2\mu_S - s) + \frac{\tau_S}{2}\right)}{4\mu_S^2 + s^2} \left(2\mu_S^2 e^{-\tau_S} + s^2 e^{-\frac{\tau_S}{2}} + 2\mu_S^2 + 2\xi_S\right).$$

588 Similarly, using Maple, we found that the eigenvalues of $\exp\left(\frac{AT}{2}\right) \exp\left(\frac{BT}{2}\right)$ when $\alpha = 1$ are

$$\Lambda(1) = \frac{\exp\left(\frac{T}{2}(2 - 2\mu_F - s) + \frac{\tau_F}{2}\right)}{4\mu_F^2 + s^2} \begin{pmatrix} 2\mu_F^2 e^{-\tau_F} + s^2 e^{-\frac{\tau_F}{2}} + 2\mu_F^2 + 2\xi_F \\ 2\mu_F^2 e^{-\tau_F} + s^2 e^{-\frac{\tau_F}{2}} + 2\mu_F^2 - 2\xi_F \\ \left(2\mu_F^2 e^{-\tau_F} + s^2 e^{-\frac{\tau_F}{2}} + 2\mu_F^2 + 2\xi_F\right) e^{-4\mu_F} \\ \left(2\mu_F^2 e^{-\tau_F} + s^2 e^{-\frac{\tau_F}{2}} + 2\mu_F^2 - 2\xi_F\right) e^{-4\mu_F} \end{pmatrix}$$

589 with

$$\begin{aligned} \tau_F &= T\sqrt{4\mu_F^2 + s^2}, \\ \xi_F &= \sqrt{\mu_F^2 \left(e^{-2\tau_S} \mu_F^2 - 2e^{-\tau_S} \mu_F^2 - 2e^{-\tau_S} s^2 + e^{-\frac{\tau_S}{2}} s^2 + e^{-\frac{3\tau_S}{2}} s^2 + \mu_F^2 \right)}. \end{aligned}$$

590 As previously ξ_F simplifies into

$$\xi_F = \mu_F \left| e^{-\frac{\tau_S}{2}} - 1 \right| \sqrt{\left(e^{-\frac{\tau_S}{2}} + 1 \right)^2 \mu_F^2 + s^2 e^{-\frac{\tau_S}{2}}} > 0$$

591 and using the same arguments we found that when $\alpha = 1$ the largest eigenvalue is

$$\lambda(1)^T = \Lambda(1)_1 = \frac{\exp\left(\frac{T}{2}(2 - 2\mu_F - s) + \frac{\tau_F}{2}\right)}{4\mu_F^2 + s^2} \left(2\mu_F^2 e^{-\tau_F} + s^2 e^{-\frac{\tau_F}{2}} + 2\mu_F^2 + 2\xi_F\right).$$

592 Therefore, the critical time T_c can be computed by solving $\Lambda(0)_1 = \Lambda(1)_1$. In practice, we were unable
593 to solve this equation. Even the numerical approximation of the solution requires particular care due to
594 the presence of large terms in the exponentials. Nevertheless, the terms of the form $e^{-c\tau_i}$ with $c > 0$ a
595 constant and $i \in \{F, S\}$ are negligible in the regime $\mu_F \ll s$. Thus, for $\alpha = 0$ it comes $\xi_S \approx \mu_S^2$ and then

$$\Lambda(0)_1 \approx \frac{4\mu_S^2}{4\mu_S^2 + s^2} \exp\left(\frac{T}{2}(2 - 2\mu_S - s) + \frac{\tau_S}{2}\right).$$

596 Similarly, for $\alpha = 0$ it comes $\xi_S \approx \mu_F^2$ and then

$$\Lambda(1)_1 \approx \frac{4\mu_F^2}{4\mu_F^2 + s^2} \exp\left(\frac{T}{2}(2 - 2\mu_F - s) + \frac{\tau_F}{2}\right).$$

597 So, the approximated critical time T_c is the solution of the equation:

$$\begin{aligned} & \frac{4\mu_S^2}{4\mu_S^2 + s^2} \exp\left(\frac{T_c}{2}(2 - 2\mu_S - s) + \frac{\tau_S}{2}\right) = \frac{4\mu_F^2}{4\mu_F^2 + s^2} \exp\left(\frac{T_c}{2}(2 - 2\mu_F - s) + \frac{\tau_F}{2}\right) \\ \Leftrightarrow & \exp\left(\frac{T_c}{2}(2 - 2\mu_S - s) + \frac{\tau_S}{2} - \frac{T_c}{2}(2 - 2\mu_F - s) - \frac{\tau_F}{2}\right) = \frac{4\mu_F^2(4\mu_S^2 + s^2)}{4\mu_S^2(4\mu_F^2 + s^2)} \\ \Leftrightarrow & \exp\left(\frac{1}{2}(\tau_S - \tau_F) + T_c(\mu_F - \mu_S)\right) = \frac{4\mu_F^2(4\mu_S^2 + s^2)}{4\mu_S^2(4\mu_F^2 + s^2)} \\ \Leftrightarrow & \frac{1}{2}\left(T_c\sqrt{4\mu_S^2 + s^2} - T_c\sqrt{4\mu_F^2 + s^2}\right) + T_c(\mu_F - \mu_S) = \log\left(\frac{4\mu_F^2(4\mu_S^2 + s^2)}{4\mu_S^2(4\mu_F^2 + s^2)}\right). \end{aligned}$$

598 Thus, the critical time is approximately

$$T_c \approx \frac{2 \log\left(\frac{4\mu_F^2(4\mu_S^2 + s^2)}{4\mu_S^2(4\mu_F^2 + s^2)}\right)}{\left(\sqrt{4\mu_S^2 + s^2} - \sqrt{4\mu_F^2 + s^2}\right) + 2(\mu_F - \mu_S)}.$$

599 However, as it stands, the contribution of each parameter to the critical time remains complex. Thus,
600 according to Taylor expansions in the regime $\mu_S \ll \mu_F \ll s$, this formula simplifies into

$$\frac{T_c}{2} \approx \frac{1}{\mu_F} \log\left(\frac{\mu_F}{\mu_S}\right) \left(1 + \frac{\mu_F}{s}\right).$$

601 D Supplementary figures

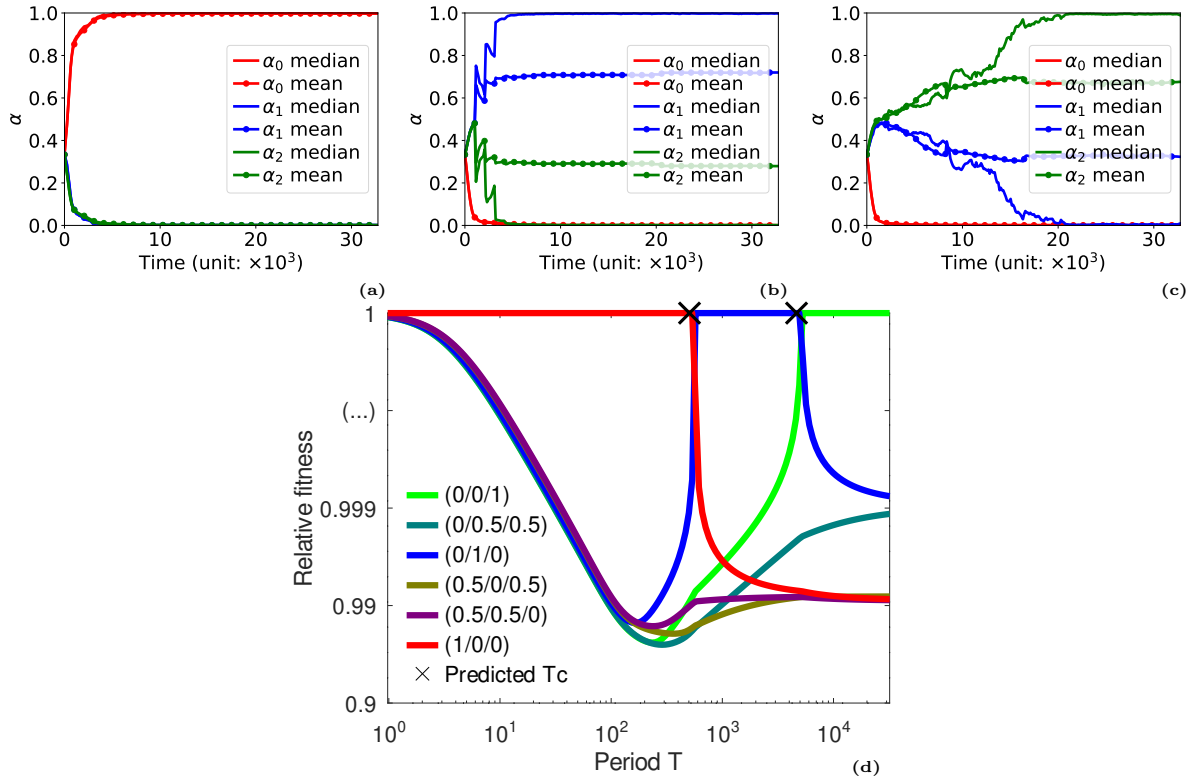


Figure 7: **Results for three media $I = 3$ and a linear selection function $\gamma = 1$.** (a-b-c) Temporal dynamics for the Monte-Carlo simulations with three determinants ($I = 3$) associated with mutation rates $\mu_i = 10^{-2}, 10^{-3}, 10^{-4}$ (analogous to Figure 2(b-c)). We observed the selection towards full contribution of one of the three determinant for each value of the time period among $T = 128$ (a: fast switching environment, selection of the largest mutation rate), $T = 2048$ (b: intermediate switching environment, selection of the intermediate mutation rate), $T = 16384$ (c: slow switching environment, selection of the slowest mutation rate) (d) Relative fitness $\frac{W(\alpha)}{\max W}$ as a function of the period T , for different values of the trait architecture α (analogous to Figure 3(a)). The maximal fitness is always attained at extremal values of the trait architecture (full contribution of a single determinant).

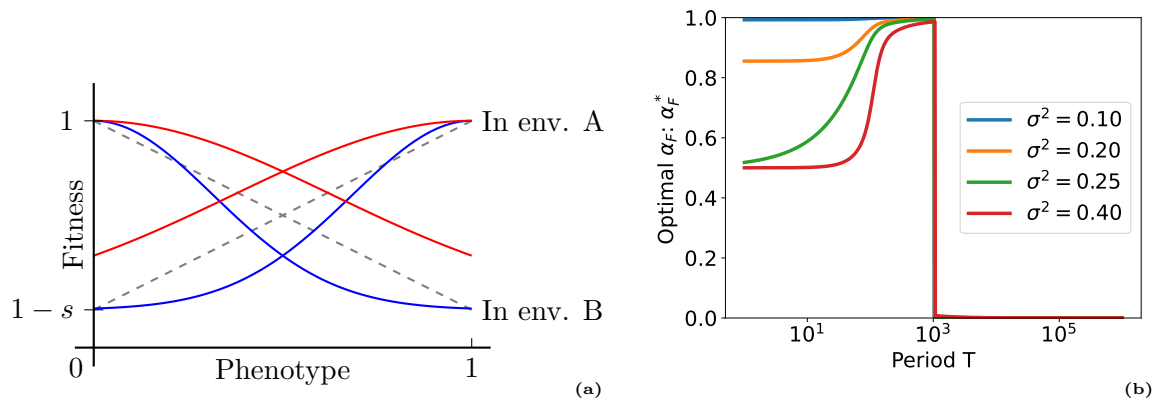


Figure 8: **Gaussian fitness function and associated optimal trait architecture:** (a) Shape of the fitness function for Gaussian selection (ie. mixed concave and convex shape): $1 - s \left(1 - \exp\left(\frac{|\Phi - \Phi^*|^2}{2\sigma^2}\right)\right)$, for $\sigma^2 = 0.1$ (plain blue) and $\sigma^2 = 0.4$ (plain red). (b) The optimal value α_F^* is represented as a function of the shape parameter σ^2 (analogous to Figure 3(b) and Figure 6(b)). Only the nearly concave fitness function ($\sigma^2 \gtrsim 0.20$) resulted in composite architectures, provided that the degree of instability overcomes the usual threshold ($T < T_c$).