Evolution and Maintenance of Phenotypic Plasticity

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Abstract

We introduce a novel framework for exploring the evolutionary consequences of phenotypic plasticity (adaptive and non-adaptive) integrating both genic and epigenetic effects on phenotype via stochastic differential equations and in-silico selection. In accordance with the most significant results derived from prior models, we demonstrate how plasticity is differentially favored when subjected to small vs large environmental shifts, how plasticity is transiently favorable while accommodating a new environment, and how, plasticity decreases during epochs where the environment remains stable (canalization). In contrast to these models, however, by allowing the same phenotypic value to be produced via two different paths, i.e. deterministic, genic, vs stochastic, epigenetic mechanisms, we demonstrate how when genic contributions alone cannot produce an optimal phenotype, plastic, epigenetic contributions will instead fully accommodate new environments, allowing for both adaptive and non-adaptive plasticity to evolve. Furthermore, we show that while rates of phenotypic accommodation are relatively constant under a wide range of selective conditions, selection will favor the most efficient route to adaptation: determinstic, genic response, or stochastic, plastic response. As a result, plasticity may evolve or canalization may occur within a given epoch depending on the relative mutation rate of genic and epigenetic contributions to phenotype, highlighting the importance of genetic conflict on the evolution of plasticity.

Introduction

Phenotypic Variability

The modern synthesis requires that all populations of organisms have some appreciable degree of phenotypic variation in order for natural selection to occur. Within this framework, phenotypic variation is a result of genetic variation, whereby selection on phenotypes acts as a feedback mechanism to control how genetic variants flow through a population. However, the extent to which variation in quantitative traits is explained by genetic variation is not fully understood. In the context of traits that vary along a continuum, phenotypic variability, often referred to as V_P, is explained by a combination of genetic and non-genetic (environmental) variability, V_G and V_E respectively, such that $V_P = V_G + V_E$. Note that in the absence of explicit parameterization, gene-by-environment interactions are often also contained within the environmental variability term Zhang and Hill (2005).

Historically, quantitative genetic models of natural selection do not incorporate the existence of non-genetic phenotypic variability Ancel (2000); Zhang and Hill (2005). Instead, such models frequently portray a one-to-one genotype-phenotype relationship, in which a particular genotype corresponds exclusively to a single phenotype, or else is expressed as a summation of the effects contributed across many loci. Any discrepancies between the additive effect of independent loci and phenotypes is often simply modeled as a linear error term, while in practice such discrepancies are dismissed by invoking the relatively poorly understood phenomenon of penetrance. However, as our collective understanding of molecular biology grows, effects previously discarded as environmental error must include an increasingly large number of effects beyond variation in behavior and life history, including more complex adaptive and non-adaptive plasticity mechanisms like behavior, epigenetic regulation, diversification, and non-genetic modes of inheritance.

Recent observations indicate the existence of variable relationships between genotype and

phenotype, in which a given genotype may in fact produce a range of phenotypes that can fluctuate dynamicallyBlake et al. (2003); Bratulic et al. (2015); McAdams and Arkin (1997); Sigal et al. (2006); Spencer et al. (2009). Even within clonal populations, individuals have been shown to display quantitative differences that may distinguish them from genetically identical individuals. Phenotypic plasticity describes the phenomenon by which such individuals within a population may differentiate from genetically similar members by non-genetic means. In the context of rapidly fluctuating environmental conditions, possessing variable phenotypes within even genetically similar populations generates the potential for individuals to be randomly suited to uncertain conditions Beaumont et al. (2009); King and Masel (2007); Levy and Siegal (2012); Libby and Ratcliff (2019); Ratcliff et al. (2015); Siegal and Leu (2014); Simons (2009). Alternatively, in the context of a single environmental shift, the ability to produce a phenotype well-suited to new conditions as a response to such changes also increases survival Ancel (2000); DeWitt (1998); Lande (2009). While hypotheses concerning the adaptive value of plasticity have been previously described, such variability largely appears to inescapably exist at the very least on a molecular level, regardless of whether or not it may provide an adaptive advantage. In fact, it has been shown that the minimization of such molecular noise requires the evolution of very specific topological constraints Ramos et al. (2015).

Understanding the potential evolutionary consequences of such variability has often been contentious, with studies suggesting that there is no evidence to show that plasticity influences adaptation Jong (2005). However, various models and observations have delved into the possible mechanisms by which plasticity may have evolved and the role that it may play in shaping biological pathwaysAncel (2000); DeWitt (1998); Donaldson-Matasci et al. (2007); Draghi and Whitlock (2012); Ghalambor et al. (2007); King and Masel (2007); Lande (2009); Mayer et al. (2017); Moxon and Kussell (2017); Pfennig (2013); Price et al. (2003); Tadrowski et al. (2018). In classical population genetics, standing genetic variation alone produces a wide variety of phenotypes upon which natural selection may act. As such, in the process of adaptation, genotype precedes phenotype under natural selection. In contrast, proponents of phenotypic plasticity have suggested

that, within a single given genotype, an organism's interactions with the environment paired with mechanisms for adaptive and non-adaptive phenotypic plasticity produce a wide variety of phenotypes. It is these phenotypes, produced by both plasticity and underlying genetic variation, that are under selection. Under such a model, phenotypic change may pave the way for genotypic change in the process of adaptive evolution in a population. Such a process has variously been referred to as either genetic assimilation Waddington (1942) or genetic accommodation West-Eberhard (2005).

West-Eberhard Model

According to Mary Jane West-Eberhard, the adaptive evolution of plastic traits may follow a three-step process. *First*, an adapting population must have a degree of phenotypic plasticity. Plastic traits will have the ability to display a range of phenotypes in response to various inputs. These inputs may be simple external variation in the environment, but they could also be novel genetic inputs as a result of mutation. West-Eberhard emphasizes that these plastic phenotypes must have a degree of responsiveness to such inputs; otherwise, environmental or even genetic changes would have no effect on phenotype. This scenario stands in contrast to fully canalized traits with such robust buffering to varying input that no alteration in phenotype would even be possible, resulting in cryptic variation Siegal and Leu (2014). *Second*, when presented with a new input, either external or internal, the plastic traits produce novel phenotypes in response. Here, a phenotype may have a wide range of adaptive and non-adaptive responses to an altered input, resulting in phenotypic accommodation. While phenotypes overall may have a broader distribution than in prior conditions, phenotypic accomodation will allow for the production of at least some individuals with an optimal phenotype. Regardless, this novel set of phenotypes now constitutes an altered substrate on which natural selection may act. *Third*, if some phenotypic response to the new input provide a selective advantage, these phenotypes may increase in frequency in the population given a recurring input. If this phenotypic response has a genetic component, genetic accommodation may occur, fixing this new phenotype within a population.

Notably, this model departs only slightly from the classic mutation-selection view of adaptation, in that the West-Eberhard model allows for the additional possibility of novelty being generated via plasticity and not only through mutational processes alone West-Eberhard (2005).

Computational and theoretical models testing various aspects of plasticity have been been previously published, but few models exist that can directly test the West-Eberhard model (see Discussion). Tests of the West-Eberhard model must possess two primary properties. Firstly, individuals in a population should be able to produce a variable, non-genetic response to the environment; and secondly, an optimal genotype should exist. The production of non-genetic responses to the environment is a pre-requisite for both steps 2 and 3 of the West-Eberhard model, while an optimal genotype must exist in order for a phenotype to be capable of becoming genetically assimilated.

With the exception of certain theoretical work concerning phenotypic plasticity or phenotypic switching, most evolutionary models continue to maintain a one-to-one genotype-phenotype relationship, and those that do incorporate some form of plasticity do not fully recapitulate the West-Eberhard model. Generally, models of plasticity and switching are concerned with understanding the role of plasticity mechanisms in adaptive processes, often addressing specific questions regarding the role of plasticity in surviving uncertain conditions, understanding how plasticity is maintained, and determining whether plasticity accelerates adaptation.

Prior Models

Intuitively, populations with greater phenotypic variation will survive a greater number of stressful conditions than those with less variation, which would impart an advantage to having greater V_E. One interesting class of models that specifically examines this phenomenon are phenotypic switching models. Here, a genotype produces binary phenotypes, which are subject to fluctuating binary environmental conditions. Such models constitute a departure from the notion that one genotype can produce a singular phenotype, particularly given that, under fluctuating environmental conditions, no single phenotype would be able to survive both conditions. One key

parameter of genotypes under these models is the phenotypic switching rate. The rate at which phenotypic diversification occurs can differ drastically among populations depending upon how beneficial variability is for survival. When change occurs more quickly than organisms are able to genetically adapt to it—as in the case of seasonal changes, sudden environmental catastrophe, etc.–other strategies, either those produced prior to or in response to external changes, must then be employed in order to avoid extinction. These models demonstrate how phenotypic switching allow populations to survive disastrous extinction events Moxon and Kussell (2017); Ratcliff et al. (2015), with the central result of these studies being that the optimal switching rate is equal to the environmental switching rate King and Masel (2007); Kussell and Leibler (2005). Some of these models have been extended to include a spatial dimension with added migration, resulting in an increased risk of disasters over space and therefore favoring an increased switching rate. Certain extensions of these models have considered scenarios in which the phenotypic or environmental switching rates may be autocorrelated. When selective environments are increasingly autocorrelated, slower switching phenotypes are favored, as the likelihood of encountering successive environments to which a phenotype is suited increases Ratcliff et al. (2015). Alternatively, when selective environments are increasingly unpredictable–specifically, when environments fluctuate on random timescales–the phenotypic switching rate will be increasingly autocorrelated Skanata and Kussell (2016).

When considering models of phenotypic switching, it is important to clarify two key facets of the models. Firstly, the distinction between heritable and non-heritable contributions to phenotype is significant, and secondly, an understanding of whether external environments are static or fluctuating is necessary. Such aspects have conceptual consequences in understanding what it means to adapt. One class of prior models has focused on the adaptation of parameters controlling non-heritable contributions, for example the phenotypic switching rate, to maximize long-term survival in fluctuating conditions Jablonka et al. (1995); King and Masel (2007); Libby and Ratcliff (2019); Moxon and Kussell (2017); Ratcliff et al. (2015); Skanata and Kussell (2016)

Alternate models, including ours, focus on how differences in parameters controlling non-

heritable contributions to phenotype affect the fixation times of beneficial alleles Ancel (1999, 2000); Tadrowski et al. (2018). As such, models of binary phenotypes may be insufficient for encapsulating certain aspects of the dynamics of phenotypes under selection. Although many models of phenotypic switching provide insight into why fluctuations are central to the evolution of variability, insight into phenotypes that exist on a continuum remains limited. While models of phenotypic switching are insightful in understanding how binary phenotypes may evolve, their applications to more continuous phenotypes are limited.

Further models of plasticity have also been developed with more continuous treatment of phenotypes. However, these models are often more complex and often capture only limited aspects of phenotypic plasticity. One such model is the Ancel model, which defines phenotype as a continuous variable Ancel (1999, 2000). Here, rather than having genetic parameters control a single-valued phenotype alone, these parameters define instead a lower and upper limit for a norm of reaction. During selection, the environmental conditions select for a single phenotypic value. In this model, selection is designed to reward having a norm of reaction that contains the optimal phenotype, but punishes large norms of reaction. Ancel Meyers finds that in the process of adaptation to an environmental shift, the norms of reaction will undergo two distinct epochs. First, the norm of reaction will expand to accommodate the new environment, greatly increasing the fitness of individuals whose norms contain the new optimal phenotype. Subsequently, the norm of reaction will shrink around the new optimum, increasing fitness even further in comparison to those individuals with a wider norm of reaction, suggesting that in static environmental conditions, plasticity will be deleterious. This model was also used to show that phenotypic plasticity may accelerate adaptation if the difference in optimal and initial phenotypes is sufficiently large. However, if this condition is not met, phenotypic plasticity appears to retard adaption.

A second class of models examines the behavior of a continuous phenotype in the context of binary states of a continuous environmental variable. While the norm of reaction in the Ancel model is defined by two bounds, in this class of models, the norm of reaction is defined as a linear function where a phenotype is strictly a product of environment given a certain

genotype Lande (2009); Via (1985). In this model, as the environmental value increases, the phenotype variable will also increase, with the degree of increase determined by the slop of the linear environment-phenotype function. The only genetically controlled variable in these models is the slope. With a high degree of plasticity, individuals may produce ideal phenotypes at both environmental conditions, with a large slope or gradient in the linear function, while less plastic individuals will be unable to produce significantly different phenotypes when phenotype is varied, resulting in a small slope or gradient. An intuitive analysis of this model shows that under static conditions, plasticity is deleterious. If the environment fluctuates locally around only one of both environmental conditions, for small perturbations in environment, a smaller norm of reaction produces phenotypes much closer to the ideal phenotype than if individuals had a larger norm of reaction. Specifically, under static conditions, it is highly favorable to be under-responsive to small perturbations. However, this lack of response produces a trade-off when large environmental shifts occur, as individuals should produce a similarly large change in phenotype to accommodate such a shift Lande (2009).

While the two models of plasticity discussed here differ significantly in interpretation, they both reach similar conclusions. First, they agree that during adaptation, phenotypic response undergoes two epochs where the norm of reaction first increases, then decreases around the new optimal phenotype. Under static conditions, strong responses to small fluctuations are deleterious. However, as the environment shifts, a higher degree of plasticity is favorable, allowing higher degrees of plasticity to increase within the population. As populations continue to adjust to the new environmental regime, sensitivity to environmental changes is then no longer favorable, instead returning to the original state where plasticity is deleterious. Because of this multi-step process, previous models have demonstrated that plasticity may accelerate natural selection but only in very limited conditions where the distance between initial conditions and optimal conditions is very large.

Though plasticity is deleterious under static conditions, as previously mentioned, an increase in phenotypic variation will allow for potential adaptation to a wider range of selective condi-

tions, potentially allowing populations to cross otherwise uncrossable fitness boundaries. While this may be beneficial in the context of highly variable and unpredictable environments, after environmental conditions have stabilized long-term, natural selection often decreases unnecessary phenotypic variation. However, phenotypic variation is often maintained in natural populations under static conditions West-Eberhard (2005). Classically, with such variation often thought to be maintained by genetic variation via mutation, selection, and epistasis Barton and Keightley (2002). Questions still remain in understanding how or why environmental variability via plasticity may be maintained in a population. Models of phenotypic switching, as well as quantitative genetic models Kondrashov and Yampolsky (1996); Zhang and Hill (2005), suggest that fluctuating environments may play a key role in this process. Graphical models comparing intrinsic trade-offs of fitness between various environmental conditions suggest that the nature of the trade-off may favor various strategies for generating non-genetic variability. Populations that have adapted to certain environmental conditions deal with an intrinsic trade-off between consistent development under normal environmental conditions and the ability to respond to alterations and new conditions. The degree of variation among extant phenotypes in a given population depends largely upon the benefit verses the cost of evolutionary trade-offs inherent to phenotypic diversification. Here, weaker fitness trade-offs tend to favor a generalist strategy, while strong trade-offs favor specialist strategies Donaldson-Matasci et al. (2007). Additionally, such models have shown that the fitness trade-off inherent to adaptive solutions may predict whether adaptation or switching will be favored Mayer et al. (2017).

Some have postulated that such plasticity may accelerate the process of genetic adaptation, and as such may provide a mechanism for maintaining environmental variability Hinton and Nowlan (1987); Simpson (1953). Others have suggested that, overall, plasticity will tend to produce slower genetic adaptation than in the case of no plasticity Draghi and Whitlock (2012), or that it will only accelerate adaptation when plasticity allows for a quicker encounter with an advantageous phenotype Ancel (2000). Regardless, results suggest that potential acceleration of adaptation is insufficient to explain the maintenance of plasticity over long periods Ancel (2000).

The models reviewed here broadly fall into many different modeling approaches, such as quantitative genetic models, neural network models, or graphical models. All incorporate different aspects of plasticity, such as a separation of phenotype and genotype or random fluctuations in environment or environmental response. However, none of these models can fully recapitulate the steps of the West-Eberhard model. Only in models of phenotypic switching are genotype and phenotype segregated, allowing phenotypic accommodation to precede the establishment of genetic accommodation of new conditions. In these models, a genotype is defined strictly as the switching rate between phenotypes, with actual phenotype being entirely independent of genotypic state. Additionally, as the occurrence of a swapped phenotype occurs independently of environmental conditions, such models may only capture certain aspects of non-adaptive plasticity.

Unlike in models of phenotypic switching, previous models of phenotypic plasticity allow for a broad range of phenotypes to exist, rather than simple binary phenotypes. In these models, phenotype is the result of genotypic state (slope of the norm of reaction) interacting with the current environmental state. As phenotype is a direct result of genotype, and all individuals in a population are subject to the same environmental conditions, phenotype thus has a one-to-one correlation to genotype. Due to this, these models of phenotypic plasticity are not able to recapiture the West-Eberhard model. However, given that new phenotypes are produced as a direct result of an environmental shift, such models may capture certain unique aspects of adaptive plasticity.

In the following section, we present a minimal model that allows for the study of adaptive and non-adaptive plasticity in a single model that satisfies the conditions for testing the West-Eberhard model.

Model

The aim of this section is to describe our minimal model of phenotypic plasticity. We compare the results of in-silico selection between populations that have either plastic or non-plastic pheno-

types. In order to model phenotypes with long-term stability and convergence, we model these self-regulating phenotypes as either the result of two feedback loops (one positive, one negative) for non-plastic traits, or three feedback loops (one positive, one negative, one negative but noisy) for plastic traits (Fig. 1). The simplest such model is a logistic growth model.

We first model non-plastic phenotypes, where an individual i in a population of size N has a phenotype P_i,

$$\frac{dP_i}{dt} = \gamma P_i - \epsilon_i P_i^2. \tag{1}$$

which is controlled by a set of genotype parameters $\{\epsilon_i, \gamma_i\}$, representing the total genic (non-epigenetic) contribution to phenotype. Phenotype is represented by an ordinary differential equation, modeled off a trait that has two feedback loops, and that therefore has the minimum requirements necessary to dynamically maintain a static trait value. There is one positive feedback loop promoting an increase of said trait according to parameter γ_i and a second, negative feedback loop repressing said trait according to parameter ϵ_i, working in concert to maintain the phenotype at a specific value $P_i = \gamma_i/\epsilon_i$ over sufficiently long periods of time. We may assume that this phenotypic value is produced as the result of a population having previously adapted to environmental conditions, such that the static phenotype is the optimal phenotype. Notably, this model does not yet have any plasticity, so that phenotype $P_i = \gamma_i/\epsilon_i$, and, all variability in phenotype (V_P) should be a direct result of population differences in parameters γ_i or ϵ_i. In a population of clones, there should be zero phenotypic variability, as there is no genotypic variablity.

As individuals are subjected to a wide variety of non-genetic changes and complex genetic interactions during development, we use a stochastic differential equation with multiplicative noise to model the genotype-phenotype relationship, resulting in log-normal-like distributions of phenotypes Kim et al. (2016); Lee et al. (2015). We may change the ordinary differential equation of non-plastic phenotypes represented in Eqn. 1 into a stochastic differential equation

$$\frac{dP_i}{dt} = \gamma P_i - (\epsilon_i + \xi_i)P_i^2, \tag{2}$$

with additional epigenetic parameter ξ_i, representing the total non-genic (epigenetic) contribution to phenotype. ξ_i represents the accumulation of non-genetic fluctuations an individual in a population encounters throughout its lifetime, including environmental, developmental, and behavioral variation, resulting in a plastic, epigenetic response ξ_i. This epigenetic response results in a decoherent feedback response via the second term of the SDE. Importantly, in contrast to the non-plastic model represented in Eqn. 1, the accumulation of random epigenetic variation results in a distribution of phenotypes within any given genotype. Similar heavy-tailed distributions have been observed for widely varied phenotypes, such as intercellular protein levels, cell size, or even clutch size Jetz et al. (2008); Osella et al. (2014); Sigal et al. (2006).

The consequences of this non-genetic variability on population phenotypes are modeled by ξ_i and its genetic control parameters, D_i and τ_i. ξ_i is a random variable with mean 0 resulting from a Wiener process. ξ_i is also autocorrelated with magnitude D_i and time τ_i such that

$$\langle \xi(t_0), \xi(t) \rangle = D_i e^{-(t-t_0)/\tau_i}. \tag{3}$$

Notably, the genetic parameters D_i and τ_i control the epigenetic value ξ_i but cannot directly dictate its value, which is still a random variable. As D_i controls simply the magnitude of plasticity, this represents genic control of the non-adaptive plastic response to environment. Similarly, τ_i controls the auto-correlation or memory of plasticity, allowing subsequent generations to have similar, favorable epigenetic responses produced in prior generations. This represents genic control of the adaptive plastic response to environment. Therefore, in contrast to 2 parameters of the the non-plastic model, individuals controlled by Eqn. 2 should have 4 total genetic parameters $\{\gamma_i, \epsilon_i, D_i, \tau_i\}$ (Table 1). We also note that as an individual's genotype does not have a one-to-one correlation to a given phenotype, phenotypic space is degenerate, where any given phenotype may have been produced by a number of different combinations of genotypes.

If the effects of ξ_i are increased (increased D_i), there is greater randomness that is not buffered and is therefore integrated into an individual's phenotype (higher phenotypic variation). Once selective pressures are applied to populations, the auto-correlation term τ_i allows for a more or less consistent response to selection. With a longer auto-correlation time (larger τ_i), offspring will produce similar responses to successive selective events (more autocorrelated), whereas with a shorter auto-correlation time (smaller τ_i), offspring are likely to have a more varied and heterogeneous response (less autocorrelated). As ξ_i has unique autocorrelated properties, ξ_i is generated by using a colored-noise Runge-Kutta method Honeycutt (1992).

This SDE has two key properties: the mean remains γ_i/ϵ_i, and the phenotypic distribution results in a steady-state distribution over sufficiently long periods of time Kim et al. (2016); Lee et al. (2015). Under a quantitative genetics framework Ancel (1999); Barton and Keightley (2002), $V_P = V_G + V_E$, so that individuals within a clonal population may have a non-zero variation of phenotype. Note that the addition of a stochastic term to a simple logistic growth model satisfies the first step of the West-Eberhard model, specifically that a trait will have differential responses to input.

Given both plastic and non-plastic models, we then apply in silico selection for haploids with Gaussian fitness, resulting in a new selective environment (Fig. 2, Supp. Fig. **S1**). Since selection is applied only to phenotype, and fitness is related simply to the phenotypic distance between the individual's phenotype and the optimal phenotype, there is no direct penalty for plasticity in this model. We note that in these simulations, individuals initially inherit the epigenetic value ξ_i in reproduction, followed by the accumulation of noise, resulting in a new epigenetic value that fits the relationship Eqn. 3. As such, this epigenetic inheritance is transient, as the values of ξ_i randomly drift during development and throughout the individual's lifetime, resulting in an inheritance of ξ_i over multiple generations that decreases according to the auto-correlation parameter τ_i **?**. Similar effects have been seen in natural populations Spencer et al. (2009). We also note that the random value ξ_i is specific to each individual/lineage, and is not shared across all individuals in the shared environment. We stress, therefore, that ξ_i should not be seen

as environmental fluctuations, but instead each individual's unique response to the common, shared environmental conditions defined by the fitness function. The optimal phenotype for the given environement, P_{opt}, does not vary between individuals - it is the same for the entire population.

We apply two selective conditions, which we refer to as "stringent" and "relaxed" selection, varying only in the parameter that determines the width of the Gaussian fitness function by an order of magnitude (See Methods) while P_{opt} is unchanged. The application of Gaussian fitness represents an environmental shift with a different phenotypic optimum, with differences in width corresponding to the degree of strictness imposed on phenotypes by the new environmental conditions. We restrict mutations to be only in one genic parameter, ϵ_i or in epigenetic parameters D_i and τ_i. The genic parameter γ_i is fixed at 1 and unmutable in all simulations presented here. We begin with initial conditions with an initial phenotype (or distribution of phenotypes) on $P_i = 1/67$, corresponding to a genotype of $\epsilon_i = 67$, and with an optimal phenotype on $P_{opt} = 1/90$, corresponding to a genotype of $\epsilon_i = 90$.

More information may be found in Supplemental Methods.

Results

Phenotypic Accomodation

The second step of the West-Eberhard model is the development of phenotypic accommodation. Specifically, in a shifting environment, certain individuals will be able to produce an adaptive phenotype in response to altered conditions. To determine whether our simulations would be able to produce phenotypic accommodation, we set the mutation rate for genotypes to 0, while allowing epigenetic parameters to evolve in populations of size N=1000 and performed 100 replicate simulations. We challenged a population of individuals with stringent and environmental conditions and allowed individuals to adapt. Given these conditions, epigenetic parameter ξ_i alone could produce fully adapted individuals (Fig. 3), even when the mutation rate for genic

parameters (γ_i, ϵ_i) is zero. This accommodation is rapid, with the population fully adapting within approximately fifty generations. As the genic parameters were not allowed to mutate, full adaptation was compensated for by a response in epigenetic variable ξ_i alone (Fig. 3). Note that, in the initial steps of adaptation, ξ_i produces a strong response out of equilibrium before eventually settling on an equilibrium value far from 0. As ξ_i is the result of a Wiener process, ξ_i should have a mean of 0, but the system is pushed far from that equilibrium value. By allowing the magnitude of plasticity D_i and the auto-correlation/memory parameter τ_i to mutate, these simulations produce a response where increased plasticity and increased memory are favorable. In this scenario, we can consider the shift in selective environment as a recurrent selection input, and due to this recurrence and the inability of the genic parameters to mutate, greater plasticity and memory is advantageous. While we have disallowed genic parameters to mutate at all in this case, a similar response of increased plasticity and memory may also be favorable in conditions where genetic mutation is significantly slower than mutation in epigenetic parameters as well (Section **Establishment and Maintenance of Plasticity**). To understand the detailed dynamic of phenotypic accommodation and epigenetic compensation under these developmental conditions, we may consider the equilibrium phenotypic value produced by this population's genotype. In this case, the genic values γ_i and ϵ_i act in concert to pull phenotypic values of the population back to the predicted steady-state distribution around γ_i/ϵ_i. However, due to selection for a phenotypic optimum that is departed from γ_i/ϵ_i, phenotype must be compensated for by the epigenetic parameter ξ_i (Fig. 2).

Being the result of the Wiener process, ξ_i should accumulate randomness, thereby returning to mean 0 with variability D_i. However, there are two demands on ξ_i. The first is the demand that epigenetic parameter ξ_i is sufficiently large so that at least some phenotypes that may be near the new optimum. Overall, plasticity magnitude alone, which is D, increases the overall variability in P_i in an unbiased, non-adaptive fashion. To increase the chance of producing offspring with the correct epigenetic parameter ξ_i when far from 0, D_i increases. The second demand is that epigenetic parameter ξ_i *remains* sufficiently large *over time*, thus not returning to being distributed

around 0. That is to say that, given a parent with an epigenetic parameter ξ_i producing fit parents, the offspring will now be likelier to have a similarly adapted ξ_i as its parents. This results in an increase in the auto-correlation parameter τ_i. Together, these steps represent the second step of the West-Eberhard model, phenotypic accommodation.

Genetic Accommodation

Given that our model can produce phenotypic accommodation, we then allowed only the genic parameter ϵ_i to mutate in our model, excluding mutations in epigenetic parameters D_i and τ_i. To test for genetic accommodation, we performed 100 replicate simulations of populations of 100 individuals under stringent and relaxed directional selection (c.f. Materials and Methods). This population size was chosen to exaggerate certain features of genetic adaptation in plastic regimes (i.e. transient fixation events due to successive bottlenecks, see below & Fig. 4). Allowing only genetic parameter ϵ_i to mutate, simulations were performed for populations with both plastic (Eqn. 2) and non-plastic (Eqn. 1) phenotypes, representing the differences in adaptation for populations with noisy genotype-phenotype relationships as opposed to those with one-to-one relationships between genotype and phenotype.

Fig. 4 provides a representation of mean genotypic (i.e. ϵ_i) changes for replicate populations with plastic and non-plastic phenotypes under two selection regimes, stringent and relaxed. By allowing only for mutations in ϵ_i alone, we can see that changes in genetic parameters allow for the eventual genetic accommodation of new environmental conditions - the last step of the West-Eberhard model. In early generations, ξ_i helps to produce selectively advantageous phenotypes (c.f. ***Phenotypic Accommodation***). However, as mutations in genic parameters allow for the production of optimal phenotypes through genetic means alone, the epigenetic response is no longer needed to produce fit individuals. Due to this, the epigenetic parameter ξ_i returns back to 0, in contrast to in the case of phenotypic accommodation (Fig. 3). Overall, in the process of adapting to altered environmental conditions, plasticity helps to ameliorate the negative consequences of an unexpected environmental shift.

For the classic non-plastic model, the genotypic responses under relaxed selection form a relatively smooth curve, with minimal noise on the upward trajectory revealing a consistent progression of all populations towards the optimal genotype. Because relaxed selection allows for a wider range of advantageous genotypes, adapting populations successively gain increasingly beneficial mutations and follow a selective gradient until reaching an optimum. The genotypes of these adapting populations rapidly converge near the predetermined genetic optimum of 90, with small deviations resulting from genetic drift. Additionally, these non-plastic populations rapidly reach an optimal state within fifty generations. By contrast, plastic populations under relaxed selection show a slower pattern of convergence on the optimal genotype within 200 generations. Rather than progressing steadily and consistently towards an optimum, the plastic populations show a very large degree of variation in phenotype, sometimes severely over- or undershooting the ideal. Such an effect occurs due to selection acting on phenotype, rather than genotype. However, phenotypic convergence on the optimum remains smooth (Fig. 5). As the range of possible phenotypes becomes larger due to plasticity, adaptation/accommodation in plastic populations is less smooth and directed than in the case of populations with less noisy genotype-phenotype relationships under conditions of broad selection. When combined with relatively relaxed selection, this phenomenon causes the genotypes of plastic populations to converge slowly on the optimum phenotype. In contrast to the non-plastic populations, they do not steadily progress directly towards the ideal and therefore do not adapt as efficiently.

Results differ significantly when one compares the effects on genotype under stringent selection for plastic and non-plastic populations. In the latter case, genotypes vary widely among replicate populations as a result of drift. As opposed to conditions of relaxed selection, non-plastic populations under stringent selection do not progress continuously along a selective gradient towards the optimum, since only phenotypes at or near the ideal confer a survival advantage. Here, phenotypes instead appear to be, in a sense, discretized, as they are either largely beneficial to selection or effectively neutral. The populations develop various neural mutations until hitting upon one at random that provides a large selective advantage. This effect results in

a series of rapid fixation events, as each population reaches an optimum and then deviates very little from it.

A measurement of the fraction of genetically adapted/accommodated populations (Fig. 4b) supports the observation that plastic populations converge on the pre-determined optimum more efficiently under stringent selection, while those that are non-plastic adapt more quickly in response to relaxed selective pressures. Within 150 generations, all non-plastic populations under relaxed selection and all plastic populations under stringent selection have genetically adapted fully to the new selection conditions. In both cases, accommodation occurred along a clearly defined selective gradient. Meanwhile, a number of populations under plastic/relaxed conditions and under non-plastic/stringent conditions have failed to adapt to their respective optima within 200 generations. In particular, non-plastic populations on average adapt far more slowly under stringent selective pressures, as they are limited by the appearance of beneficial alleles through mutations alone.

While our models do not incorporate disasters and total-population extinction due to our fixed-population-size simulations, it should be noted that under conditions of stringent selection, all non-plastic replicate populations would have experienced total extinction in the first few generations of applied stress. Rather than allowing for such scenarios, the model instead allowed populations to undergo genetic drift. Such results indicate that there is a certain degree of plasticity that is required for survival under extreme selective conditions Libby and Ratcliff (2019); Ratcliff et al. (2015). Regardless, findings suggest that, in general, plasticity does not necessarily expedite adaptation. In the scenario of broad selection, a non-plastic population may more rapidly adapt to an altered environment when compared to plastic populations. However, in the scenario of stringent selection, plastic populations adapt more rapidly than non-plastic populations.

Genetic Turnover and Mutation-Selection-Drift Balance

To further examine how phenotypic plasticity affects MSD balance, we determined the degree of genetic turnover for all populations shown in Fig. 4. We performed an auto-correlation analysis to determine the degree of turnover in mean genotype values (ϵ_i) for plastic and non-plastic populations (Fig. 6). Specifically, we took replicate populations at this MSD equilibrium, and plot the auto-correlation of mean population genotype values.

The results of the auto-correlation analyses reveal a much higher degree of genetic turnover for plastic populations in comparison to non-plastic populations. Regardless of the degree of selection, each generation of plastic individuals gradually diverges from its previous state under plastic conditions. Meanwhile, non-plastic populations do not display this same, continuous turnover. Under relaxed selection, the degree of auto-correlation rapidly diminishes for non-plastic populations, while those under stringent selection show an extremely low rate of genetic turnover, with the auto-correlation value varying very little in the examined time frame. Overall, populations display a buffering of the degree of turnover from various selective conditions.

Loss of Variability

The previous sections have demonstrated how plasticity is beneficial under conditions of dramatic selective changes. Additionally, we have shown that plasticity buffers genetic turnover from variations in selection. We now consider whether it is deleterious during static selective conditions. To test whether phenotypic plasticity presents a selective disadvantage at MSD balance, we performed in-silico selection on diversified and non-diversified populations, making the only mutable parameter the degree of variability (D_i).

In accordance with expectations, populations under stringent selective pressures show a strong downward trend in phenotypic plasticity over many generations (Fig. 7). Most of these populations show a significant decrease in their degree of variability, with some having their average plasticity decreased by nearly half. Therefore, while plastic populations under stringent

selection can reach an MSD balance more quickly than non-plastic populations, once the system has come to an equilibrium by reaching an ideal phenotype, the potential for great phenotypic variety becomes less useful.

By contrast, populations under relaxed selection do not show a decrease in plasticity after 1000 generations. Unlike in the case of stringent selection, small populations under relaxed selection have a broader range of phenotypes which could be considered beneficial. So long as the result of phenotypic variability, which includes both V_E and V_G, is sufficiently smaller than the width of the Gaussian fitness function, the degree of plasticity within a population should not be highly detrimental. Under these conditions, the variability originating from plasticity is not as harmful as it may be for populations under stringent selection.

Establishment and Maintenance of Plasticity

While prior studies have shown how plasticity is often deleterious under constant environmental conditions (c.f. **Prior Models**), at best serving to avoid extinction during dramatic environmental shifts, we have demonstrated that under similar static conditions, plasticity can both be advantageous (Fig. 3) or deleterious (Fig. 7). In our model, phenotype is a single-value variable, produced by a combination of both genic and non-genic/epigenetic contributions. As multiple mechanisms can produce the same phenotype, any given phenotypic value in our model is highly degenerate, with a broad set of genotypic parameters (genic and non-genic) being able to produce the same outcome. However, while phenotype may be degenerate, allowing individuals to survive a single selection event, the degree to which a phenotype is produced through genic pathways vs epigenetic pathway produces trade-offs in subsequent generations. The more a phenotype is dependent on epigenetic compensation, the less likely that subsequent generations will produce a similar response in comparison to producing the same phenotype through mostly genic means. Intrinsically, this effect forces a strong trade-off during the evolution of plasticity - progeny may be better optimized for current conditions but will be less likely to survive environmental changes.

Consideration of this trade-off leads to the natural conclusion that under constant conditions, quantitative traits should begin to canalize and lose plasticity. However, under recently changed environmental conditions, natural selection will also favor the fastest route to accommodation of a new environment, whether it be by genic or non-genic means. Indeed, this effect manifests itself as the Baldwin Expediting Effect Ancel (2000); Lande (2009), where plasticity appears to be transiently beneficial during adaptation, first increasing, then subsequently being selected against. Similarly, optimization of adaptation rate also explains why the switching rate in models of phenotypic switching Jablonka et al. (1995); King and Masel (2007); Libby and Ratcliff (2019); Moxon and Kussell (2017); Ratcliff et al. (2015); Skanata and Kussell (2016) will match the rate of environmental fluctuations.

While previous studies suggest phenotypes would begin to canalize under static conditions, we have demonstrated under certain conditions that plasticity may in fact be advantageous (Fig. 3). To further explore this tradeoff, we constrain the relative mutation rates of genic and non-genic control parameters. We define a new variable $r = \mu_{genic}/\mu_{epigenetic}$, where μ_{genic} and $\mu_{epigenetic}$ are the mutation rates for genic and epigenetic control parameters respectively. We can see now that in the case of full epigenetic compensation, plasticity increases when $r = 0$ (Fig. 3), and when genic control is mutable, decreases when $r = 1$ (Fig. 8).

We applied in-silico selection to 100 replicate populations of 1000 individuals while varying the relative mutation rate r (Fig. 8). As r is varied, the relative rate of phenotypic accommodation remains roughly the same in all cases (Fig. 8A), though, slightly more rapid accommodation is seen at higher r values. While the mean phenotype in these populations remains similar, the genic contribution to phenotype (Fig. 8B) varies dramatically as the relative mutation rate for genic contributions is decreased. In the case of low r, as the new environment is phenotypically accommodated, the epigenetic value ξ_i instead compensates for the inability to produce an optimal phenotype using genic means alone (Fig. 8C). As seen in previous sections, ξ_i compensates for sub-optimal genotypes initially, then within the given epoch, for large r, ξ_i is no longer needed, returning to a mean of zero reflecting the canalization of this phenotype by genic

means. However, for small r, ξ_i continues important for the production of optimal phenotypes, subsequently increasing again. The genetic control of ξ_i similarly stratifies depending on r (Fig. 8D-E). As r decreases, epigenetic compensation becomes an increasingly important mechanism for survival, causing both non-adaptive and adaptive plasticity to be more advantageous within the given epoch. Should a further shift in environment occur after the current epoch, the net result would be that both adaptive and non-adaptive plasticity are overall increased within a population, rather than canalizing.

Discussion

West-Eberhard Model

Mary Jane West-Eberhard has proposed that plasticity plays a central role in the process of adaptation. Under this model, phenotypes that produce differential responses to input encounter a newly recurring input that is both phenotypically and genotypically accommodated. However, previous genetic models have been limited in their capacity to recapitulate this idea. In particular, quantitative genetic models involving explicit and parameterized phenotypes, while able to provide insight into forces acting on overall non-genetic phenotypic variability, typically cannot produce differential responses to a new input and do not allow for the possibility of phenotypic accommodation Lande (2009); Price et al. (2003); Via (1985); Wagner et al. (1997); Zhang and Hill (2005). Even models of phenotypic switching–which allow for the possibility of variable responses to a new input, degenerate genotype-phenotype relationships, and phenotypic accommodation King and Masel (2007); Kussell and Leibler (2005)–cannot model genetic accommodation beyond adjusting the switching rate to maximize survival to fluctuating environmental conditions.

The model used in this study provides a way of examining the behavior of populations that are phenotypically responsive to novel environmental inputs. As demonstrated by replicate simulations of populations in which only phenotypic parameters were allowed to mutate in response

to stringent selection, full adaptation to new environmental conditions occurred within fifty generations (Fig. 3). All populations reached a new optimum phenotype that was then maintained solely through phenotypic rather than genotypic change, as shown by the fact that the epigenetic parameter ξ_i remained at a quantity above 0. As such, our model not only shows the progression of plastic populations' phenotypic change in response to novel inputs, but our model also has the capacity to distinguish between genic and epigenetic methods of accommodation. It therefore stands in contrast to otherwise similar models, including neural network models of gene regulation Draghi and Whitlock (2012); Wagner (1996). Such models, which can provide differential responses to input, may demonstrate complex behaviors given relatively few assumptions and have even been shown to depict canalization when applied to real data Manu et al. (2009*a*,*b*). However, they cannot phenotypically accommodate environments that have not been previously encountered. Such models are able to produce networks that are robust to fluctuating environmental conditions; however, such networks must be evolved genetically/trained to be able to produce such responses. As such, segregation of phenotypic accommodation and genotypic accommodation is difficult in such models.

Changing Environments

Our model shares conceptual similarities to other models of phenotypic plasticity, as well as to learning behaviors Ancel (1999, 2000); Hinton and Nowlan (1987); Lande (2009); Via (1985). In prior models Ancel (1999, 2000); Lande (2009); Via (1985), the survival of an individual depends upon whether or not the selected phenotype is within an individual's norm of reaction when selection is applied. Similarly, in our model, a genotype is more likely to survive depending on whether or not the optimal phenotype is contained within the phenotypic distribution produced by a given genotype. However, this result is contingent upon the individual with said genotype being in a favorable phenotypic state at the time of selection, a key difference between these prior models and our model. Specifically, the former are unable to distinguish between genetic and epigenetic effects. To wit, in prior models, genotype strictly defines the bounds of the

591 norm of reaction, where individuals possess elevated fitness only if a new optimal phenotype is contained within that norm of reaction. Such a model is not only unable to recapitulate the West-Eberhard model, but also assumes that plasticity may only be adaptive in response to an 594 environmental shift. This stands in contrast to our model, where an optimal phenotype may be well outside the associated phenotype distribution determined by the genotype but can still be produced regardless. Alternatively, it is possible for an optimal phenotype to indeed be within 597 the phenotypic distribution associated with a given genotype but for no individuals of said genotype producing such a phenotype.

Nevertheless, prior models provide insight into the how plasticity may ameliorate the effects 600 of an environmental shift Ancel (1999, 2000); Lande (2009); Via (1985). It is primarily concerned with understanding whether plasticity/learning may accelerate adaptation by examining the ideas behind the Baldwin expediting effect Hinton and Nowlan (1987). Using her model, the 603 author is able to demonstrate that plasticity may only "expedite the search from an initial population distribution to the first encounter with the optimum phenotype" and that this effect is observed for "initial genotype distributions sufficiently distant from the target." Ancel (2000).

606 Our model produces similar results in that plasticity does indeed expedite a population's first encounter with a more fit phenotype, in the case of both relaxed and stringent selection. However, whether or not plasticity ultimately increases a population's rate of adaptation depends 609 upon the conditions under which selection occurs. Further effects not previously described are also seen with our model. In the case of populations under stringent selection, once both genic and epigenetic parameters are allowed to mutate, plastic populations show a much more 612 consistent and directed progression towards the optimum genotype as opposed to non-plastic simulations. Unlike in the case of the non-plastic simulations, many of the individual plastic populations transiently display several extremely sharp spikes followed by plateaus. As such, 615 the populations adopt genotypes progressively nearer to the optimum. The genotypic development of the plastic populations under stringent selection forms a well-defined curve before reaching a plateau around 90, with deviations caused by genetic drift. Plasticity thus allows

them to adapt more quickly as they progress along a selective gradient that has become sufficiently smoothed in comparison to the non-plastic populations. This same trend is not seen in plastic populations under relaxed selection, however, which fail to converge on an optimum phenotype in the number of generations that non-plastic populations do in following a selective gradient.

In summary, we find that the rate of adaptation, as reflected by the cumulative fraction of genetically adapted populations, is dependent on both the manner of selection and the degree of plasticity in a population. This result is in agreement with the Ancel model, which states that plasticity does retard adaptation when both plastic and non-plastic populations readily adapt to a new optimum. However, in contrast to the Ancel model, genotype in this case may be segregated from phenotype, and as such, initial genotypic distributions for all simulations in this section were identically delta distributions with $\epsilon_0 = 67$. Our results also suggest that while non-plastic populations are highly sensitive to the conditions of selection that are applied, plasticity allows populations to be more robust to such variation, a feature that is absent from the Ancel model. Such results may have broader implications for interpreting substitution rates based on sequencing data.

Given these limited conditions, a question remains regarding the maintenance of plasticity and V_E. For plasticity to be maintained in a population, the results of the Ancel model as well as models of phenotypic switching King and Masel (2007); Kussell and Leibler (2005) suggest that a constantly and randomly fluctuating environment may be the only method by which plasticity could be maintained. How, then, may plasticity be maintained under static conditions?

Maintenance of Plasticity Under Static Conditions

The maintenance of plasticity under static conditions remains an open problem in the field. A model proposed by Zhang and Hill (Zhang and Hill (2005)) agrees with the results in prior sections, stating that fluctuating environments may help to maintain plasticity. The Zhang and Hill model additionally proposes that certain ”engineering” costs to precise expression of phenotypes

may allow for the maintenance of non-genetic phentypic variability within a population. This analysis agrees with chemical models of gene regulation where the expression variability may exist in an "infra-Fano" regime only under extraordinarily specific conditions Ramos et al. (2015). A model proposed by Wagner, Booth, and Bagheri-Chaichian shows how pleitropy or associations between decreases in plasticity (environmental variability) and changes in the mean phenotype may also allow plasticity to be maintained under static conditions Wagner et al. (1997).

Our model has shown how plasticity may variously increase, decrease, or be maintained under different selective conditions. Specifically, we have shown that when mutation of genic parameters is disallowed, increased plasticity is selected for under static conditions (c.f. ***Phenotypic Accommodation***). We also have shown that, so long as the range of phenotypes produced both by genotypic and environmental variability is sufficiently within the bounds of directional selection, plasticity may be maintained in a population under static conditions. Alternatively, if the range of phenotypes produced exceeds the bounds set by directional selection, decreased plasticity is selected for (c.f. ***Loss of Variability***). Our results indicate the existence of a trade-off. When undergoing change to adapt to unfavorable environments, populations that express a variety of phenotypes are more likely to be able to adapt quickly, since beneficial phenotypes are more likely to be present and selected for. However, this same trait may act as a detriment under steady-state conditions, as the potential for variation causes the phenotypes to deviate from the ideal. As such, the plasticity of the populations is reduced over time, under certain conditions.

Our results demonstrate how plasticity may be favored and subsequently increase within a population within static environmental conditions. Central to this result is variation in the relative mutation rate for genic and non-genic control of phenotype. Various factors could contribute to r, as pleiotropy, linkage, epistatsis, essentiality, or other genetic conflict can prevent the occurance of certain types of changes. Similarly, the underlying architecture of the genetic networks underlying both genic and non-genic control of phenotype may also provide for an overall larger or smaller substrate for mutations by simply having a larger number of mutable positions within the genome. Such genic-plastic conflict may be a wide-spread mechanism by which plasticity

evolves within a population.

We also note that the trajectory of genetic control of plasticity is not only dependent on r, but also the epoch of time considered. Indeed, if conditions remained static for sufficiently large times, all traits would eventually undergo canalization. However, consideration must be given to how we define a given epoch. The simplest way to define the end of an epoch would be a subsequent shift to a new environment. In this case, plasticity would continue to increase in a population so long as the time before a subsequent environmental shift is shorter than the time required to undergo genetic accommodation of a new environment. Alternatively, the considered epoch may also end when the relative mutation rate r is altered. Given that in our model, the primary driver of the evolution of plasticity is genic-plastic conflict, such conflict may also be resolved via gene duplication or new gene evolution Long (2013), altering r either upwards or downwards.

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Additional information

All authors declare no competing interests.

The authors affirm that all data necessary for confirming the conclusions of the article are present within the article, figures, and tables.

Code to simulate and generate figures may be found at : https://github.com/avianalter/sde_evo

Symbol	Variable
N	Population size
i	Individual $i \in \{1, 2, ..., N\}$
P_i	Phenotype of individual i
ξ_i	Epigenetic value of individual i
γ_i	Deterministic growth parameter/genotype of individual i
ϵ_i	Deterministic repression parameter/genotype of individual i
D_i	Magnitude of plasticity (non-adaptive) parameter/genotype of individual i
τ_i	Auto-correlation of plasticity (adaptive) parameter/genotype of individual i

Table 1: ***Summary of variables.***

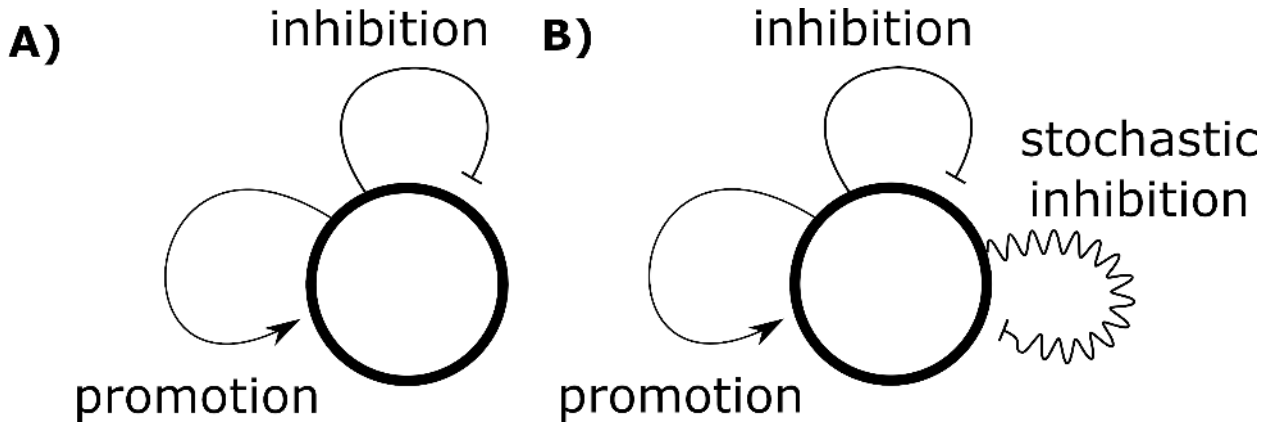

Figure 1: ***Self-regulating traits.*** Phenotypes are modeled as the result of a minimal self-regulating system. Non-plastic phenotypes **(A)** have two feedback loops, one positive and one negative, while plastic phenotypes **(B)** have three feedback loops, one positive and two negative, one deterministic, and one stochastic.

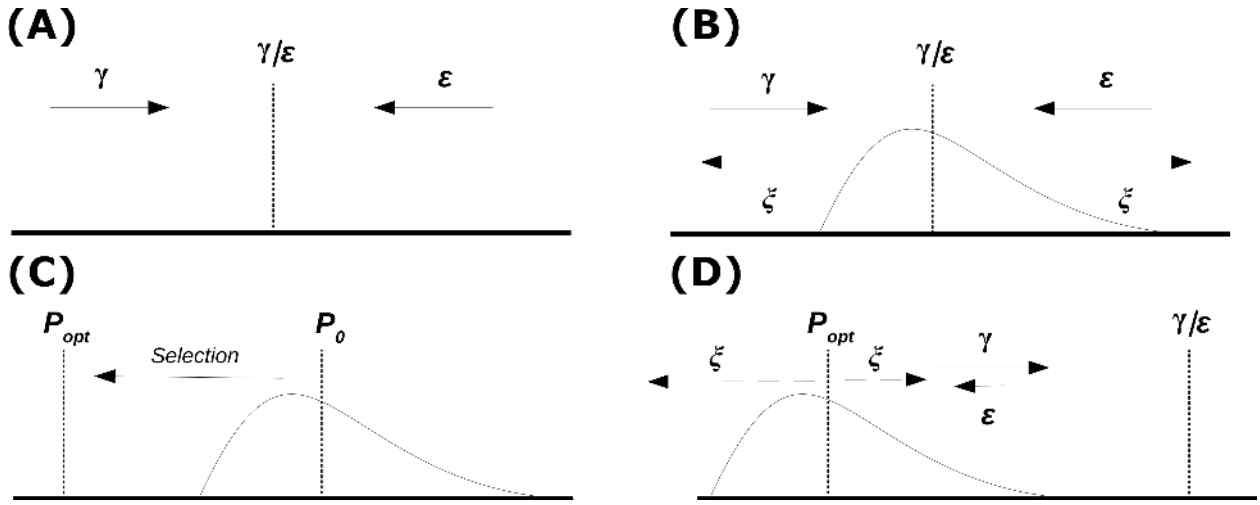

Figure 2: ***Differential equation illustration. (A) Non-plastic phenotypes.*** For non-plastic phenotypes, phenotype is strictly defined by genic control parameters, γ and ϵ, where the trait value is the equilibrium between the "forces" of growth (ϵ) and repression (γ). ***(B) Plastic phenotypes.*** For plastic phenotypes, phenotype is defined by genic control parameters, γ and ϵ, as well as the random epigenetic parameter ξ, which is controlled by (magnitude of plasticity) and τ (auto-correlation). With plasticity, trait value is random, but converges on a steady-state distribution around γ/ϵ. ***(C) Adaptation.*** Populations are challenged with a new environmental condition, favoring an optimal phenotype far from the initial conditions. ***(D) Phenotypic accommodation.*** By disallowing mutation of genic control parameters, when challenged with a new environmental condition, populations adapt to the new environmental conditions through epigenetic means alone. As a whole, the genic control parameters pull populations towards a distribution around γ/ϵ. To maintain populations around the optimum, epigenetic parameter ξ compensates by favoring larger, non-zero values of ξ, while increasing the degree of plasticity and auto-correlation (c.f. Fig. 3).

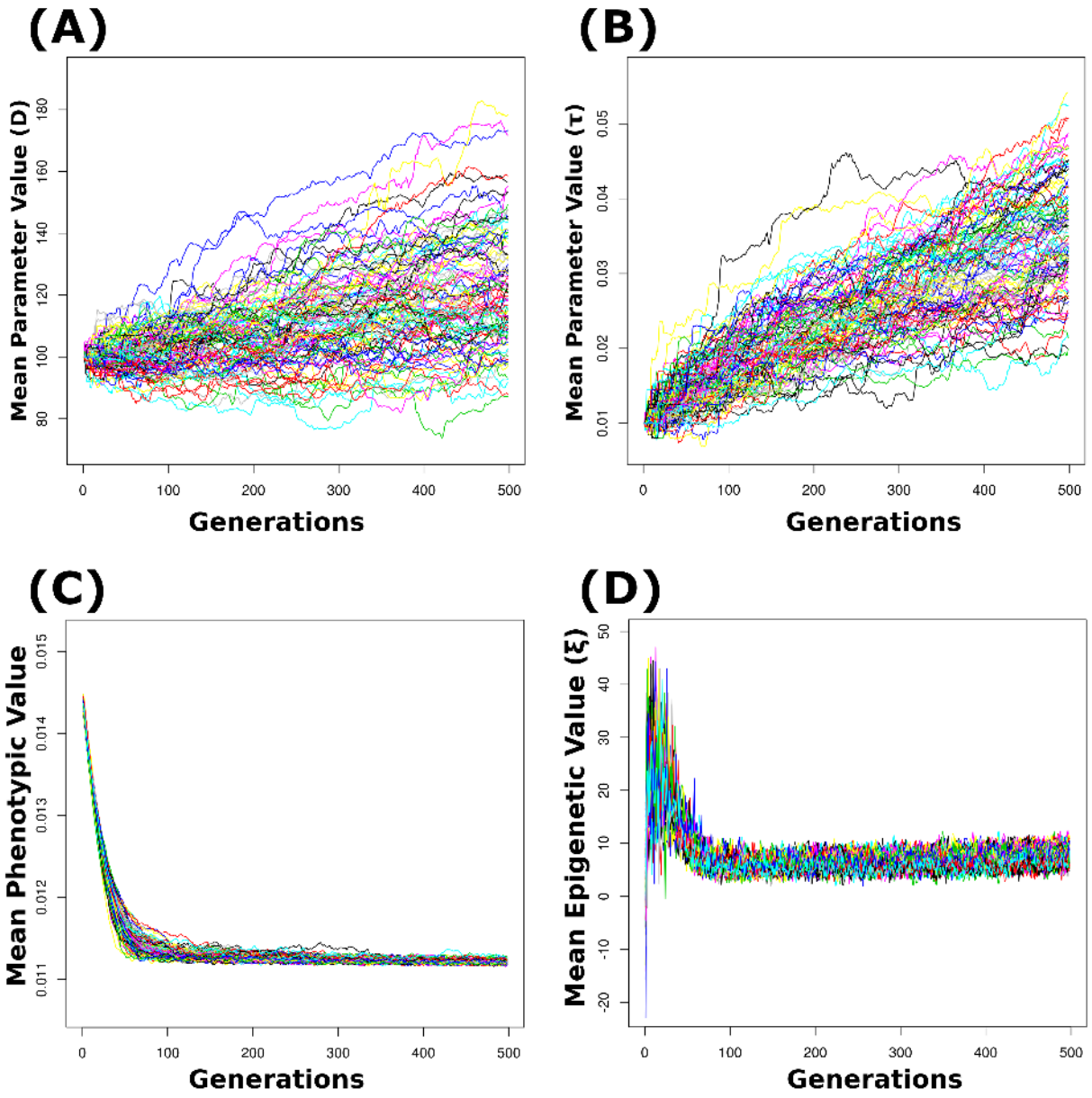

Figure 3: ***Phenotypic accommodation favors increased plasticity and auto-correlation*** 100 replicate populations of 1000 plastic individuals ($T = 2\tau$) were subjected to stringent ($\mu = 1/90, \sigma = 10^{-4}$) selection, with mean parameter values for each replicate population shown above for D_i ***(A)*** and τ_i ***(B)***, one line per replicate population. Though genic parameters were not allowed to mutate, population phenotypes fully adapted to new environmental conditions ***(C)*** through epigenetic compensation ***(D)***. The epigenetic parameter (ξ_i) compensates for a non-optimal genic configuration (γ/ϵ far from P_{opt}), consistently remaining far the expected value of 0. Under such conditions, increased D_i (non-adaptive plasticity) and τ_i (adaptive plasticity) are favored.

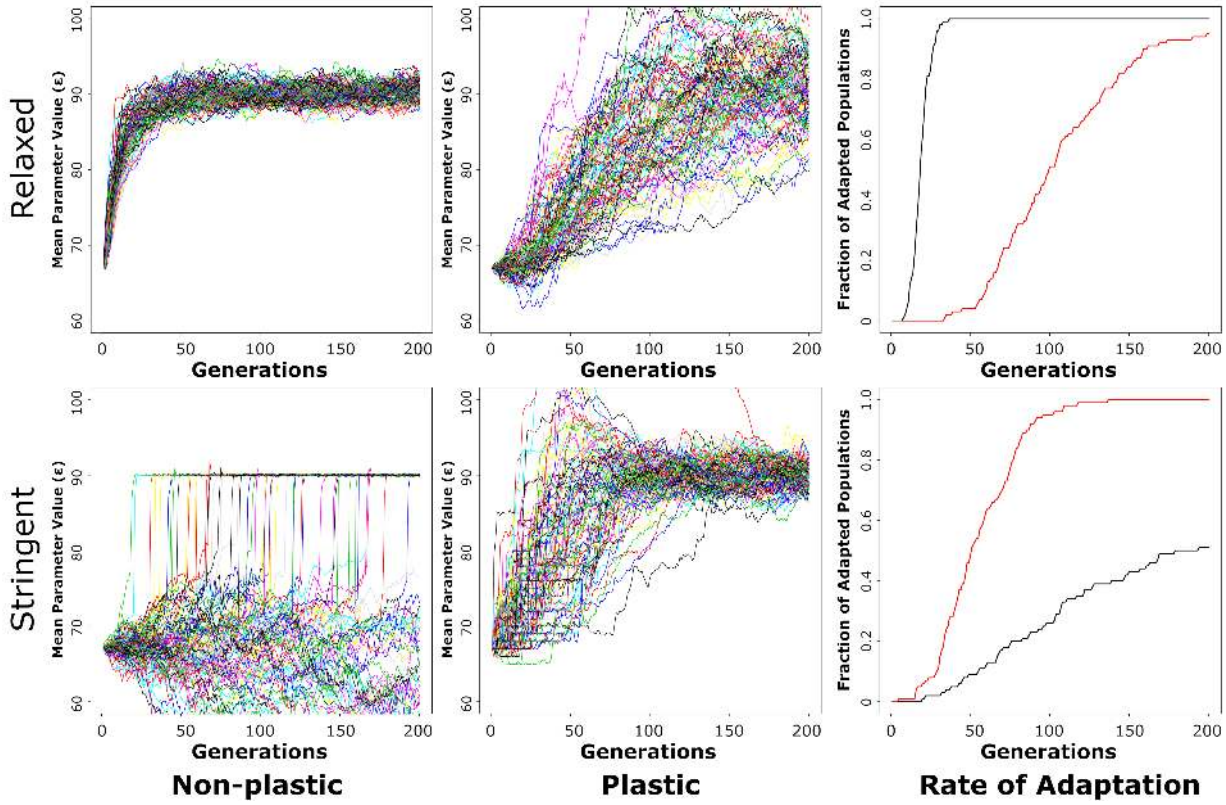

Figure 4: ***Plastic populations are robust to changes in selective forces.***100 replicate populations of 100 individuals were subjected to stringent ($\mu = 1/90, \sigma = 10^{-4}$) and relaxed ($\mu = 1/90, \sigma = 10^{-3}$) selection regimes for non-plastic or plastic traits. The mean genotypic values for ϵ_i are shown, one line per replicate population, demonstrating how plasticity allows populations to have more robust responses to changes in selection pressures. When relaxed selection is applied, non-plastic populations converge more rapidly and smoothly to the optimal genotype than plastic populations (top row). However, when stringent selection is applied, non-plastic populations undergo drift until an advantageous genotype is found, followed by rapid fixation, while plastic populations converge smoothly and rapidly on the optimal genotype (bottom row). The cumulative fraction of genetically adapted replicate populations ($\pm 5\%$ of ϵ_{opt}) within non-plastic simulations are significantly more sensitive to differences in selection than plastic simulations. In conditions of relaxed selection, non-plastic populations adapt faster than plastic populations, however in conditions of stringent selection, plastic adapt first.

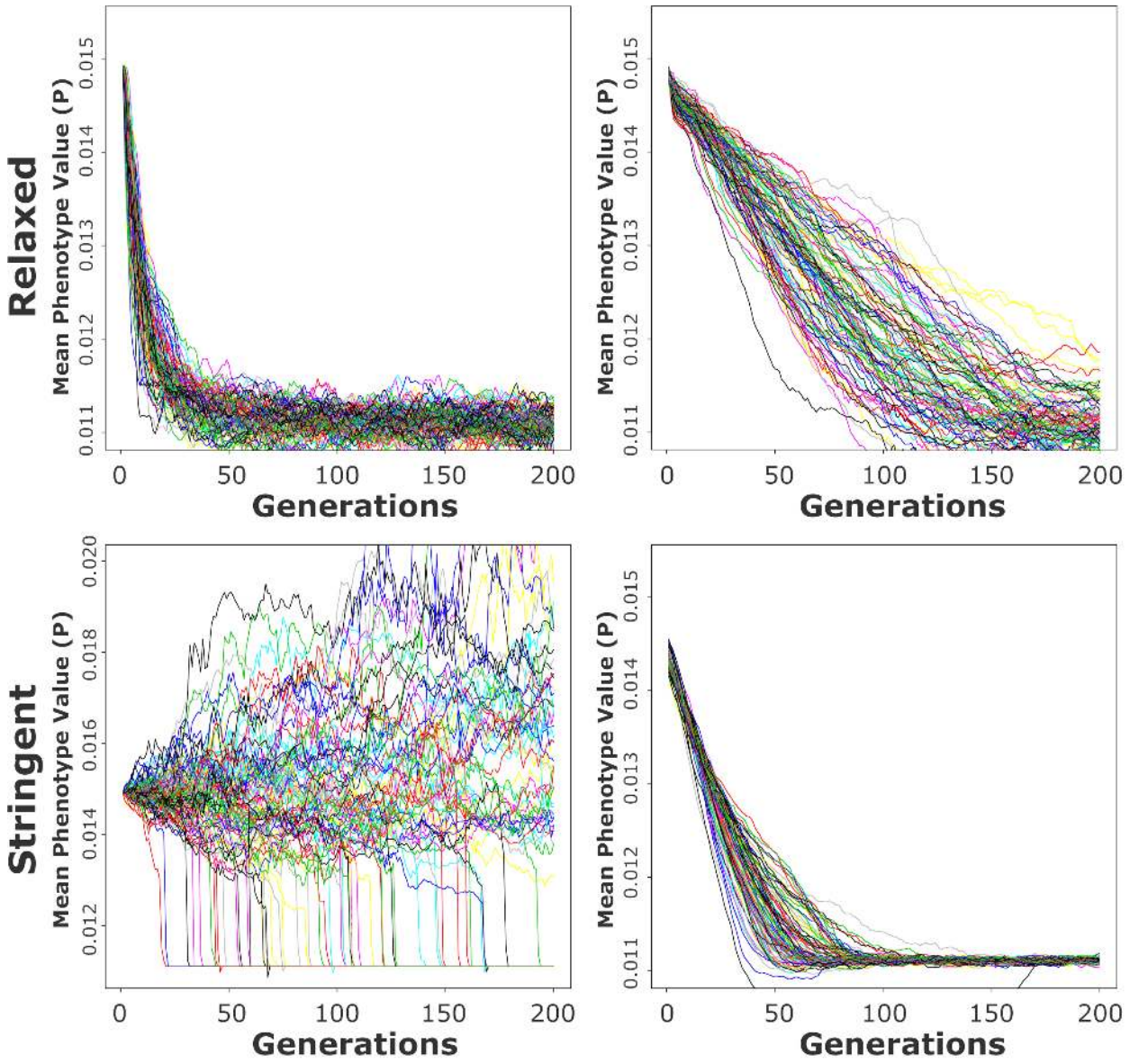

Figure 5: ***Populations with plastic phenotypes converge smoothly on optimum*** Mean phenotypic values for populations shown in Fig. 4 are plotted, one line per replicate population. The behavior of non-plastic phenotypes match the behavior of population genotypes due to the one-to-one relationship between genotype and phenotype. However, while these phenotypic trajectories for non-plastic populations vary greatly (left), phenotypic trajectories for plastic populations converge smoothly on the pre-defined optimum (right). This effect is more pronounced in conditions of stringent selection (bottom).

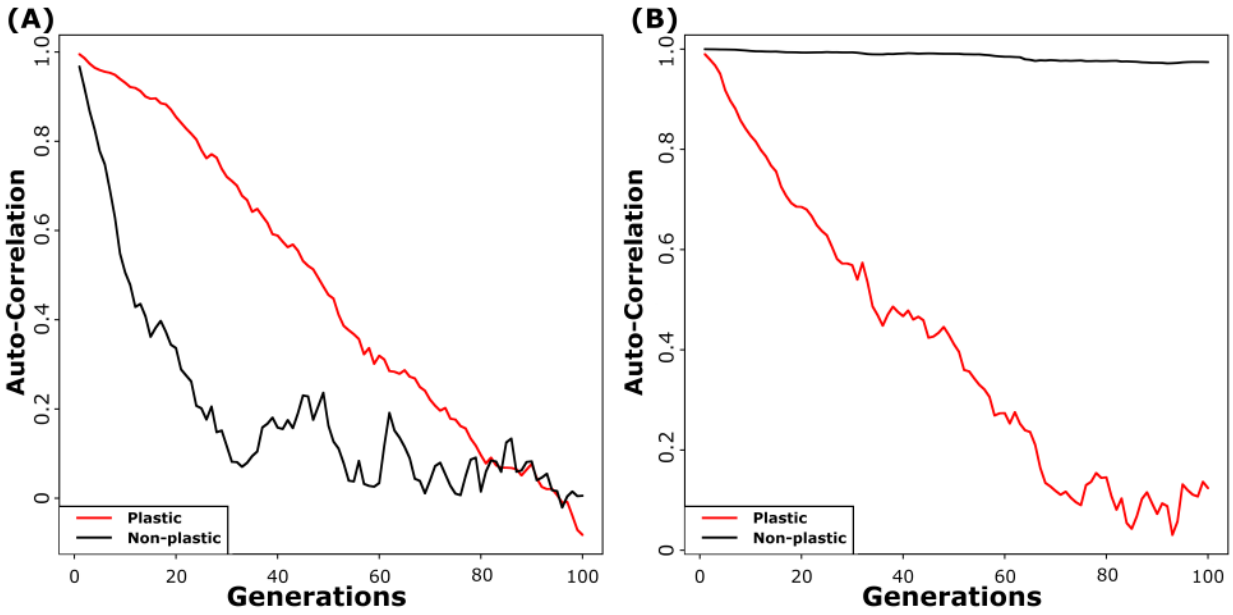

Figure 6: ***Genetic turnover in plastic populations is robust to varying selection conditions.*** At mutation-selection-drift (MSD) balance, turnover of alleles still occurs. Using 100 replicate populations of 1000 individuals at MSD balance, the degree of genetic turnover is represented here by the auto-correlation of the mean genic parameter ϵ_i for the set of 100 replicate populations. Under relaxed selection conditions, non-plastic populations turn over more frequently than plastic populations (***(A)***). Under stringent selection conditions, plastic populations turn over less frequently than non-plastic populations (***(B)***). Plastic populations appeared to be less responsive to various selection conditions (relaxed ***(A)***, stringent ***(B)***) than non-plastic populations.

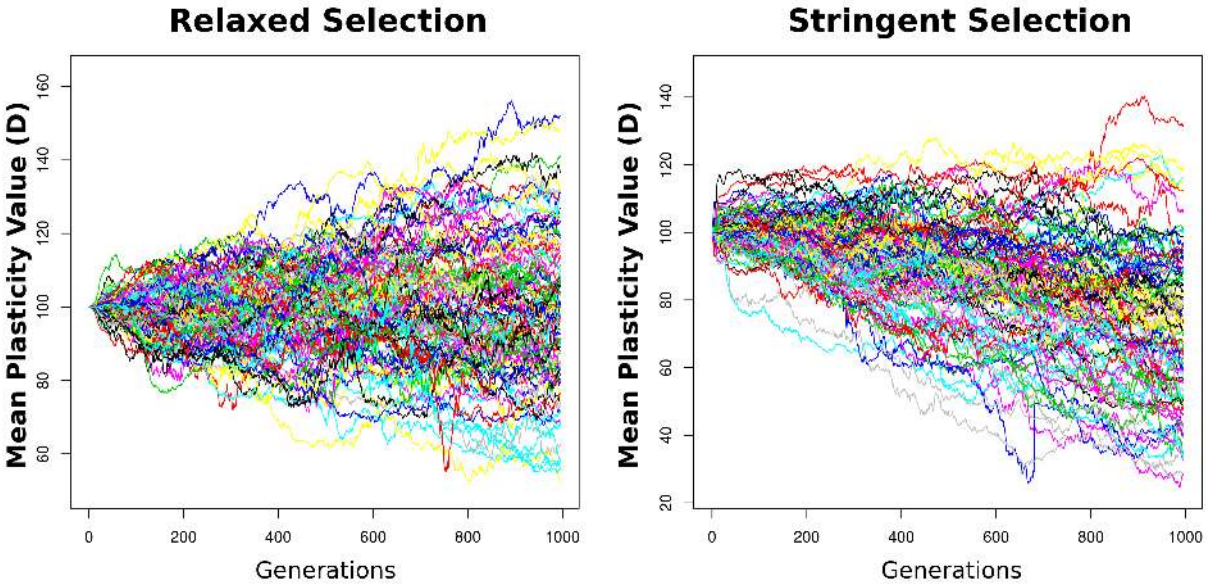

Figure 7: ***Phenotypic plasticity under static conditions is weakly deleterious.*** At mutation-selection-drift balance, plasticity does not to contribute any meaningful selective advantage. Shown are mean D_i values for 100 replicate populations of 1000 individuals at mutation-selection-drift balance, one line per replicate population. So long as the phenotypic variability is sufficiently within the bounds of applied selection, as in the case of relaxed selection, plasticity is near neutral and thus may be maintained in a population for extended periods (left). However, if the stringency of selection is increased, plasticity is weakly deleterious (right).

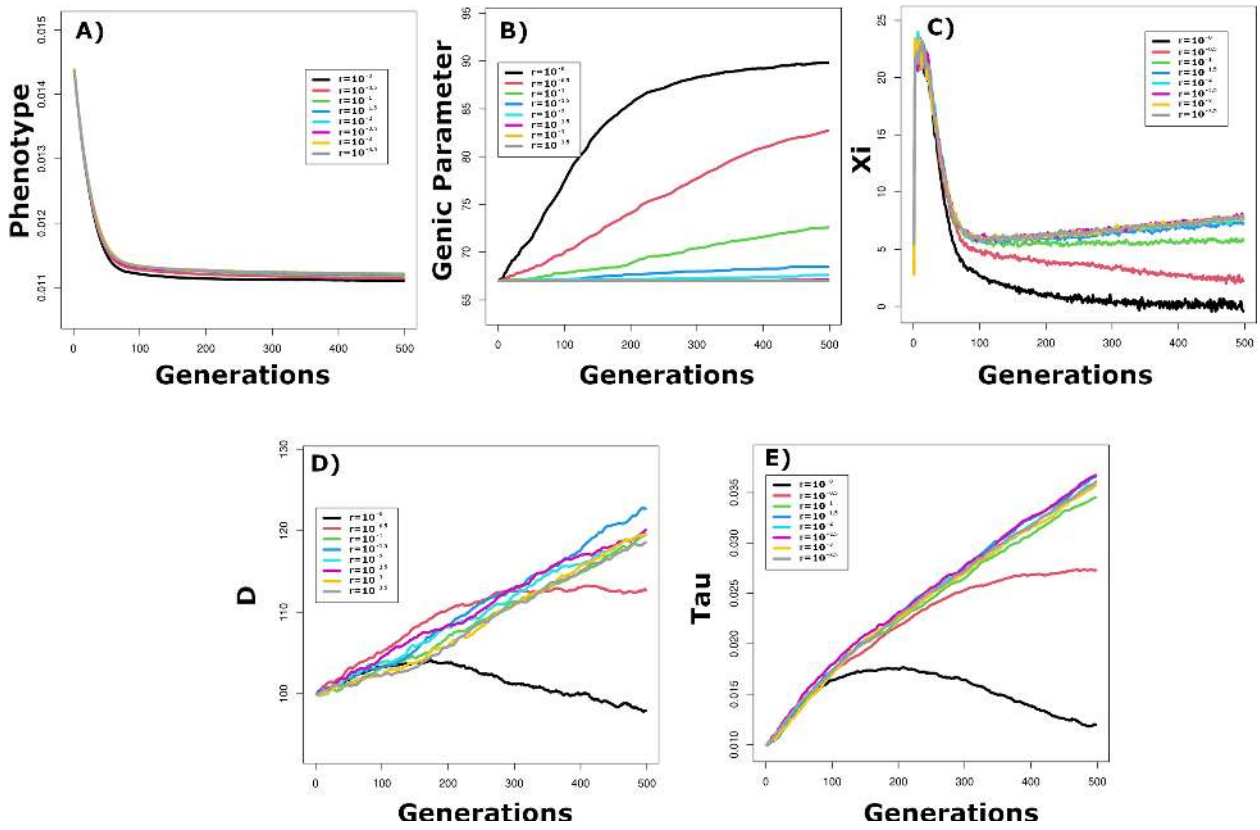

Figure 8: ***Relative mutation rate determines evolution of plasticity*** Populations (100 replicates) consisting of plastic individuals ($N = 1000$) were presented with a new environment while the relative rate of mutation of genic and non-genic parameters (r) was varied. Shown here is the mean population behavior at each r value, averaged over 100 replicate populations, one line per r value. While in all cases, phenotypic accommodation of the new environment occurred rapidly ***(A)***, the ability of individuals to provide a genic solution ($_i$) to new conditions was hindered ***(B)***. Where genic solutions were not easily produced, epigenetic compensation occurred ***(C)***, allowing both non-adaptive and adaptive plasticity to be advantageous within the given epoch ***(D-E)***.