Evolvability

A Unifying Concept in Evolutionary Biology?

Edited by: Thomas F. Hansen, David Houle, Mihaela Pavličev, Christophe Pélabon
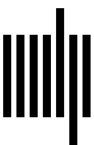
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14 Does Lack of Evolvability Constrain Adaptation? If So, on What Timescales?

Kjetil L. Voje, Mark Grabowski, Agnes Holstad, Arthur Porto, Masahito Tsuboi, and Geir H. Bolstad

The relevance of genetic constraints for evolutionary change beyond microevolutionary timescales is debated. The high evolvability of natural populations predicts rapid adaptation, but evolvability is often found to correlate with phenotypic divergence on longer timescales, which makes sense if evolvability constrains divergence. This chapter attempts to reconcile the observation of high evolvability of populations with the idea that genetic constraints may still be relevant on long timescales. We first establish that a relationship between evolvability and divergence is a common empirical phenomenon both among populations within species (microevolution) and among species (macroevolution). We then argue that a satisfactory model for the prevalence of this empirical relationship is lacking. Linking microevolutionary theory with the dynamics of the adaptive landscape across time—moving toward a proper quantitative theory of phenotypic change on macroevolution timescales—is key to better understanding the relative importance of genetic constraints on phenotypic evolution beyond a handful of generations.

14.1 Introduction

The study of adaptation—how natural selection improves organisms' fit to their environment—is central to evolutionary biology. Adaptations enable lineages to survive and thrive in vastly different habitats, or they may represent fine-tuned differences among populations, like the relationship between pericarp thickness in the fruits of populations of *Camellia japonica* and the length of the rostrum of the seed-predatory weevil *Curculio camelliae* (Toju and Sota 2006). But not all populations are well adapted. For example, *Crescentia alata* and several other plant species in Central America have large fruits that do not get dispersed due to the late-Pleistocene extinction of the many large herbivores that acted as their agents for seed dispersal (Janzen and Martin 1982). Why is fruit size evolving fast in populations of *Camellia japonica* in Japan while the large and energy-expensive fruit of *Crescentia alata* is not? In this chapter, we ask whether lack of evolvability—the potential (or disposition) of a population to evolve—may be an explanation for why "evolutionary failure is commonplace" (Bradshaw 1991, 289). We find that evolvability and phenotypic divergence are often positively correlated, both on short and on longer timescales, an intriguing result, given the lack of models that readily predict this correlation.

To say something meaningful about a potential relationship between adaptation and evolvability, we first clarify what we mean by adaptation, as the term has accumulated numerous definitions (e.g., Reeve and Sherman 1993). In the context of evolvability in quantitative

genetics (see Hansen and Houle 2008; Hansen and Pélabon 2021), adaptation can be understood and defined in relation to an adaptive landscape. Simpson (1944) outlined the concept of the adaptive landscape as a representation of possible combinations of phenotypic traits where elevations in the landscape represent higher population fitness. Adaptation can be both a process and an outcome. In the context of an adaptive landscape, the process of adaptation is about climbing peaks, and selection will always push the population up along the steepest slope of a fitness surface it resides on (Lande 1979; 2007). The outcome of this climbing process is increased adaptation (and a reduced maladaptiveness); a well-adapted population will be at or close to a peak in the landscape. Because elevation on this landscape reflects the fitness of the population, the degree of maladaptation increases with the vertical distance to the closest peak. The different populations of *Camellia japonica* in Japan probably reside at or close to local peaks in the adaptive landscape for pericarp thickness. The South American plants lacking large-bodied agents for seed-dispersal are probably closer to the foot than the top of a mountain in the adaptive landscape or are trapped on a local peak that has been reduced from a high summit to a small hill.

Changes in the environment experienced by a population can affect the adaptive landscape and thus decrease adaptiveness (i.e., cause maladaptation). The extinction of a seed disperser is an obvious example. But several other processes can also displace a population from a peak or hinder it from efficiently ascending peaks in the adaptive landscape. Gene flow among populations may hinder local adaptation (Savolainen et al. 2007), small population size will increase the prevalence of mildly deleterious alleles (Ohta 1992) and enable genetic drift to play an increasing role on the evolutionary dynamics (Walsh and Lynch 2018). Genetic architecture (e.g., pleiotropy) may generate a deviation in the response to selection, causing the evolving population to take a curved path toward the peak (Lande 1979). Different degrees of maladaptation may therefore be a common state in nature (Crespi 2000), even for apparently well-adapted populations. Indeed, a large-scale analysis of selection gradients indicated that most of the populations studied (64%) had a trait mean that deviated more than 1 standard deviation from the estimated optimum and about one third had a mismatch between trait mean and optimum of more than 2 standard deviations (Estes and Arnold 2007).

The ample evidence of maladaptation in natural populations suggests that the ability to evolve—and potentially a lack thereof—matters on short timescales. When the position of the optimum changes, a highly evolvable population will track and re-ascend the peak, while less evolvable populations will remain displaced from the peak. Lineage extinction is the ultimate failure of adapting sufficiently rapidly to changes in the environment (Gomulkiewicz and Houle 2009), a fate common to the great majority of all lineages that have ever existed (Jablonski 2004).

Are constraints imposed by the lack of evolvability relevant on timescales beyond microevolution? This question has a long and controversial history in evolutionary biology (e.g., Simpson 1944; Kluge and Kerfoot 1973; Schluter 1996). Low genetic variation in the direction of selection is commonly assumed to be a soft constraint, because it can be overcome given enough time (Maynard Smith et al. 1985). Therefore, as long as a sustainable population size is maintained during the time interval in which the population reclimbs the peak, extinction will be avoided. Indeed, currently living species must have been able to surmount changes in the adaptive landscape in their past, which suggests little relevance

of evolvability on macroevolutionary timescales. A growing body of empirical work suggests otherwise.

Genetic constraints are influencing evolution if the closest adaptive peak has not been reached by the population due to lack of available genetic variation (Arnold 1992). Schluter (1996) was the first to detect that phenotypic differentiation between populations and species tended to be biased in the multivariate direction containing the greatest additive genetic variance (i.e., the direction with highest evolvability). Later studies have found a similar pattern between evolvability and divergence, sometimes across macroevolutionary timescales. For example, Houle et al. (2017) showed that the evolvability of a population of the fruit fly *Drosophila melanogaster* strongly correlated with trait divergence among Drosophilid species that shared a common ancestor 40 million years ago. Empirical evidence in favor of evolvability constraining the process of adaptation on both long and short timescales is paradoxical, given the apparent high evolvability of natural populations (Bolstad et al. 2014). On short timescales, evolvability depends on the amount of additive genetic variation, and most quantitative traits seem to contain enough variation to quickly respond to directional selection (Hansen and Pélabon 2021). Directional selection on traits is also common in nature (Hereford et al. 2004), and populations typically respond rapidly—just as predicted by theory (Hendry and Kinnison 1999; Kinnison and Hendry 2001). Many populations are therefore seemingly sufficiently evolvable to readily overcome even serious cases of maladaptation and to rapidly ascend peaks in the adaptive landscape. But why then are the large fruits of *Crescentia alata* rotting close to the individual producing them?

This chapter discusses how to reconcile the apparent high evolvability of natural populations with the hypothesis that a population's ability to evolve might act as a constraint on the process of adaptation. After introducing the quantitative genetic concept of evolvability, we discuss methodological issues when investigating correlations between evolvability and divergence. Reviewing published studies, we show that a positive correlation between evolvability and phenotypic divergence is a common empirical pattern. We then briefly discuss trait evolution models and conclude that we currently lack a satisfactory model that fully explains the commonness of the relationship between evolvability and phenotypic divergence. Because the realism of the different models depends on the dynamical nature of the adaptive landscape, we discuss new developments in our understanding of how adaptive landscapes change on different time intervals. We end by pointing to future directions of research that will help us further assess the relevance of evolvability for adaptation and phenotypic divergence.

14.2   General Introduction to Evolvability

To understand the relationship between evolvability and constraint, we need first to understand the measurement of evolvability. Quantitative genetic theory posits that short-term evolvability can be quantified using a metric reflecting standing genetic variation. Houle (1992; see also Hansen, chapter 5; Houle and Pélabon, chapter 6)[1] proposed that evolvability, *e*, can be operationalized using the mean-scaled additive genetic variance:

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1. References to chapter numbers in the text are to chapters in this volume.

$$e = \frac{V_A}{\overline{z}^2},$$

where V_A and $\overline{z}$ are respectively the trait's additive genetic variance and mean before selection. Hansen et al. (2003a) showed that e can be interpreted as the proportional evolutionary response of a trait to 1 unit strength of directional selection, where the unit is defined as the strength of selection on fitness itself. This definition of evolvability serves as a metric, allowing us to assess and compare the ability of different types of traits to evolve.

Reported estimates of univariate evolvabilities suggest abundant additive genetic variation for virtually any trait of interest (Hansen et al. 2011). On a trait-by-trait basis, that would suggest a sufficiently large supply of "fuel" for the evolutionary process to cast doubt on any hypotheses claiming evolvability could act as an evolutionary constraint. Still, observed evolutionary rates are often orders of magnitude smaller than predicted from univariate evolvabilities. For example, Lande (1976, 333) found that only about 1 selective death per million individuals per generation is needed to explain the observed evolution in tooth characters of Tertiary mammals in the fossil record (see also Lynch 1990). One possible explanation is that univariate evolvability estimates are not representative of the true capacity for traits to evolve. Empirical studies indicate that variation in single traits is often bound to variation in other traits of the same organism due to genetic correlations (e.g., Walsh and Blows 2009). The immediate implication is that evolutionary change for any one trait is often not possible without substantial changes in other traits. Strong stabilizing selection on pleiotropically linked traits may therefore severely reduce the amount of "free" additive genetic variance available for a given trait to evolve (Hansen and Houle 2004).

Suggestions of multivariate constraint as an essential component of adaptation have been made for decades (e.g., Dickerson 1955), and evolutionary biology has witnessed an increasing use of quantitative genetic approaches aimed at understanding evolution in multivariate morpho-space. Most of these approaches rely on the genetic variance-covariance matrix, **G**, as the central entity with which to study evolvability. For example, several studies have attempted to find dimensions of **G** with little to no additive genetic variance and have framed issues surrounding evolvability in terms of "nearly null spaces" (e.g., Gomulkiewicz and Houle 2009), that is, subspaces of **G** with very low evolvability. These studies argue that finding such dimensions is essential to understanding evolvability, as they would represent multivariate constraints due to diminished evolutionary potential in these directions. However, studying these dimensions is complicated, because estimating variance in nearly null spaces may be confounded with measurement error. It may also be that the absence of genetic variance in short time spans is not representative of long-term evolvability, as both new mutations or changes in allele frequencies (because of dominance or epistasis) may lead to increased additive variance.

Another popular approach to studying multivariate evolvability is framed in terms of lines of least evolutionary resistance (sensu Schluter 1996). The term "lines of least evolutionary resistance" refers to dimensions of multivariate space with a larger-than-average amount of the total additive genetic variance along which evolution could proceed at a fast pace (Hansen and Houle 2008). Although lines of least resistance are often much easier

to estimate and study than are nearly null spaces, they also have shortcomings. Most notably, there are usually multiple dimensions with abundant additive genetic variance in a population, so lack of population divergence along the primary axis of genetic variance is not an indication that those populations did not diverge along an axis associated with greater-than-average additive variance (Hansen and Voje 2011).

Hansen and Houle (2008) proposed an approach to unify these perspectives on multivariate evolution into a single framework, suggesting multiple direct measurements of evolvability that take into account the extent to which variation in individual traits are bound to other traits during adaptation. These are defined as unconditional and conditional evolvabilities and depend on assumptions about the adaptive landscape. Unconditional evolvability is measured as the magnitude of the projection of the response on the selection vector; it represents the magnitude of the evolutionary response in the direction of selection. Conditional evolvability is measured as the response along the selection vector when no other directions (with measurements) of response are allowed (Hansen et al. 2003b). This represents a situation where evolvability is the genetic variation available for selection in one direction when other multivariate directions are under strong stabilizing selection. The importance of such operational definitions of evolvability is that they provide a truly multivariate view of evolution.

Although some researchers have argued that explanations for stasis are "far outside the domain of genetic constraints" (Arnold 2014, 743), others have argued that the multivariate nature of evolution may provide a partial resolution to the problem of stasis (Hansen and Houle 2004; Walsh and Blows 2009). Indeed, most conditional evolvabilities can be much smaller than unconditional evolvabilities, highlighting once again that most individual trait variance is bound to other traits (Hansen 2012). One explanation for a lack of adaptation despite abundant variation may therefore be that we simply do not have a good understanding of all the relevant traits that make up $\mathbf{G}$, or how a high-dimensional $\mathbf{G}$ impacts and is impacted by natural selection. To complicate the matters further, studies of multivariate evolvability and divergence are also plagued with methodological issues.

14.3 Methods Matter!

Analyzing the relationship between evolvability and divergence is not straightforward. A first challenge is that $\mathbf{G}$ is hard to measure with high accuracy (Cheverud 1988), making the comparison to divergence imprecise. A second methodological issue is the use of correlation matrices. In a genetic correlation matrix, elements are standardized by the trait variances, removing the magnitude of variation and, therefore, obscuring the relationship between the genetic variance and divergence. A third methodological issue is the tendency to solely assess the angle between the divergence vector and the dominant eigenvector of $\mathbf{G}$ (g_{max}) when investigating for a relationship between evolvability and divergence, as there may be many directions in phenotype space with high evolvability (Hansen and Voje 2011). There are additional issues with interpreting several of the matrix comparison methods (see discussion in Bolstad et al. 2014), and their power to detect a true evolvability-divergence relationship might be weak (e.g., see the reanalysis of Lofsvold's data later in this section).

To analyze the relationship between evolvability and divergence, we advocate using mean standardization or natural log transformation before employing the framework suggested by Hansen and Houle (2008). These two methods are interchangeable for small variances, as mean standardization is the first order (local) approximation of the natural log (see Grabowski and Roseman 2015). Not all traits can be meaningfully log-transformed or mean standardized, however (see Houle et al. 2011; Pélabon et al. 2020). After such standardization, the estimated evolvabilities in a direction of divergence can be compared with the average evolvability of all traits (Hansen and Houle 2008; Hansen and Voje 2011), or evolvabilities can be compared to divergence variance or rates across traits (e.g., as in Bolstad et al. 2014). For the latter approach, one would typically do a regression with log divergence variance or rate as response and log evolvability as predictor, to estimate the scaling relationship between the two.

The approach we advocate also has methodological issues. A first issue is that traits of different dimensionality will have systematically different evolvabilities and divergence rates (Gingerich 1993; Hansen et al. 2011). Note, however, that these differences are not statistical artifacts but should be interpreted as a dimensionality-scaling effect rather than a potentially constraining effect of evolvability. Therefore, to test for a relationship between evolvability and divergence, it is advisable to include only traits measured in the same physical dimension in the same analysis. A second issue is the choice of how to linearly transform the traits before fitting the regression between evolvability and divergence (for more on this point, see Houle et al. 2020; Jiang and Zhang 2020).

We illustrate the impact that different methodologies can have on the conclusions regarding the relationship between **G** and the among-population variance-covariance matrix, **D**, by reanalyzing the data on different subspecies of the genus *Peromyscus* presented in Lofsvold (1986, 1988). Lofsvold (1988) concluded that, overall, there is no significant similarity between **G** and **D** (**L** in Lofsvold 1988). His analysis was based on comparing angles of the first 5 eigenvectors between matrices, computing matrix correlations, and performing Mantel tests. Conveniently, the variance-covariance matrices presented by Lofsvold are based on natural log transformed traits, and hence the genetic variances (V_A) can be interpreted as evolvabilities and the among-population variances (V_D) are on the same scale. We analyzed the scaling relationship between **D** and **G** by using a simple least squares regression with log V_D as response and log V_A as predictor. We detected moderate to strong relationships between the **D**s and **G**s, with scaling exponents (*b*) in the range 0.70–0.93, and R^2 in the range 29–89% (figure 14.1a). In two of the subspecies, the among-population divergence was best explained by the **G** of the same subspecies, indicating that constraints break down over time, whereas in the other subspecies (*P. maniculatus bairdii*), this was not the case. Interestingly, the relationships are generally steeper and stronger when using **P**, the phenotypic variance-covariance matrix, in place of **G** (figure 14.1b). This may be because **G** is poorly estimated compared to **P**, and therefore the shape of **P** is a better representation of the shape of the true **G** (see Cheverud 1988). Alternatively, it can be caused by a component of plasticity shared by **P** and **D**. In any case, our analysis reaches the opposite conclusion of Lofsvold (1988).

With the data of Lofsvold (1988), we can also test whether there is a relationship between **G** and divergence among species and subspecies. Because there are only 3 species, calculating **D** at this level is not informative. However, we can quantify whether the divergence vectors
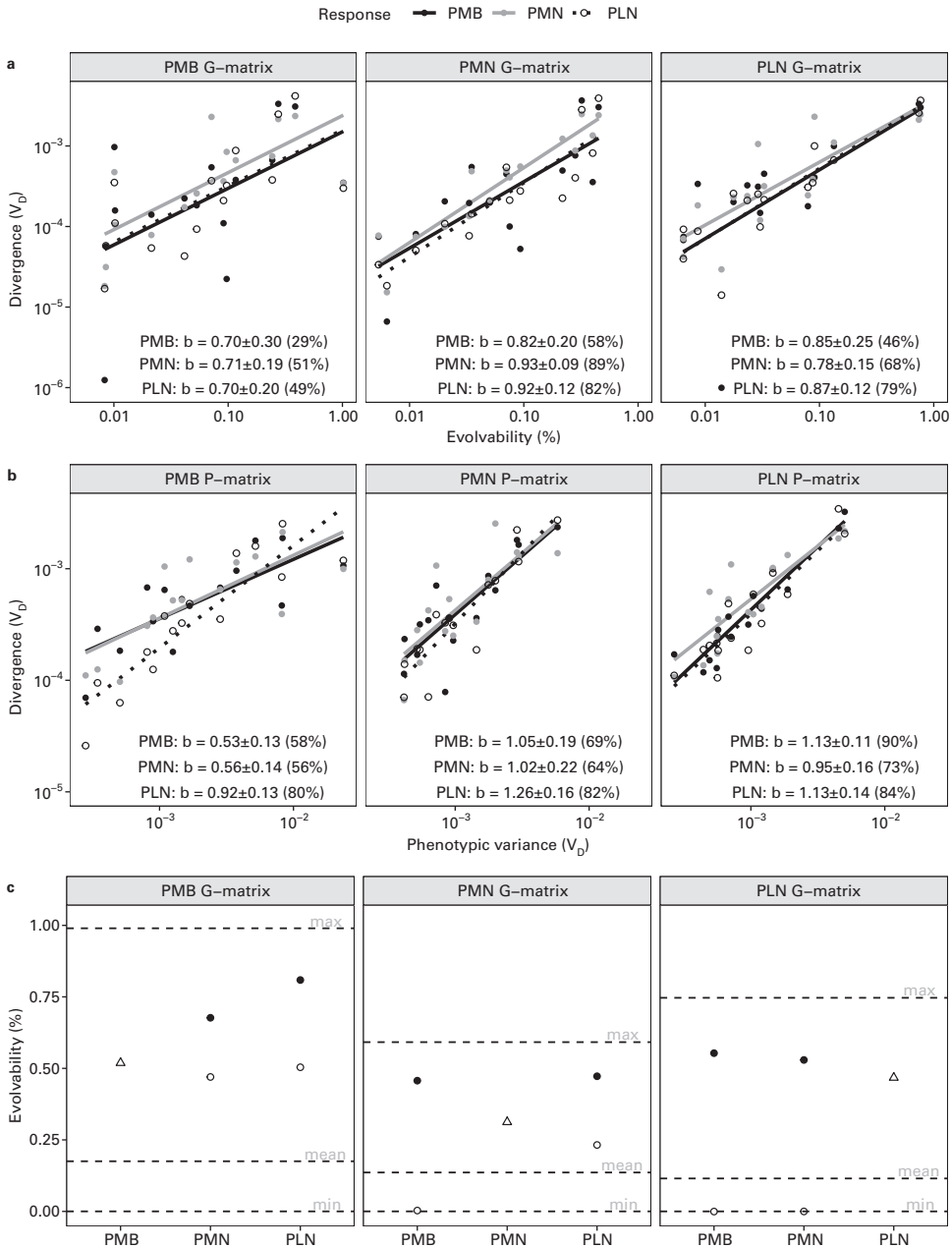
Figure 14.1

Analysis of scaling relationship between divergence and (a) evolvability and (b) phenotypic variance in different subspecies of the genus *Peromyscus* ("deer mouse," PMB = *P. maniculatus bairdii,* PMN = *P. maniculatus nebrascensis,* PLN = *P. leucopus noveborascensis*). Divergence (V_D) and phenotypic variance (V_P) are in units of ln²(mm), and evolvability is in units of $100 \times$ ln²(mm) (i.e., $100 \times V_A$), which can be interpreted as percentage change in the trait mean under unit selection. The scaling exponents $b \pm$ SE (R^2) were estimated from the slope of least squares regression on log transformed variances of the 15 traits at the 2 levels. The traits used in the analysis were defined by the eigenvectors of the corresponding **P** when **G** was used as the explanatory variable and by the eigenvectors of the corresponding **G** when **P** was used as the explanatory variable (data are from Lofsvold 1986, 1988). We used the original **G**-matrices presented in Lofsvold (1986) and not the bent **G**-matrices presented in Lofsvold (1988). One obvious sign error was corrected. (c) Evolvability in the direction of divergence from the focal subspecies, for which **G** was estimated, to the subspecies indicated on the x-axis. For comparison, the open triangles show the average evolvability of the 2-dimensional plane with highest divergence in each subspecies (this plane accounted for approximately 70% of the divergence). The vertical lines show (from top to bottom) maximum evolvability, average evolvability, and minimum evolvability, respectively, of the **G**-matrix. Filled circles show evolvability, and open circles show conditional evolvability. The average conditional evolvabilities are not shown as they were visually indistinguishable from the minimum evolvabilities. The figure is based on the bent **G**-matrices published in Lofsvold (1988), to avoid negative minimum evolvabilities.

among these taxa are along lines of low genetic resistance by comparing the evolvability in these directions with the minimum, average, and maximum evolvability of the **G**-matrices using the "evolvability" R-package (Bolstad et al. 2014). Our analysis (figure 14.1c) shows that the evolvabilities in the directions of divergence are high compared to the average evolvabilities. This suggests that the relationship between divergence and evolvabilities is retained up to the species timescale for these data. The conditional evolvabilities were very low in three instances (open circles in figure 14.1c). This may not reflect reality, as the estimated **G** has several dimensions with very little evolvability. Low conditional evolvabilities can arise from estimation error in the orientation of **G**. If the direction of divergence is only slightly correlated (due to estimation error) with a direction of **G** with close to zero evolvability, its conditional evolvability will be very small.

14.4   Empirical Evidence for a Relationship between Evolvability and Divergence

Evolvability should correlate with divergence if the former constrains the latter, but as we argued in section 14.3, meaningful assessments of a relationship between divergence and evolvability can be obscured by methodological issues. Therefore, in our review of studies assessing such a relationship (table 14.1), we have briefly summarized the methods used.

  The first thing to notice from table 14.1 is that more studies are reporting a relationship rather than failing to find one. Several of the studies that did not find a relationship may also have failed to do so because of methodological issues, as we have shown with Lofsvold's (1988) study. In contrast, some of the observed relationships between evolvability and divergence might be due to comparison of traits with different dimensionality or with different units (see the "DC" column). However, even if we only consider studies that have used dimensionally consistent traits, the evidence for a relationship between evolvability and divergence is strong. Holstad et al. (in preparation) found a positive relationship between evolvability and divergence across 409 univariate traits collected from 123 different species. Variation in evolvability explained 30% of the variation in among-population variance and 12% of the among-species variance (figure 14.2). A detailed analysis of the plant subset of this data further supports these findings but also identifies an important role of the trait function, which together with evolvability, explained 40% of the variation in population divergence (Opedal et al. 2023). Hence, a preliminary answer to the first question of the title of this chapter—Does lack of evolvability constrain adaptation?—is yes, in the sense that plenty of circumstantial evidence indicates that evolvability does constrain evolution and therefore also adaptation. This result aligns well with the many studies reporting a relationship between within-population phenotypic variation and covariation (i.e., the **P** matrix) and divergence (e.g., Hunt 2007b; Grabowski et al. 2011; Baab 2018; Tsuboi et al. 2018).

  The evolvability-divergence relationship is commonly observed both on the population and the species timescales (table 14.1). Hence, the answer to the second question of the title is that constraints appear to be common even on a macroevolutionary timescale, where divergence times are often on the order of millions of years. Holstad et al. (in preparation) observed a weakening in the evolvability-divergence relationship at the species timescale compared to the relationship observed at the timescale of population divergence. Other
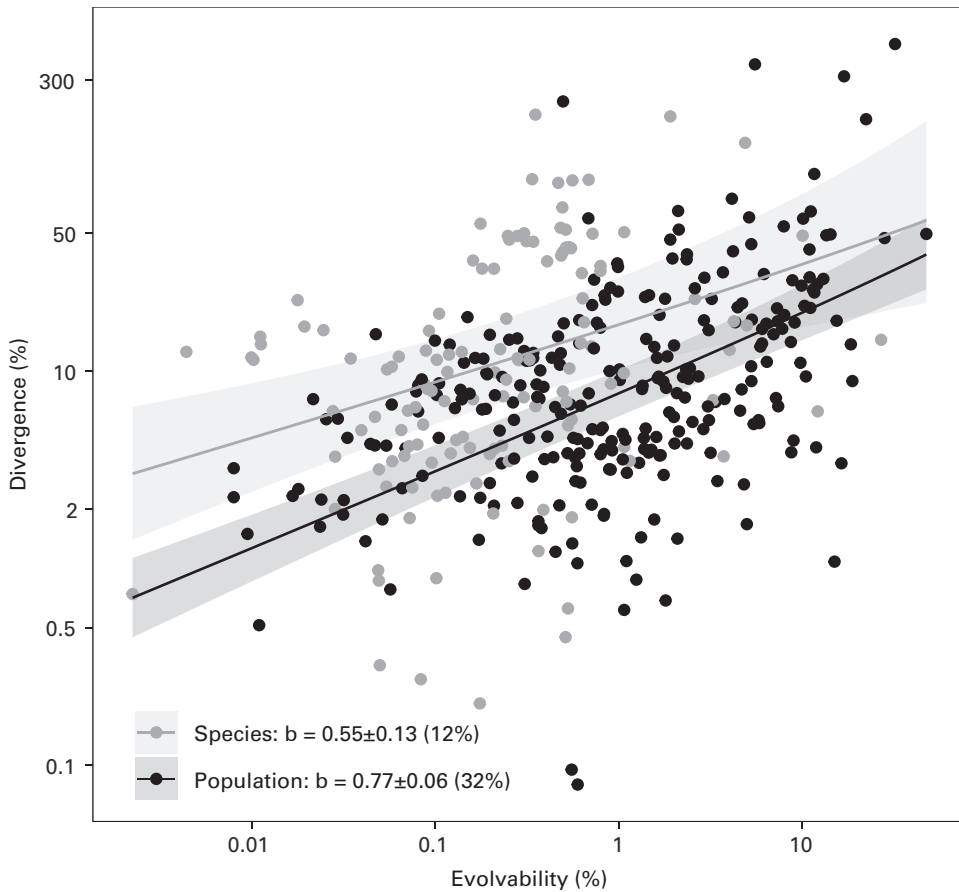
Figure 14.2
Divergence among populations and species predicted by evolvability. Divergence is expressed as expected proportional divergence in percentage change from the mean of the measured populations per trait. Evolvability is expressed as the mean percentage potential evolutionary change. The scaling exponents $b \pm SE$ (and marginal R^2) are obtained from mixed-effect models on natural log-transformed variables (divergence and evolvability) with closest shared taxa as random effect. The figure is rendered with permission from Holstad et al. (in preparation).

studies likewise report a weakening relationship with divergence time (Schluter 1996; Berger et al. 2014; Chakrabarty and Schielzeth 2020; but see Innocenti and Chenoweth 2013), supporting the idea that constraints break down over time.

The studies listed in table 14.1 cover a variety of traits, including thermal reaction norms, cuticular hydrocarbons (CHCs), morphological shape, and gene expression, as well as a wide variety of taxa. Hence, the positive relationship between **G** and divergence seems to be very general, at least within each trait group.

The positive relationship between evolvability and divergence is not a given, considering that most quantitative traits seem to harbor levels of additive genetic variance that could generate rates of evolution that far exceed those we observe. Furthermore, both evolvability and divergence are estimates of variance at particular levels of biological organization, which require substantial amounts of data to be estimated with high accuracy. The estimates reported in the studies listed in table 14.1 thus all come with rather large errors, which will

Table 14.1
Studies comparing genetic variance and divergence

Study	N/tx*	Scale‡	DC§	**G**-divergence comparison method**	Traits
Population timescale: studies reporting a relationship between G and divergence					
Mitchell-Olds (1996)	3/10	same	Y	Regression slopes	Plant life history
Schluter (1996)	5/21	log	N	$\angle$ g-max	Stickleback body shape
Andersson (1997)	7/12	corr	Y	Matrix correlation	Plant morphology
Blows and Higgie (2003)	4/6	log	Y	Common PCA	*Drosophila* CHCs
Hansen et al. (2003a)	24/5	mean	N	V_A and V_D	Blossom morphology
McGuigan et al. (2005)	21/8	log	Y	$\angle$ g-max; $\angle$ p_i	Fish body shape
Chapuis et al. (2008)	12/16	mean	N	Matrix proportionality test	Snail life history
Colautti and Barret (2011)	12/20	var	Y§§	Krzanowski method	Plant life history
Berger et al. (2013)	5/7	mean	Y	$\angle$ g-max	Fly thermal reaction norms
Boell (2013)	24/50†	same	Y	$\angle$ genetic effect vectors	Mouse mandible shape
Bolstad et al. (2014)	6/23	mean/log	Y	V_A and evolutionary rate	Bract morphology
Bolstad et al. (2014)	5/23	mean/log	N	V_A and evolutionary rate	Blossom morphology
Costa e Silva et al. (2020)	4/10	mean	N	$V_A(\boldsymbol{\beta})$ vs. mean V_A	Wood property traits
Royauté et al. (2020)	7/4	none	N	$\angle$ h_i	Cricket behavior
Reanalysis of Lofsvold (1988)	15/59	log	Y	V_A and V_D	Mouse cranial morphology
Population timescale: studies reporting no relationship between G and divergence:					
Lofsvold (1988)	15/59	log	Y	$\angle$ eigenvectors; matrix correlation	Mouse cranial morphology
Venable and Búrquez (1990)	12/6	corr	Y§§	Matrix correlation	Plant morphology /life-history
Badyaev and Hill (2000)	5/7	corr	Y§§	$\angle$ eigenvectors	House finch morphology
Chenoweth and Blows (2008)	8/9	log	Y	Sign of covariances; eigenvectors	*Drosophila* CHCs
Kimmel et al. (2012)	10/22	same	Y	$\angle$ eigenvectors; $V_A(\boldsymbol{\beta})$ vs. mean V_A	Stickleback opercle shape
Species timescale: studies reporting a relationship between G and divergence					
Schluter (1996)	5/26	log	Y	$\angle$ g-max	Bird and mouse morphology
Baker and Wilkinson (2003)	9/15	corr	Y	Matrix correlation	Stalk-eyed fly morphology
Bégin and Roff (2003)	5/3	log	Y	$\angle$ g-max	Cricket morphology
Bégin and Roff (2004)	5/7	log	Y	$\angle$ eigenvectors	Cricket morphology
Marroig and Cheverud (2005)	39/16	same	Y	$\angle$ g-max	Monkey cranial morphology
Hansen and Houle (2008)	8/20	same	Y	$V_A(\boldsymbol{\beta})$ vs. mean V_A	*Drosophila* wing shape
Boell (2013)	24/50†	same	Y	$\angle$ genetic effect vectors	Mouse mandible shape
Innocenti and Chenoweth (2013)	36/7	same	Y	$V_A(\boldsymbol{\beta})$ vs. mean V_A	*Drosophila* gene expression
Porto et al. (2015)	30/6	same	Y	V_A and V_D	Marsupial cranial morphology
Houle et al. (2017)	17/117	same	Y	V_A and evolutionary rate	*Drosophila* wing shape
Lucas et al. (2018)	69/8	corr	Y	PCA similarity index	Butterfly wing pattern
McGlothlin et al. (2018)	8/7	log	Y	V_A and V_D; $\angle$ h_i	*Anolis* lizard skeletal shape
Polly and Mock (2018)	14/13	same	Y	$\angle$ eigenvectors; matrix correlation	Shrew molar shape
Chakrabarty and Schielzeth (2020)	10/3	same	Y	V_A and V_D	Grasshopper morphology
Reanalysis of Lofsvold (1988)	15/3	log	Y	$V_A(\boldsymbol{\beta})$ vs. mean V_A	Mouse cranial morphology

Table 14.1
(continued)

Study	N/tx*	Scale‡	DC§	**G**-divergence comparison method**	Traits
Species timescale: studies reporting no relationship between G and divergence					
Hohenlohe and Arnold (2008)	2/39	same	Y	Matrix size, shape and orientation	Snake vertebral number

Note: The studies are categorized by the timescale of divergence (population or species) and whether they report a relationship between the two levels of variation.

* N = number of traits; tx = number of taxa.

† Total number of taxa (mix of species, subspecies, and populations within subspecies).

‡ Same = measured in same units; log = naturally log transformed; corr = correlation matrices; mean = mean scaling; var = phenotypic variance scaling; mean/log = variances mean scaled, evolutionary rates log transformed; none = no standardization.

§ Dimensional consistency.

§§ The traits have different dimensions, but their correlations are comparable.

** V_A = genetic variance, V_D = among taxa variance, $\angle$ = angle between divergence vector(s) and PCA = Principal Component Analysis, p_i = ith resultant projection of genetic variance closest to the direction of phenotypic divergence, $V_A(\beta)$ = genetic variance along a vector of species divergence, h_i = ith eigenvector from Krzanowski's common subspace analysis of several **G**s.

tend to obscure a potential relationship between evolvability and divergence. One interpretation of the data is that the underlying relationship is so strong that even rather poor estimates are sufficient to detect the signal. If a strong signal between divergence and evolvability is the norm, this can inform us about the likely historical trait dynamics, as different models make different predictions regarding a relationship between divergence and evolvability. Section 14.5 therefore reviews various theoretical models of phenotypic divergence and the relationships between evolvability and divergence that they predict.

14.5 Predicted Relationships between Evolvability and Divergence

In this section, we present a sample of models predicting scaling relationships between evolvability and divergence. Some models of trait evolution predict a relationship, while others do not (Hansen and Martins 1996). The models differ primarily in their assumptions about the adaptive landscape and how it changes over time. Contrasting data with theoretical predictions is a fruitful approach to better understand correlations between evolvability and divergence.

14.5.1 Neutral and Linear Selection

Models of neutral evolution (flat adaptive landscape) or constant or fluctuating linear selection (tilted adaptive surface) predict a positive, linear relationship between evolvability and divergence. Predicted levels of trait divergence, however, are far larger than empirical observations (e.g., Lynch 1990; Estes and Arnold 2007; Houle et al. 2017).

14.5.2 Fixed Optimum

Lande (1976) developed a model with a single optimum, where the variance among taxa is given by a balance between selection and genetic drift. The stationary variance of the trait mean under this model (assuming weak selection) is $\text{Var}(\bar{z}) = 1/(4sN_e)$, where N_e is

the effective population size, and s is the curvature of the quadratic fitness function (i.e., the selection gradient $\beta = -2s(\bar{z} - \theta)$, where θ is the optimum; see also Hansen and Martins 1996). Hence, at equilibrium, this model does not predict any relationship between evolvability and divergence. The initial approach to the optimum generates a positive relationship between evolvability and divergence, but it requires an assumption of short timescale, very weak stabilizing selection, and/or low evolvability.

14.5.3   Moving Optimum (Ignoring Genetic Drift)

Bolstad et al. (2014) analyzed an evolutionary model in which the optimum moved according to an Ornstein-Uhlenbeck (OU) process (figure 14.3). The OU process of the optimum is given by $d\theta = -\alpha(\theta - \bar{\theta})dt + \sigma dB$, where α describes the "pull" of the trait toward the primary optimum $\bar{\theta}$, and σ is a parameter scaling the white noise (dB) process. Under this model, the stationary variance in the species means is given by $\mathrm{Var}(\bar{z}) = 2Ves/(2es + \alpha)$, where $V = \sigma^2/(2\alpha)$ is the stationary variance of the OU-process, and e is the evolvability. If the movement of the optimum is much faster than the response to selection, then the population cannot track the optimum and the variance of the trait mean goes toward 0. If adaptation is much faster than the movement of the optimum, the populations would track it perfectly, and variance of the trait mean would converge on the variance of the optimum V. Between these two extremes, the relationship between evolvability and among population variance is concave (i.e., negative second derivative), and we therefore expect a scaling relationship between evolvability and divergence between 0 and 1. The value of the relationship depends on the value of α relative to the product $2es$. If $\alpha \approx 2es$, populations lag far behind their optimum, and the scaling becomes close to isometry. When α is smaller than $2es$, populations will track the optimum faster, and the scaling coefficient will decrease.

If trait means evolve according to a stationary OU-process, the phylogenetic signal decreases over time. Therefore, if we replace α with $2es$ and use reasonable values of e
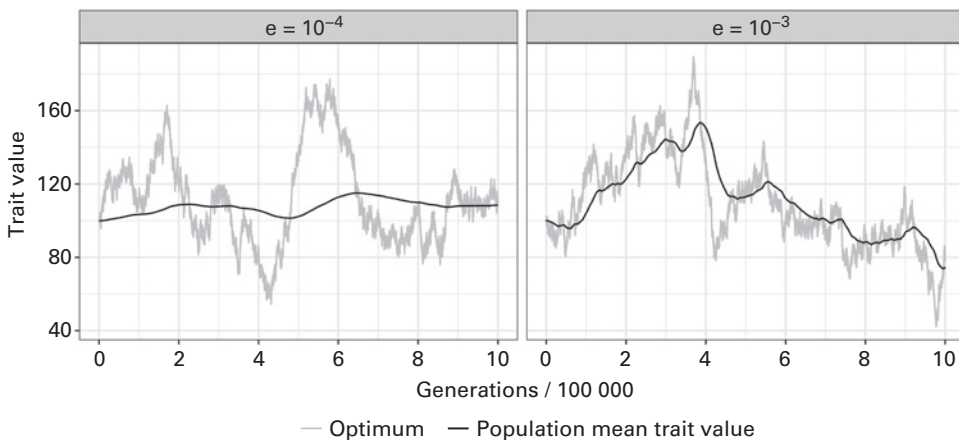
Figure 14.3
Tracking a moving optimum. Shown are the dynamics of two traits differing in evolvability (10^{-4} and 10^{-3}), both tracking a moving optimum following an OU-process with parameters $\alpha = 10^{-5}$, $\bar{\theta} = 100$, and $\sigma = 0.1$, with weak stabilizing selection ($s = 0.01$). The trait with the highest evolvability tracks the optimum much better than the trait with low evolvability. Consequently, the evolvability will be positively related to population divergence in this scenario (given that trait optima move independently among populations).

and s, we can evaluate at what timescales we would expect to observe both a nearly isometric scaling relationship and a phylogenetic signal in the traits. Mean-scaled evolvability is often around 10^{-3} (Hansen et al. 2011), while moderately strong stabilizing selection would be given by $s = 1$. These values give a half-life ($\ln(2)/\alpha$) of about 350 generations, showing that this model is only consistent with observing a phylogenetic signal on very short timescales. For traits varying around a low level of evolvability, say $e = 10^{-4}$, and experiencing very weak stabilizing selection, say $s = 0.01$, the half-life would be about 350,000 generations, which would be consistent with observing a phylogenetic signal on the population timescale but not the species timescale. The latter would require even weaker selection or lower evolvability. This model can explain a relationship between evolvability and divergence but only in a very restricted part of parameter space.

The above OU-model converges on a Brownian motion when $\alpha \rightarrow 0$, and σ is finite. In this situation, the variance in the trait means settles on the same rate of increase as the variance in the optimum, but with a constant lag that is inversely proportional to the evolvability, resulting in a weak relationship between evolvability and divergence.

14.5.4   Natural Selection Shaping within and among Species Variances

A relationship between divergence and evolvability may result from selection shaping evolvability to align with the adaptive landscape (e.g., Pavličev et al. 2011; Jones et al. 2014), which in turn may align with directions of divergence among populations. Following Arnold et al. (2001), this alignment can happen if peak movement follows directions of "selective lines of least resistance." In this model, the adaptive landscape is Gaussian in all trait dimensions, and directions with weaker stabilizing selection (wider bell curves) are assumed to be more prone to peak movement, and hence, divergence. In addition, the strength of stabilizing selection must be negatively related to evolvability, but this is not necessarily the case (Hermisson, et al. 2003; Le Rouzic et al. 2013).

14.5.5   Local Adaptation with Gene Flow

In a system with gene flow between populations, among-population variance in a trait will be determined by the balance between gene flow reducing variation and local adaptation to different optima increasing variation. Because the response to natural selection depends on the evolvability, we would expect traits with high evolvability to reside closer to their optima compared to traits with low evolvability, and therefore a positive relationship between evolvability and among-population variance. In addition, we would expect an increase in the evolvability due to the build-up of linkage disequilibrium (Bulmer 1980; Tufto 2000; Pélabon et al., chapter 13). The increase in evolvability due to linkage disequilibrium would depend on the among-population variance, which would further strengthen the relationship between evolvability and divergence. However, this model cannot explain the observed relationship at the species level.

14.6   Dynamics of the Adaptive Landscape across Time

Understanding the nature of how the adaptive landscape changes across time is key to assessing whether evolvability is likely to constrain adaptation. Evolvability as a constraint should be common if peak movements generally outpace the ability of populations to track

the topological changes; in contrast, it should not be important if landscape changes are slow or rare relative to the evolvability (see section 14.5.3 on moving-optimum models). The observation that populations generally are displaced from their optimum (Estes and Arnold 2007) might indicate that the adaptive landscape is in constant flux (see also Chevin et al. 2015 and Gamelon et al. 2018). Studies of the fossil record on the sub-million-year timescale support this view. Changes in trait means within a limited range, which we term stationary trait dynamics, are a common mode of evolution in lineages on this timescale (e.g., Gingerich 2001; Hunt 2007a; Uyeda et al. 2011; Voje 2016). The magnitudes of trait change during such a stationary phase are frequently too large for a fixed optimum model to explain (e.g., Arnold 2014; Voje et al. 2018).

If the adaptive landscape changes on short timescales, optima must be able to show larger changes on macroevolutionary timescales. Despite many verbal models of macroevolution—for example, adaptive radiation (Schluter 2000), punctuated equilibrium (Eldredge and Gould 1972), and Red Queen (Van Valen 1973)—there are currently few formal models of the dynamics of the adaptive landscape on macroevolutionary timescales. Existing models are phenomenological in the sense that they are derived solely from the fit of stochastic models, such as Brownian motion or Ornstein-Uhlenbeck processes, to empirical data (e.g., Hansen 2012; Uyeda and Harmon 2014). For example, several studies have explored shifts in the adaptive landscape along branches of a phylogeny using Ornstein-Uhlenbeck models (e.g., Mahler et al. 2013). Whether these estimated shifts represent cumulative changes in the position of adaptive peaks across time or they represent sudden large-scale changes in the adaptive landscape is currently hard to disentangle (e.g., Uyeda and Harmon 2014). Unifying analyses of microevolutionary, fossil, and phylogenetic data is one way forward to improve our understanding of adaptive landscape dynamics. For example, analyses of evolutionary sequences describing how single linages evolve on a sub-million-year timescale (e.g., Hunt et al. 2008; Reitan et al. 2012; Voje 2020) could assess whether large-scale shifts in adaptive optima happen more frequently than predicted based on phylogenetic comparative data. Incorporating measurements of evolvability into comparative methods is also likely to better our understanding of the relationship between evolvability and divergence along the timescale continuum (for a statistical framework, see Hansen et al. 2021).

14.7   Conclusion

The predicted effectiveness of adaptation suggested by univariate estimates of evolvability strongly indicates that maladaptation should be a transient phenomenon in natural populations. Still, maladaptation seems to be a common state in nature. The large body of work showing a correlation between phenotypic divergence and evolvability may suggest that genetic constraints are important, but we lack evolutionary models adequately explaining how constraints can be so pervasive. Contrasting data with clear theoretical predictions on the role of evolvability in phenotypic divergence can help answer a range of currently unanswered questions:

• Does the relationship between divergence and evolvability weaken with time?

• What is the relative explanatory power of genetic constraints and selection on observed correlations between divergence and evolvability?

• How much is evolvability reduced when conditioning on traits known to be under stabilizing selection?

• How similar are the inferred dynamics of the adaptive landscape when analyses are based on different types of data spanning different time intervals?

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