

Quantitative Genetics of Evolutionary Divergence and Diversification

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Key Points

- This chapter investigates how the genetic architecture of populations—summarized by the **G-matrix**—shapes long-term patterns of phenotypic **divergence** and **diversification** across evolutionary lineages.
- We explore whether genetic constraints bias the direction of evolution, examining the alignment between microevolutionary variation (within populations) and macroevolutionary divergence (among lineages).
- A key focus is the **paradox of predictability**: despite abundant genetic variation and strong selection, macroevolutionary divergence often aligns with microevolutionary patterns, suggesting complex interactions between genetic architecture and adaptive landscapes.
- Finally, we discuss how changes in genetic architecture, such as the loss of phenotypic integration, may influence diversification patterns, particularly during adaptive radiations and the evolution of key innovations.

Glossary

adaptive landscape G.G. Simpson's phenotypic adaptive landscape, which can be conceptualized as a surface describing the relationship between a population's mean values for a set of continuous traits and relative fitness (cf. Wright's adaptive landscape, in which population fitness is a function of allele frequencies).

additive genetic variation The variance in breeding values (mean genetic values of offspring for a given population) for a quantitative trait in a population. Additive genetic variation is the component of genetic variation that leads to parents-offspring resemblance and is, therefore, most relevant for evolutionary change. See Evolvability.

Brownian Motion A simple continuous-time stochastic model often used to model quantitative trait evolution. The model describes the random movement of trait means through phenotypic space.

constraints hypothesis The hypothesis that patterns of divergence among lineages are constrained by the amount and structure of genetic variation within populations, with divergence being limited by genetic constraints along certain axes of trait space.

correlational selection Selection that favors combinations of traits rather than acting on traits independently.

D-matrix A matrix describing the variance and covariance of among-population or among-species mean trait values.

demographic constraints A demographic constraint is an inability for a population to maintain a viable population size while approaching an adaptive peak, leading to its extinction before the arrival at the optima.

divergence Evolutionary change in phenotypes between lineages.

diversification An increase in the number of evolutionarily distinct lineages.

diversifying selection Natural selection that drives divergence and increases phenotypic variation among populations or lineages.

evolvability A measure of the amount of additive genetic variation in a trait or along an axis of multivariate trait space. Formally, evolvability is the additive genetic coefficient of variation (Houle, 1992).

G-matrix A matrix describing the amount of additive genetic variation and covariation for phenotypic traits in a population.

genetic constraints Insufficient genetic variation in the direction of selection to produce an evolutionary response. An absolute genetic constraint exists if no genetic variation exists along a certain axis of trait space.

key innovations Novel traits that allow or trigger diversification and/or divergence of phenotypes and often accompany adaptive radiations and the colonization of novel niches.

M-matrix A matrix describing the variance and covariance of mutational effects of new mutants affecting a set of phenotypic traits in a population.

paradox of predictability Coined by (Tsuboi et al., 2024), the apparently frequent but difficult to explain pattern in which macroevolutionary divergence closely corresponds with microevolutionary variation, despite no quantitative evidence for genetic constraints.

phenotypic integration A term used to describe the state of having a set of correlated phenotypic traits, generally integrated together as a functional unit. Phenotypic de-integration then represents the loss of genetic correlations that allows traits to evolve independently from one another in the population.

Qst A measure of population differentiation that describes the partitioning of quantitative genetic variation in continuous traits within and among populations.

stabilizing selection Natural selection that favors intermediate values and selects against extreme values.

Wright's F-statistic A measure of population differentiation that describes the partitioning of genetic variation within and among populations.

Abstract

A key question in evolutionary biology is understanding how the genetic properties of populations affect long-term patterns of adaptation, divergence and diversification. Quantitative genetics provides a framework for understanding how genetic variation within populations allows phenotypic divergence via genetic drift and natural selection. This chapter examines whether or not the structure of genetic variation within populations provides meaningful insight into the evolutionary processes and patterns of divergence and diversification across evolutionary lineages.

Introduction

Disentangling the evolutionary processes that shape the divergence and diversification of lineages requires an understanding of the inheritance of quantitative traits. While quantitative genetics provides a powerful and effective framework for studying short-term response to selection and genetic drift (Lande, 1979; Lande and Arnold, 1983), it is less clear how the complex interplay between selection, standing genetic variation, mutation, migration, and demographic stochasticity results in realized patterns of divergence and diversification among lineages over longer evolutionary timescales (Arnold et al., 2001; Tsuboi et al., 2024; Schluter, 2024; Rolland et al., 2023; Melo et al., 2016). This chapter examines to what extent the properties of quantitative genetic variation within populations can inform our understanding of the evolutionary processes influencing lineage divergence and diversification over “macroevolutionary” time. Our goal is not to predict the exact course of evolution in natural populations over such scales, as this is likely infeasible; instead, we seek to understand whether and how the variational properties in evolving populations bias or constrain divergence and diversification.

As described in previous chapters, the structure of genetic variation within populations can be summarized for quantitative traits by the genetic variance-covariance matrix (the G-matrix, Lande, 1979). The G-matrix describes the set of genetic constraints present in a population (Arnold, 1992). The amount of additive genetic variation for a given phenotypic trait determines a population's response to selection (Lande, 1979; Lande and Arnold, 1983) and the rate at which variation among lineages accumulates in response to genetic drift (Lande, 1976, 1979). Furthermore, the genetic covariation between traits resulting from pleiotropy and linkage disequilibrium determines correlated responses to selection that can skew the trajectory away from the direction of selection (Lande, 1979; Schluter, 1996; Hansen and Houle, 2008).

The G-matrix is, therefore, a key parameter for predicting the behavior of specific evolutionary models and, more generally, for understanding whether genetic constraints bias patterns of divergence among lineages. Furthermore, when phenotypic traits are tied to reproductive or ecological isolation, quantitative genetic variation may influence the process of speciation and help explain disparate patterns of diversification across lineages (Lande and Kirkpatrick, 1988; Lande, 1982). Here, we address the effect of quantitative genetic variation on among-lineage evolutionary patterns at three distinct levels: (1) Can the observed divergence patterns among lineages be attributed to a specific evolutionary process (e.g. drift or selection)? (2) Does the structure of genetic variation bias patterns of phenotypic divergence across lineages? (3) Does the amount of genetic variation within or among populations affect speciation and diversification?

Is Divergence Among Populations the Result of Drift or Selection?

The quantitative genetic model of genetic drift provides a neutral model of phenotypic evolution (Lande, 1976; Lynch, 1990; Turelli et al., 1988) in much the same manner as Kimura provided a neutral expectation for molecular evolution (Kimura et al., 1968; Kimura, 1983). Just as Kimura's model allows for tests of selection from gene sequences, the neutral model of quantitative genetics

generates predictions for patterns of divergence expected under genetic drift. Significant deviations from this expected pattern provide a useful tool for detecting adaptive trait differentiation and determining the nature of selection.

A neutral expectation for phenotypic divergence of a single character under genetic drift can be obtained by first assuming constant genetic variation. Each generation drift erodes genetic variation, while mutation (and, potentially, migration) increases genetic variation, resulting in mutation-drift equilibrium (Phillips et al., 2001). Assuming that the effective population size remains constant, genetic drift is expected to shift the phenotypic mean of the population each generation at a rate proportional to the additive genetic variation in the population, and inversely proportional to effective population size (N_e ; Lande, 1976). Under such a model of drift, divergence among lineages is expected to evolve via Brownian Motion and the variance among replicate population's mean phenotypes is expected to increase linearly with time. One can also relax the assumption of constant genetic variation, since the amount of genetic variation itself is expected to depend on N_e . Specifically, Lynch & Hill (1986) showed that at mutation-drift equilibrium, genetic variance is expected to be approximately equal to $2V_mN_e$, where V_m is the mutational variance added each generation. Under these assumptions, effective population size cancels out when predicting divergence among replicate populations, and variance increases at a rate proportional only to the mutational variance.

These models allow rough estimates for the amount of divergence expected under neutrality in typical natural populations. Lynch (1990) and later Estes and Arnold (2007) showed that most macroevolutionary divergence between species occurs at a rate that is substantially slower than expected under genetic drift. Comparing across a wide-range of paleontological divergence estimates, Lynch (1990) found that only hominid divergence in cranial capacity fell within the range predicted by genetic drift. Of course, this does not indicate that hominid cranial capacity is a neutrally evolving trait, but rather, shows that most macroevolutionary divergence is considerably slower than predictions from genetic drift, indicating that stabilizing selection is prevalent in nature (but see Hansen and Houle (2004); Schroeder et al. (2014); Schroeder and von Cramon-Taubadel (2017); Machado et al. (2022, 2023)). This observation is consistent with the paleontological observation of stasis (Eldredge and Gould, 1972; Gingerich, 1983; Estes and Arnold, 2007; Uyeda et al., 2011), or little to no accumulation of evolutionary change over long timescales (whereas genetic drift predicts steady increase in divergence over time). Similarly, neutral expectations for patterns of divergence for multiple, covarying traits can be modeled under drift as a multivariate Brownian Motion process. Estimates of the G-matrix and effective population sizes can be used to generate predictions for the amount of divergence among lineages (Felsenstein, 1988; Zeng, 1988). This provides a null expectation for the amount of divergence consistent with genetic drift (Rogers Ackermann and Cheverud, 2002; Marroig and Cheverud, 2004). In addition to predicting the amount of expected divergence among populations, it is also possible to test whether correlations among lineages' multivariate trait values reflect within-population genetic covariance between traits (Rogers Ackermann and Cheverud, 2002; McGuigan et al., 2005; Tsuboi et al., 2024). Frequently, it is difficult to obtain reliable estimates of relevant parameters (e.g., effective population size, time since divergence) to make specific predictions about the amount of divergence under drift. Furthermore, the assumptions necessary to make direct predictions are frequently violated in natural populations (e.g., no migration). Studies below the species level in natural populations commonly encounter complex population histories of gene flow, population fission and fusion. These processes greatly complicate direct prediction of expectations under genetic drift using quantitative genetic models. An alternative approach is to compare the amount of phenotypic divergence to divergence at putatively neutrally evolving genetic loci (Wright, 1951; Lande, 1992; Spitze, 1993). This approach compares Wright's F-statistic (Wright's F-statistic) for a neutral genetic locus with an analogous quantity for a quantitative trait (Q_{st}). Both quantities describe how variation is partitioned within and among populations. A value of 0 is indicative of no divergence among populations in allele frequencies, while the theoretical maximum value of 1 would indicate that all variation is partitioned between populations (with no variation shared between populations). Under the neutral model, Q_{st} is expected to behave as a single neutrally evolving molecular locus (Whitlock, 2008). Assessing significance of a given value of Q_{st} can be obtained by comparing its value to the distribution of F_{st} for neutrally evolving loci (Whitlock, 2008; Whitlock and Guillaume, 2009). A Q_{st} significantly higher than F_{st} would indicate a phenotypic trait is under diversifying selection, while a Q_{st} significantly lower than F_{st} would indicate stabilizing selection. Multivariate extensions of Q_{st} - F_{st} tests allow exploration of the relationship between orientation and direction of divergence in quantitative traits within and among-populations (Kremer et al., 1997; Chenoweth and Blows, 2008). Empirical studies reveal that at the relatively short time scales of population differentiation, it is quite common for phenotypic traits to exhibit diversifying selection (Merilä and Crnokrak, 2001; Leinonen et al., 2013). Given that the traits under study are often assumed to be ecologically relevant, it is perhaps unsurprising that these traits evolve and adapt to local conditions faster than neutral expectation. However, note that this is in contrast to macroevolutionary comparisons of trait divergence relative to neutrality that were discussed above, which typically show rates of phenotypic divergence slower than predicted under drift. This disparity likely reflects a difference in timescales. By analyzing a large database of divergence estimates collected from generational to macroevolutionary timescales, Estes and Arnold (2007) showed that empirical estimates of phenotypic divergence in body-size related traits across a large range of taxa are generally larger than neutral expectation at microevolutionary and population divergence timescales. However, at longer timescales, divergence lags behind neutral expectation. These differences underscore that traits such as body size are not likely to evolve neutrally for very long, but rather, have long-term dynamics driven by the evolution of adaptive landscape (Hansen, 2012). Furthermore, predictable patterns of timescaling in rates across both genes and traits, whether due to estimation artifacts or real biological processes, can make the outcomes of such comparisons potentially inevitable given specific timescales (Harmon et al., 2021).

One potential work around this problem was shown by Latrille et al. (2024), who first developed an index of neutrality for macroevolutionary data, which is analogous to the F_{st} - Q_{st} test. Specifically, they scale the additive genetic variance of a trait by the amount of variation in neutral loci, and likewise scale the rate of trait evolution among species by the rate of divergence in those

same neutral loci. Under some assumptions, like similar mutation rates between neutral and non-neutral loci, they find that those two scaled metrics should be equal, devising a test analogous to the McDonald–Kreitman test for identifying selection on genetic data [McDonald and Kreitman \(1991\)](#). By applying their method on body size in both Primates alone and mammals as a whole, they were able to retrieve a signal of diversifying selection in macroevolutionary data. The generality of these findings is still an open question ([Machado et al., 2022](#); [Schroeder and von Cramon-Taubadel, 2017](#)).

Does Genetic Architecture Bias the Direction of Evolution (Or Vice Versa)?

Under most circumstances, complex phenotypic traits closely tied to organismal fitness are not expected to be selectively neutral. A more interesting question is whether within-population genetic variances and covariances bias the pattern of phenotypic divergence among lineages. This so-called “constraints hypothesis” posits that the pattern of divergence among lineages will reflect the evolutionary constraints present within populations ([Schluter, 1996](#)).

[Schluter \(1996\)](#) conjectured that divergence among lineages proceeds, at least temporarily, along “lines of least resistance” in phenotypic space. In particular, he posited that the “genetic line of least resistance”—or the combination of traits with the most available genetic variation in a population—would bias divergence to occur primarily in this direction. Mathematically, this axis is described by the leading eigenvector of the G-matrix, or g_{max} . The hypothesis may be viewed from two sides. First, it may be viewed as a hypothesis about genetic constraints, in which divergence is limited due to low levels of genetic variation, particularly along multivariate axes of trait variation ([Fig. 1A–B](#), [Arnold, 1992](#); [Blows and Hoffmann, 2005](#); [Walsh and Blows, 2009](#)). On the other side of the coin, one may view genetic covariance among traits as not limiting divergence, but rather by positively channeling divergence along lines of least resistance in the adaptive landscape ([Fig. 1C](#), [Lande, 1979](#); [Gould, 1989](#); [Brakefield, 2006](#); [Eroukhmanoff, 2009](#); [Agrawal and Stinchcombe, 2009](#)). Patterns of divergence among lineages can be described in a manner analogous to within-population divergence, via the divergence matrix (D-matrix, a variance-covariance matrix of changes among lineage-specific phenotypic means, [Lande, 1979](#); [Blows and Higgie, 2003](#)). Schluter’s model predicts that the D-matrix and the G-matrix will be proportional, providing a test for whether the genetic architecture of populations affects the structure of phenotypic diversification. Indeed, under both drift and selection, genetic covariance will bias divergence of covarying traits ([Fig. 1A–D](#)). Empirical tests of the constraints hypothesis commonly find a relationship between multivariate axes of high genetic variance and divergence ([Schluter, 1996](#); [Mitchell-Olds, 1996](#); [Chenoweth et al., 2010](#); [Hohenlohe and Arnold, 2008](#); [Rogers Ackermann and Cheverud, 2002](#); [Blows and Higgie, 2003](#); [Bégin and Roff, 2004](#); [Marroig and Cheverud, 2004](#); [McGuigan et al., 2005](#); [Bolstad et al., 2014](#); [Haber, 2016](#); [Houle et al., 2017](#); [McGlothlin et al., 2018](#); [Machado, 2020](#); [Rohner and Berger, 2023](#); [Machado et al., 2023](#); [Opedal et al., 2023](#); [Holstad et al., 2024](#)). Even more compelling, [Houle et al. \(2017\)](#) demonstrated not only a strong alignment between g_{max} and d_{max} in *Drosophila* wing shape, but also in the leading eigenvector of the M-matrix—the mutational variance-covariance matrix. This matrix describes the mutational phenotypic effects of new mutations in a population and was estimated from inbred lines, meaning that few studies will be capable of estimating it. Further studies on fly wings ([Rohner and Berger, 2023, 2025](#)) have suggested that developmental variation, as measured by fluctuating asymmetry, also aligns with D, G and M-matrices. This suggests that development might play a significant role in either structuring this alignment between genetic variation and evolutionary divergence or itself might be affected by it through the action of natural selection ([Riedl, 1978](#); [Cheverud, 1984](#); [Melo and Marroig, 2015](#); [Mongle et al., 2022](#); [Machado et al., 2023](#)).

Despite strong evidence for the alignment of genetic variation and divergence, some have argued that this is not enough to favor the constraint hypothesis [Houle et al. \(2017\)](#). This is because biases induced by trait covariance are expected to be temporary so long as the constraints are not “absolute constraints” (all eigenvalues of the G-matrix are non-zero) and populations are given sufficient time to reach an adaptive peak [Schluter \(1996\)](#). In fact, many studies find abundant genetic variation along all axes of variation ([Mezey and Houle, 2005](#); [Walsh and Blows, 2009](#); [Houle et al., 2017](#)), and others have reported strong directional selection is also frequently observed ([Hereford et al., 2004](#); [Siepielski et al., 2009](#); [Kingsolver and Diamond, 2011](#)). In combination, these two patterns predict rapid adaptation to adaptive peaks (relative to macroevolutionary time) and would seem to suggest limited potential for genetic constraints to shape divergence ([Hansen and Houle, 2004](#); [Houle et al., 2017](#)). This contrast has led [Tsuboi et al. \(2024\)](#) to coin the “paradox of predictability” for the frequent observation of correspondences between microevolutionary variation and macroevolutionary divergence, despite the apparent lack of true genetic constraints. A corollary of this paradox is that G-matrices and their constraints are relatively stable over macroevolutionary times, even while there are theoretical and empirical reasons to expect Gs to evolve. While there are theoretical and empirical reasons to expect Gs to evolve ([Turelli et al., 1988](#); [Roff, 2000](#); [Steppan et al., 2002](#); [Berger et al., 2013](#)). Despite this, empirical investigations have suggested that Gs might be relatively stable over the macroevolutionary timescales of interest ([Bégin and Roff, 2004](#), [Marroig and Cheverud, 2001](#) but also see [Hubbe et al., 2016](#), [Machado et al., 2018](#), [Rossoni et al., 2019](#) for some exceptions). This stability thus allows for the existence of a causal connection between micro and macroevolution through the action of genetic constraints.

The dual observation of abundant genetic variation, or evolvability, in most measured directions and the existence of strong directional selection is not a death blow to the constraints hypothesis. Multivariate genetic constraints with unmeasured traits experiencing stabilizing selection may limit adaptation while simultaneously allowing limited but rapid short-term evolutionary responses ([Walsh and Blows, 2009](#); [Hansen, 2012](#); [Bolstad et al., 2014](#); [Jiang and Zhang, 2020](#)). This latter pattern is widely observed for phenotypic divergence across timescales, which find that although divergence is often quite rapid in the short-term, it is bounded and does not accumulate until much longer, million-year timescales ([Uyeda et al., 2011](#)). Such a pattern may arise by considering the concept of “conditional evolvability” ([Hansen and Houle, 2008](#)), which is defined as the amount of available

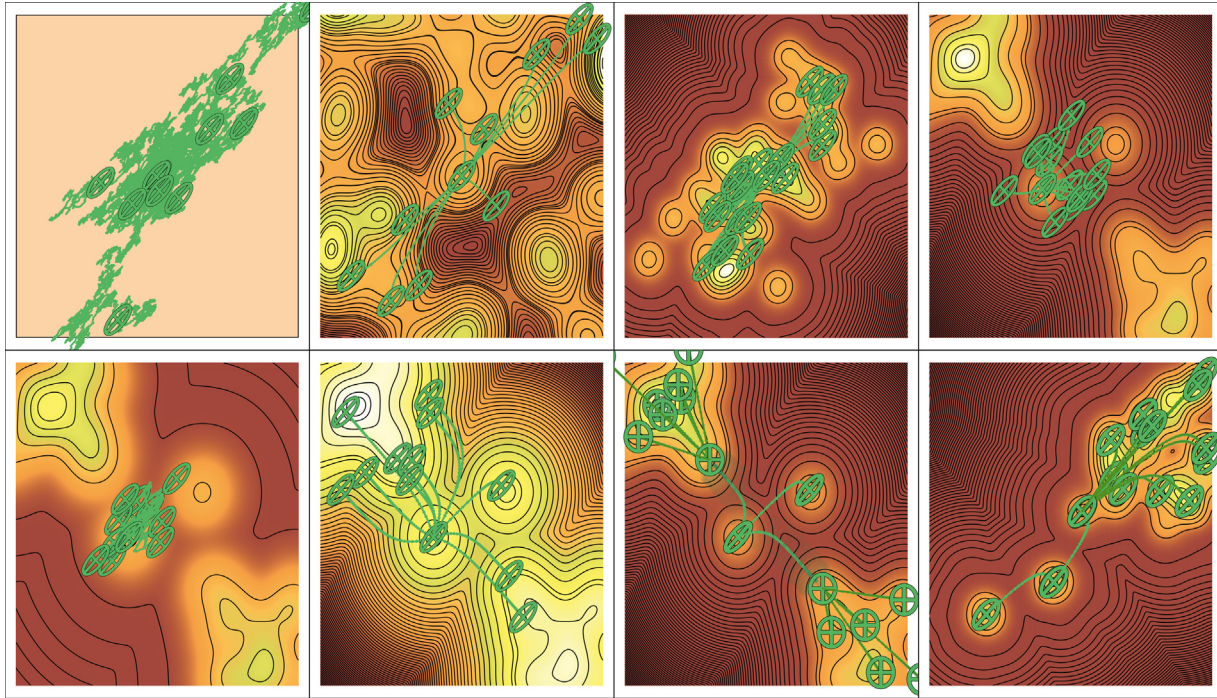


Fig. 1 Conceptual figure illustrating potential relationships between the adaptive landscape and the G-matrix. The G-matrix is indicated by the ellipses, which represent the 95% confidence interval for the bivariate distribution of genetic values in the population. X and Y-axes indicate mean values for two phenotypic traits, while the contour lines and colors indicate mean fitness of the population. Note that we cannot depict spatially or temporally varying adaptive landscapes in only two dimensions. Hence, we show the location of adaptive peaks from several different regions accessible to the source population on a single plot. However, in a given population we assume only a single adaptive peak. Trajectories therefore illustrate paths between the ancestral adaptive peak (center) and novel adaptive peaks in surrounding regions. (A) Genetic drift- A flat adaptive landscape allows diverging species to freely explore phenotypic space. Divergence is biased along genetic lines of least resistance. (B) Randomly-oriented adaptive peaks- In this scenario no region of the adaptive landscape is favored over any other. However, peaks along g_{max} are reached more quickly, leading to greater divergence along this axis. Nevertheless, given sufficient time for selection, all populations will reach their optimum. Thus, the correspondence between g_{max} and d_{max} will erode over time. However, if demographic constraints prevent species of reaching distant peaks along constrained axes of variation, a correspondence between g_{max} and d_{max} may remain. (C) Positive constraints- This scenario depicts so-called “positive constraints”, where the correlation between traits channels variation in directions likely to be adaptive in novel habitats. (D) Negative constraints- This scenario depicts an ill-formed G-matrix. High fitness “adaptive ranges” are located nearby, but approach to these peaks is slow, and combined with demographic constraints, prevents populations from colonizing these areas of phenotypic space. Scenarios E-H depict different types of ecological release and key innovations leading to an increase in phenotypic divergence. (E) Decrease in stabilizing selection- In accordance with the hypothesis of Yoder et al. (2010), stabilizing selection can decrease the valleys between adaptive peaks and thus allow lineages to traverse to novel adaptive peaks. However, this occurs at a slower rate due to weaker selection favoring novel peaks. This scenario resembles genetic drift. (F) Increase in absolute fitness- Demographic constraints may prevent species from reaching distant peaks. Therefore, an increase in absolute fitness in accordance with ecological release can allow lineages to traverse fitness valleys to new adaptive peaks without risking extinction. In this scenario, relative fitness remains the same, and thus divergence proceeds at the same rate as in (D), but with less extinction of evolving populations. (G) Loss of phenotypic integration- Key innovations are thought to allow the rapid differentiation of species into novel regions of phenotypic space. Here a loss of phenotypic integration allows lineages to more rapidly colonize novel adaptive peaks which were always present and accessible, but could not be reached due to genetic constraints. (H) Novel area of phenotypic space- This type of key innovation can result simply from a shift in the mean that allows access to novel habitats with an abundance of adaptive peaks. This is typical when, for example, a species invades a novel niche or is introduced to a novel bioregion.

genetic variation along the vector of selection that is uncorrelated to variation along perpendicular axes (i.e., the amount of evolutionary change possible in a given direction without change in other traits). Because only a small subset of traits are typically measured, this may mean that conditional evolvabilities are considerably lower than evolvabilities measured in natural populations (Bolstad et al., 2014) and some statistical biases may be prone to overestimating evolvability of specific genetic architectures (Jiang and Zhang, 2020). Furthermore, genetic constraints need not be absolute if populations are constrained by finite population sizes. If populations are maladapted and off their fitness optima, they may incur demographic costs and decrease in population size. Even temporary lags resulting from insufficient genetic variation could impose “demographic constraints” on adaptation, preventing colonization of peaks along axes of low evolvability despite the absence of absolute genetic constraints (Gomulkiewicz and Houle, 2009).

As an alternative to constraints hypotheses, selective explanations of these patterns suggest that among-lineage patterns of divergence may be driven primarily by the dynamics of adaptive peaks over time, with most populations residing close to their adaptive

optima. If we accept this view, the primary determinant of evolutionary divergence among lineages is the long-term dynamics of adaptive peaks themselves with the specifics of genetic architecture playing little role in the pattern of divergence (Simpson, 1944; Arnold et al., 2001; Hansen, 2012; Uyeda et al., 2011). Alternatively, the trajectory of evolution may still be biased by the G-matrix if the landscape has multiple peaks, and local peaks in certain directions of phenotypic space are favored over others, leading to biased exploration of the adaptive landscape (Hine and Blows, 2006; McGuigan and Blows, 2007; Schluter, 2024; Melo et al., 2016; Holstad et al., 2024). Different views on this process differ in whether macroevolutionary alignment with G-matrices is primarily due to correlational selection (Melo et al., 2016; Schluter, 2024), or biases induced by fluctuating selection with strongly biased G-matrices (Holstad et al., 2024). One tempting unifying hypothesis for the alignment of M, G, and D-matrices is that it M and G-matrices are themselves shaped by selection and the shape of the macroevolutionary adaptive landscape. Thus, rather than genetic architecture biasing divergence, divergence along adaptive ridges in phenotypic space may shape genetic architecture to orient g_{max} along so-called “selective lines of least resistance” (Arnold et al., 2008). Indeed, simulation studies have shown that the G-matrix evolves as a balance between the shape and orientation of the adaptive landscape—which may be skewed by correlational selection—and the shape and orientation of the mutation matrix (M-matrix), which describes the phenotypic effects of new mutations that enter into the population (Jones et al., 2003, 2007, 2012). Directional selection and migration between populations can likewise orient the G-matrix along the axis of divergence between populations by introducing alleles with correlated effects on phenotypic traits—albeit weakly and with transient effects (Guillaume and Whitlock, 2007). Finally, simulation studies suggest that the M-matrix itself can evolve, especially in the presence of epistatic interactions between genes, to conform to the shape of the adaptive landscape, resulting in triple alignment between the M-matrix, G-matrix and the axis of divergence among populations (Jones et al. 2007, 2014; Hether and Hohenlohe, 2014). Studies of how developmental architecture shapes both genetic and environmental variation suggest possible mechanistic pathways for this alignment (Rohner and Berger, 2023; Machado et al., 2023; Alba et al., 2021), and also suggest that underlying developmental architectures are far more constrained than what simple measures of genetic variance would suggest. Better connecting developmental biology to measures of variation and reconstructing the origins of developmental architectures would do much to reveal the plausibility of these alternative mechanisms. These alternative explanations and their underlying processes are not necessarily mutually exclusive and may be reinforced in natural populations. While this general condition of alignment seems likely under many circumstances, instances of misalignment between the G-matrix and the D-matrix certainly do occur. Furthermore, it seems likely that genetic constraints are underestimated in natural populations. Nonetheless, understanding to what extent the genetic architecture drives patterns of divergence remains an outstanding question in scaling between microevolutionary processes and macroevolutionary patterns (Tsuboi et al., 2024; Schluter, 2024; Rolland et al., 2023).

Does Genetic Architecture Affect Rates of Diversification?

Until now, we have focused on phenotypic divergence and ignored speciation and diversification. Yet, a vast disparity exists between rates of diversification among clades. Furthermore, radiations can both encompass dramatic diversifications in phenotype, as well as “cryptic radiations” in which species diversify without phenotypic change. To what extent does the structure of quantitative genetic variation within a species affect these patterns of diversity and phenotypic divergence? Under some evolutionary processes, the structure and amount of genetic variation can play a key role in driving phenotypic divergence in traits important for reproductive isolation. For example, quantitative genetic models of sexual selection predict that amounts of genetic variation for sexual preference and ornament traits under a variety of circumstances can affect the rate of evolution of reproductive isolation (Lande, 1981; Mead and Arnold, 2004; Gavrillets, 2000; Gavrillets and Hayashi, 2005; Uyeda et al., 2009). Similar arguments can be made for other types of coevolution, so long as a mechanistic link exists between phenotypic divergence and the evolution of reproductive isolation (Felsenstein, 1981; Kiestler et al., 1984, but see Yoder and Nuismer, 2010). Adaptive radiations characterized by large amounts of phenotypic divergence and lineage diversification have long captured the attention of evolutionary biologists. This correspondence between lineage diversification and phenotypic divergence in these clades suggests a potential role for changes in genetic architecture, or of the adaptive landscape, in driving these patterns. Yoder et al. (2010) argue that ecological opportunity drives these patterns and can be conceptualized as a weakening of the strength of stabilizing selection, allowing populations to traverse fitness valleys more easily (Fig. 1E). However, such a model is somewhat inconsistent with the seemingly rapid pace of adaptation in many adaptive radiations, as weakened stabilizing selection results in pattern akin to expectations under genetic drift rather than the rapid, niche-based divergence of lineages typically envisaged in such radiations (Fig. 1A). Alternatively, “ecological release” of populations can be defined as an overall increase in the absolute fitness of populations, resulting in relaxation of demographic constraints while still maintaining stark differences in relative fitness among peaks and strong selection (cf. Wellborn and Langerhans, 2014, Fig. 1F). Adaptive radiations are sometimes attributed to “key innovations” that allow colonization of previously unattainable niches. Two types of key innovations are possible: (1) an innovation resulting from novel phenotypic values (Figure 1H) and (2) a change in the genetic architecture that removes genetic constraints (i.e., a loss of phenotypic integration, Fig. 1G). This latter type of innovation is of primary interest to the subject of this chapter, as it would indicate that the potential for adaptive radiation may be predicted from genetic architecture of trait variation. A change in the effective dimensionality of trait covariance can affect the overall rate of phenotypic divergence along novel axes of phenotypic space (Nosil and Sandoval, 2008). If these traits are related to mechanisms of speciation and diversification, adaptive radiation may result. This is because higher-dimensionality in trait variation results in more axes along which divergence can occur, and sexual isolation can result if the trait is tied to reproductive isolation (Hohenlohe and

Arnold, 2010; Kemp, 2007; Wainwright, 2007; Doebeli and Ispolatov, 2010; Young et al., 2010). For example, Maia et al. (2013) showed key innovations in pigmentation cells resulted in an increase in the dimensionality of color phenotypes, which are simultaneously correlated with both increased rates of phenotypic evolution and diversification. Non-sexually selected key innovations with de-integrated phenotypes have been found with more equivocal effects on diversification (Alfaro et al., 2009; Fr  d  rich et al., 2014). Instead, a common pattern is for the increase in diversification to lag behind the evolution of the key innovation or require a sequence of innovations or secondary shifts in environmental context (Alfaro et al., 2009; Near et al., 2012; Sanderson and Donoghue, 1996; Kemp, 2007). These patterns suggest that diversification rate shifts likely results from a shift into novel regions of the adaptive landscape itself (Fig. 1G), rather than changes in genetic architecture directly influencing diversification rates (Fig. 1H, Wainwright, 2007).

Conclusion

Bridging the divide between micro and macroevolution requires understanding the degree to which the structure of genetic variation influences macroevolutionary patterns of divergence and diversification among lineages. Quantitative genetics provides a means to generate quantitative and empirically testable predictions that help disentangle the evolutionary processes of drift and selection in explaining divergence. Furthermore, the evolutionary constraints hypothesis posits that among-lineage patterns of divergence are constrained by patterns of genetic variation within lineages. In general, an emerging picture is one in which divergence among lineages generally correlates with within-lineage patterns of trait variation. Naive extrapolation of measured levels of genetic variation, however, appears inconsistent with absolute constraints on divergence. Nevertheless, genetic constraints may still play a role and empirical estimates of evolvability may be affected by unobserved trait correlations limiting divergence in certain directions. Additional empirical research is also necessary on the evolution of genetic architecture itself in a comparative framework to establish the degree to which divergence G-matrix itself evolves among lineages and in response to patterns of selection (Steppan et al., 2002). While the degree of integration among phenotypes has long been suggested to impact rates of species diversification, relatively few macroevolutionary tests of the effect of phenotypic integration on rates of diversification have been conducted. Increased dimensionality and evolvability for some phenotypic traits may increase diversification rates. However, as with phenotypic diversification, the relationship may be more complex than naive extrapolation would indicate. Rather, the specific means by which patterns and processes can be reconciled across scales and macroevolutionary time require significant further exploration. In general, connecting “microevolution”—the variational properties of populations—and “macroevolution”—the divergence and diversification of lineages—remains a challenging but fertile research avenue with many enigmatic challenges (Tsuboi et al., 2024; Schluter, 2024; Melo et al., 2016). The strong predictive power of quantitative genetic models combined with the increasing availability of parameter estimates obtained from empirical studies provides a powerful framework for pursuing these important goals.

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