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Overview Article

Evolvability: progress and key questions

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Abstract

Since the 1990s, evolutionary biologists have recognized the importance of explaining the ability of biological systems to evolve and how this ability itself evolves. This recognition of the need to explain evolvability emerged from an awareness that the kind and the amount of heritable variation available for natural selection require explanation. The concept of evolvability is now the focus of many research programs in diverse subdisciplines within evolutionary biology. In the present article, we first review and synthesise progress made in evolvability research. We then present key questions to set an agenda for future research on evolvability, identify challenges to answer these questions, and discuss opportunities to apply results from the evolvability research to conservation biology.

Keywords: evolvability, evolutionary quantitative genetics, evo-devo, paleobiology, evolutionary systems biology

Rates of evolution are highly variable within and among traits, populations, and species and at both micro- and macroevolutionary timescales (Simpson 1953, Uyeda et al. 2011). We also often observe large differences in species diversity and morphological divergence among related lineages (figure 1). For example, in angiosperms, clades displaying bilateral symmetric (zygomorphic) flowers combined with other traits that increase precise pollination, include more species than their sister clades displaying the alternative character states including radially symmetric (actinomorphic) flowers (O'Meara et al. 2016). This may be explained by differences in selective histories, as would be expected if bilateral symmetry increases the precision of pollination by directing pollinator movement and increases the likelihood of visitation by specialist pollinators, both of which would increase the speciation rate (Armbruster 2014). However, these differences in diversity among clades may also reflect differences in evolvability—that is, differences in the ability to produce and maintain variation on which natural selection acts (Wagner and Altenberg 1996). This suggestion was already made by Simpson (1953) but only in the last 30 years has interest in the concept of evolvability become widespread.

The origins of phenotypic variation and how differences in the amount and type of variation affect the potential for evolution have interested biologists since Darwin (Crother and Murray 2019, Distin 2023). This interest has shaped research in the study of evolutionary morphology, paleobiology, and macroevolution (e.g., Simpson 1953, Olson and Miller 1954, Vermeij 1973), but this work was often overlooked in other areas of evolutionary biology. In the 1990s, however, several research programs emerged that seek to explain differences in rates of evolution, divergence, and evolutionary innovation not only through variation in natural selection but also through the production and maintenance of heritable variation (Brigandt 2015, Nuño de la Rosa 2023). Evolvability rapidly became the focus of research in diverse disciplines such as evolutionary developmental biology (evo-devo; e.g., Alberch 1991, Raff 1996, Wagner and Altenberg 1996,

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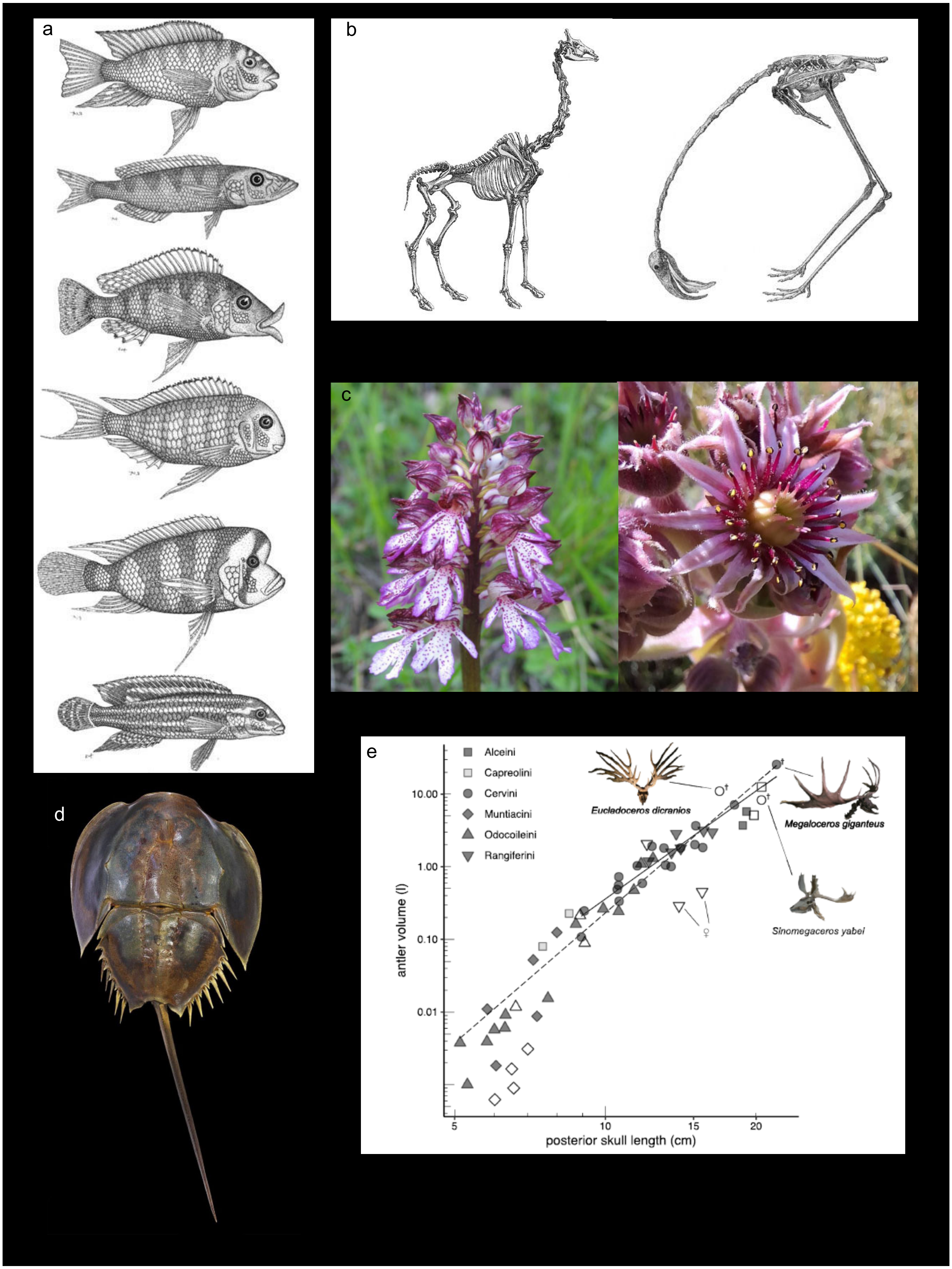
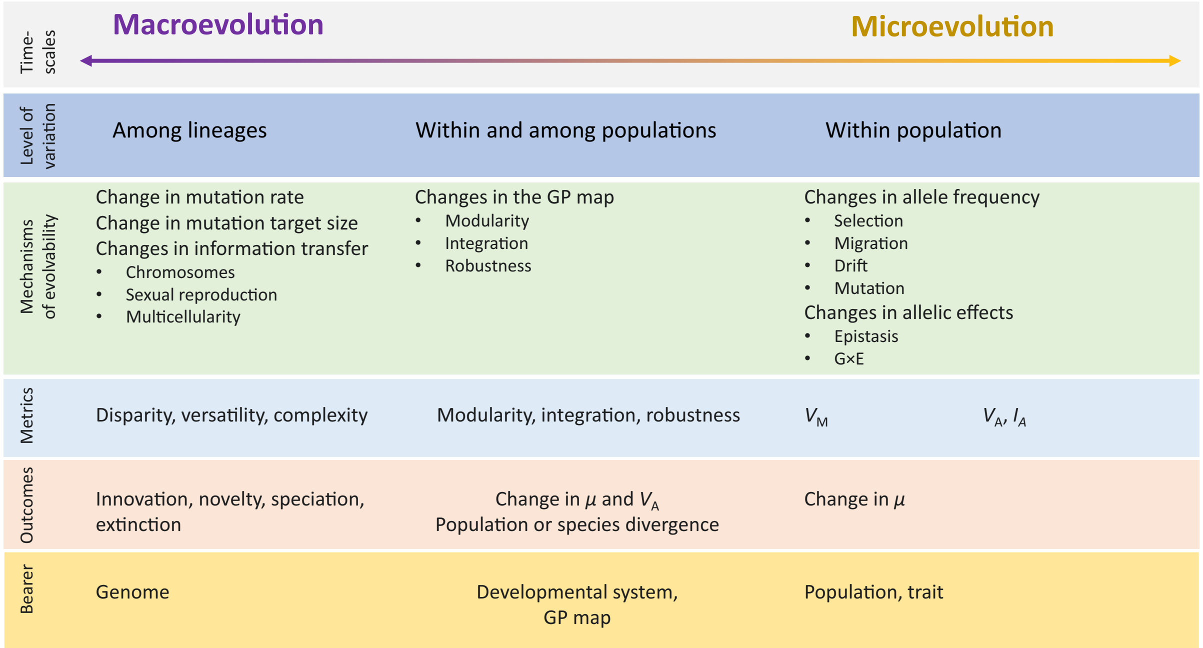


Figure 1. Example of evolutionary questions involving evolvability. (a) Species of cichlids in lake Tanganyika differ extensively in their craniofacial morphology and in their feeding regimes. Galis and Drucker (1996) suggested that the evolution of such diversity was made possible by developmental changes that allowed independent movements of the upper and lower pharyngeal jaws, thereby increasing the evolvability of the feeding apparatus.

Figure 1. *(Continued)* (b) Although almost all mammalian species have only seven cervical vertebrae whatever the length of their neck, bird species differ extensively in the number of cervical vertebrae; this allows the evolution of long and flexible neck, as in flamingoes. Why is the number of cervical vertebrae not evolvable in mammals? Galis (2023) suggested that the constraint in mammals results from the deleterious pleiotropic effects associated with changes in the induction of cervical vertebrae. (c) O'Meara and colleagues (2016) showed that clades with bilateral flowers (e.g., ***Orchis purpurea***, Orchidaceae, left) contain many more species than clades with radial flowers (e.g., ***Sempervivum montanum***, Crassulaceae, right). Whether this results from differences in the selection pressures generated by specialist or from generalist pollinators or from differences in evolvability remains unresolved (Woźniak and Sicard 2018). (d) The morphology of the horseshoe crabs (Xiphosurida) has changed little since the Jurassic. Whether this lack of evolution can be explained by natural selection or by low evolvability is unresolved (Bicknell et al. 2022). (e) The allometric relationship between antler size and body size in cervids, with the iconic ***Megaloceros***, is a key example of evolutionary constraints where body size and antler size are supposedly forced to evolve along a trajectory imposed by the development (Gould 1974, Tsuboi et al. 2024). However, the low evolvability in static allometric slopes but the high evolvability in static allometric intercepts (Bolstad et al. 2015) suggest that allometric constraints alone cannot fully explain the origin of evolutionary allometry observed in deer antlers and in many other systems. Sources: (a) from Albertson and Kocher 2006; (b) from Galis 2023 (http://creativecommons.org/licenses/by/4.0), left reproduced from Owen (1866), and right reproduced from Evans (1900). Photographs: (c) Christophe Pélabon, (d) Didier Descouens, (e) Tsuboi et al. 2024 (http://creativecommons.org/licenses/by/4.0)



Time-scales	Macroevolution		Microevolution
Level of variation	Among lineages	Within and among populations	Within population
Mechanisms of evolvability	Change in mutation rate Change in mutation target size Changes in information transfer • Chromosomes • Sexual reproduction • Multicellularity	Changes in the GP map • Modularity • Integration • Robustness	Changes in allele frequency • Selection • Migration • Drift • Mutation Changes in allelic effects • Epistasis • G×E
Metrics	Disparity, versatility, complexity	Modularity, integration, robustness	V_M V_A, I_A
Outcomes	Innovation, novelty, speciation, extinction	Change in μ and V_A Population or species divergence	Change in μ
Bearer	Genome	Developmental system, GP map	Population, trait

Figure 2. Evolvability at different biological and temporal scales. Top row: levels at which variation in evolvability can be studied. Second row: mechanisms affecting evolvability. Third row: evolvability measures or proxies for it at different organismal levels and timescales ($\mathbf{V_A}$, additive genetic variance; $\mathbf{I_A}$, mean-scaled evolvability; $\mathbf{V_M}$, mutational variance). Fourth row: evolutionary events expected to be affected by evolvability, and therefore how variation in evolvability is expressed ($\boldsymbol{\mu}$, population mean). Last row: typical bearers of evolvability.

Gerhart and Kirschner 1997), evolutionary systems biology (Kauffman 1993, Wagner 1996), and evolutionary quantitative genetics (Houle 1992, Hansen et al. 2003).

Defined as the ability of organisms to produce and maintain heritable variation, evolvability depends on the ability of developmental systems, in interaction with the environment, to convert differences in DNA sequences into phenotypic variation. Over a few generations (i.e., at microevolutionary timescales), evolvability mostly depends on population-level additive genetic variance V_A (figure 2; Houle 1992), which is the component of phenotypic variance due to additive effects of alleles (i.e., directly heritable and independent of context). Over tens to hundreds of generations, V_A and, therefore, evolvability is affected by the combined effects of mutation, natural selection, migration, and genetic drift (Bürger 1999, Pélabon et al. 2023). Over longer time periods (i.e., at macroevolutionary timescales), ongoing evolution of developmental processes that map DNA sequence variation onto phenotypic variation affects the production of V_A and therefore affects the evolvability of genomes and lineages (Wagner 2014). The resulting differences in evolvability among lineages affect their ability to adapt and diverge. For example, the greater variation of the feeding apparatus of fish species in the family Cichlidae (figure 1) than in the Centrarchidae may have been spurred by developmental changes that allowed independent movements of the upper and lower pharyngeal jaws (Galis and Drucker 1996). Over even longer time periods, changes in evolvability may result from the evolution of mutational processes and of new forms of variation. For example, the evolution of sexual reproduction and multicellularity has facilitated new modes of individual organization and information transfer that led to new sources of variation such as recombination and new patterns of variation allowed by cell differentiation and modularity (Maynard Smith and Szathmary 1995, Gerhart and Kirschner 1997).

These different perspectives illustrate the plurality of the evolvability concept and the need for integrated studies across all biological levels and timescales to generate overarching understanding of the causes and constraints on the potential for evolutionary change (figure 2). In the present article, we further demonstrate this plurality and the need for a multidisciplinary approach of the concept by reviewing progress in evolvability research since the 1990s. We then outline a series of twelve key remaining questions concerning evolvability to provide an agenda for future research.

Progress in evolvability research

Conceptualization of evolvability: Evolvability describes the potential of biological entities to evolve, and it should be understood as an intrinsic capacity or dispositional property (Wagner and Altenberg 1996, Brigandt et al. 2023). Accordingly, over long time periods evolvability depends on variability, meaning the variation that can potentially be generated by developmental systems, irrespective of the current observed variation. This distinction has contributed to focusing attention on the processes that generate and maintain heritable variation and their evolution. It has also enabled the recognition that these processes influence evolutionary possibilities in a generative manner (i.e., by generating viable phenotypes), overcoming the limiting notion of constraint by rendering the processes compatible with evolutionary explanations involving selection (Brigandt 2015). Recognizing the dispositional nature of evolvability has also clarified several conceptual issues, including distinguishing what entities are evolvable (e.g., genes, traits, genomes), the features causally contributing to their evolvability, and the characterization of ways in which evolvability contributes to evolutionary changes (figure 2; Brigandt et al. 2023, Houle and Pélabon 2023, Villegas et al. 2023).

Evo-devo and evolutionary systems biology: The concept of evolvability is central to evo-devo research, which aims to understand the mechanisms generating and structuring phenotypic variation and how these mechanisms evolve (Hendrikse et al. 2007). Accordingly, evo-devo research has revealed some core principles and complexities of the developmental mechanisms that map sequence variation onto phenotypic variation (Hallgrímsson et al. 2009, 2023). Key points include demonstrating how new phenotypic variants in many systems result from small changes in developmental mechanisms, such as changes in gene regulation (e.g., Stern 2000, Hinman and Cheatle Jarvela 2014), and how the generation of phenotypic variation can be biased in that some variants are more likely to arise than others (e.g., Oster and Alberch 1982, Cano et al. 2023).

This research has placed the genotype–phenotype map (GP map) concept at the center of the evolvability research. This concept provides a framework for studying how properties of developmental systems affect phenotypic variation and its evolution (Hallgrímsson et al. 2023, Pavlicev et al. 2023). Studies of empirical GP maps representing gene-regulatory networks, regulatory interactions between genes, have been instrumental for understanding the mechanisms underpinning crucial stages during development, whereas comparing orthologous gene-regulatory networks across species further revealed specific features about the evolution of these networks. For example, comparative studies of the mesoderm–endoderm specification in echinoderms have shown how specific motifs such as positive feedback circuitry are conserved across species and may represent constraints on the evolution of developmental systems (Levine and Davidson 2005, Hinman and Cheatle Jarvela 2014). These studies also revealed that large phenotypic changes and novelties can be generated via cooption of important motifs (for a review, see Wittkopp and Kalay 2012). These studies have advanced our understanding of the evolutionary changes in molecular and developmental processes responsible for phenotypic variation among species. However, they have so far provided limited insights into how developmental processes generate the within-population heritable variation on which natural selection acts and how these processes themselves evolve under natural selection (Houle and Jones 2021).

Theoretical and empirical studies of GP maps have also identified properties of those maps that can influence evolvability. For example, *modularity*, the organization of development into relatively autonomous modules, could increase evolvability by reducing the effective dimensionality of variation and therefore reducing evolutionary trade-offs among different parts of the organism (e.g., Wagner and Altenberg 1996, Gerhart and Kirschner 1997, Wagner 2014, but see Hansen 2003). Similarly, *robustness*, the ability of developmental systems to remain unaffected by genetic or environmental perturbations (e.g., family level characters such as scutellar bristles number in *Drosophila*, Rendel 1959, or the uniform expression of five petals in the phlox family, Huether 1968), could increase evolvability by allowing the accumulation of cryptic genetic variation that may facilitate adaptation under new conditions (Wagner 2005). Mathematical modeling of GP maps has further highlighted how specific features of gene-regulatory networks can generate modularity and robustness and thereby influence evolvability (e.g., Kauffman 1993, Nijhout et al. 2017). Recently, the integration of such models into a quantitative genetic framework has suggested how GP maps could evolve under natural selection on phenotypic traits (Milocco and Salazar-Ciudad 2020, 2022).

Evolutionary quantitative genetics: One central principle of evolutionary quantitative genetics is that the ability of a population to show an evolutionary response to selection is determined by its additive genetic variance, V_A (Lande 1979, Houle 1992). This parameter has been estimated for many kinds of complex (i.e., polygenic) traits during the last 50 years and is often standardized by the total phenotypic variance V_P to yield the heritability ($h^2 = V_A/V_P$). However, heritability should not be considered as a comparative metric of evolvability because it does not measure evolvability independently from natural selection (Hansen et al. 2003, 2024). To overcome this issue, Houle (1992) introduced mean-scaled measures of additive genetic variance (e.g., $I_A = V_A/\mu^2$, where μ is the trait mean) as a method to quantify evolvability that is independent of selection. Because mean-scaled evolvability can be interpreted as the expected proportional response to selection when selection is as strong as selection on fitness (i.e., when the mean-scaled selection gradient $\beta_\mu = 1$; Hansen et al. 2011), it provides a metric for the evolutionary potential of quantitative traits when they are exposed to selection of similar strength. Comparisons of mean-scaled evolvabilities have led to the realization that the heterogeneity in evolutionary potential among traits is mainly influenced by differences in the amount of variation generated by mutations (Houle 1998), instead of being due to patterns of selection as is often argued (Mousseau and Roff 1987). Accordingly, life-history traits are more genetically variable than morphological traits, despite being more closely related to fitness (table 1; Houle 1992, Hansen and Pélabon 2021).

Beyond simply the magnitude of V_A in any trait, Lande and Arnold (1983) highlighted the influence of genetic correlations on the evolution of complex characters. Their framework later led to the development of multivariate measures of evolvability such as *conditional evolvability*, which quantifies the remaining evolvability of a trait when other genetically correlated traits are (hypothetically) not allowed to change. Conditional evolvability therefore quantifies the evolutionary consequences of pleiotropy (i.e., when a single locus affects several traits) and operationalizes the concept of modularity within a quantitative genetic perspective (Hansen and Houle 2008).

Another important insight for evolvability in evolutionary quantitative genetics stems from the recognition that patterns

Table 1. Median evolvabilities and heritabilities for different trait categories.

			Evolvability I_A				*Heritability h^2*	
Trait type	**Trait**	***n***	***Median* (%)**	**t_2 *(gen)***	**25th percentile (%)**	**75th percentile (%)**	***n***	***Median***
Morphology		1665	0.23	301	0.05	0.82	1560	0.37
	Size length	1025	0.10	715	0.03	0.47	929	0.40
	Size volume or mass	231	0.50	139	0.17	1.5	223	0.31
	Size count	333	0.45	154	0.21	0.98	332	0.36
	Shape	50	1.19	58	0.18	5.4	50	0.27
Growth		255	0.65	107	0.22	1.9	250	0.26
Pattern		18	0.84	83	0.50	3.3	18	0.36
Life history		474	0.86	81	0.05	3.8	470	0.18
	Fertility	182	2.28	30	0.54	8.1	182	0.25
	Dev. time	157	0.18	385	0.03	0.77	153	0.25
	Longevity	33	0.81	86	0.06	1.5	33	0.11
	Fitness	102	1.28	54	0.001	4.9	102	0.02
Physiology		175	1.45	48	0.38	3.6	170	0.20
Behavior		69	1.95	36	0.24	8.1	59	0.26
	Nonsexual	39	1.93	36	0.26	7.8	29	0.34
	Sex. selected	30	2.28	30	0.16	9.2	30	0.25
Total		2656	0.37	187	0.06	1.6	2527	0.31

Note: For ease of interpretation of the median evolvability, the column t_2*(gen)* reports the time in generation it takes to double a trait under unit directional selection. This is calculated as $t_2 = ln(2)/I_A$, where I_A is the mean-scaled evolvability. For example, an evolvability of 0.10% as in size length means that the trait will change by 0.10% per generation when selection is as strong as selection on fitness, and it will take 715 generations to double the trait. Abbreviation: *n*, the number of traits in each category. Source: From Hansen and Pélabon (2021).

of gene interaction can modify evolvability under directional selection. Specifically, *epistasis* occurs when genetic changes at loci influencing a trait modify the effects of genetic changes at other loci also influencing the trait. Because net effects are expected to be small when epistatic interactions cancel each other, with some increasing and some decreasing allelic effects, the role of epistasis in driving evolutionary dynamics has often been considered negligible. However, if there is *directional epistasis*, meaning that genetic changes influencing the trait systematically increase (or decrease) the effects of changes at other loci, genetic variation and therefore evolvability changes as the trait evolves (figure 3; Carter et al. 2005, Hansen et al. 2006). Such directional epistasis can be conceptualized as the population genetical manifestation of nonlinear GP maps. Directional epistasis may arise from any sources of nonlinearity, including genetic, developmental, or physiological feedback mechanisms; enzyme or transcription factor saturation; constraints on phenotypic expression produced by hard ceilings (e.g., figure 3; Morgan et al. 2020); or dichotomous or other forms of discrete phenotypic outcome (Dempster and Lerner 1950, Acker et al. 2023). A recent meta-analysis showed that directional epistasis is common and often strong, even in morphological traits that are continuously distributed on the phenotypic scale (Bourg et al. 2024). Consequently, epistasis can no longer be ignored and may in fact be a key force driving the dynamics of evolvability. Indeed, directional epistasis implies that evolvability changes as trait means evolve, violating the assumption of constant genetic variance with respect to mean phenotype that underpins foundational models of microevolutionary change (Lande 1979). By modifying the phenotypic impact of mutations and allele substitutions and, consequently, by modifying additive genetic variance, directional epistasis also provides an explanation for the evolution of robustness and evolvability (Hansen et al. 2006, Hansen and Wagner 2023).

Paleobiology: Although the modern synthesis postulates that macroevolution can be explained by microevolutionary processes, leading twentieth century biologists and paleontologists (including Eldredge and Gould) argued that processes causing microevolutionary changes within populations are not sufficient to explain macroevolution occurring among populations or among species (Futuyma 2015). Using observations such as the discontinuity of evolutionary patterns in the fossil record, they argued that macroevolution should be explained by evolution occurring at different biological levels and involving different processes (e.g., speciation, extinction, species sorting). They also questioned the ultimate power of selection for shaping evolution and introduced the concept of developmental constraints to explain patterns of evolutionary stasis (figure 1; Raup 1966, Gould 1980). Preceding the emergence of the field of evo-devo, these authors emphasized the importance of development for producing the variation on which selection could act, including concepts such as allometry (e.g., Gould 1974), versatility (Vermeij 1973), and phenotypic integration (Olson and Miller 1954).

A key hypothesis that emerged from the paleobiology research program is that genetically more variable populations and species should evolve more or faster. In the first effort to quantitatively test this hypothesis, Simpson (1953) failed to observe the predicted relationship. However, subsequent studies have reported positive correlations between within-population phenotypic variation or additive genetic variance and rates of evolutionary divergence (e.g., Kluge and Kerfoot 1973, Hunt 2007, Bolstad et al. 2014, Holstad et al. 2024). By revealing the influence of within-population evolvability on evolutionary patterns at timescales up to hundreds of thousands of years, these studies reestablish a link between micro- and macroevolution but also raise new questions concerning the evolutionary mechanisms that can generate such a link.

Key research questions about evolvability

The rich background briefly summarized above highlights the broad multidisciplinary interest in evolvability that has recently regained integrative momentum. This research activity yields a range of key questions that now need to be addressed to advance our overarching understanding of the causes and the consequences of variation in evolvability.

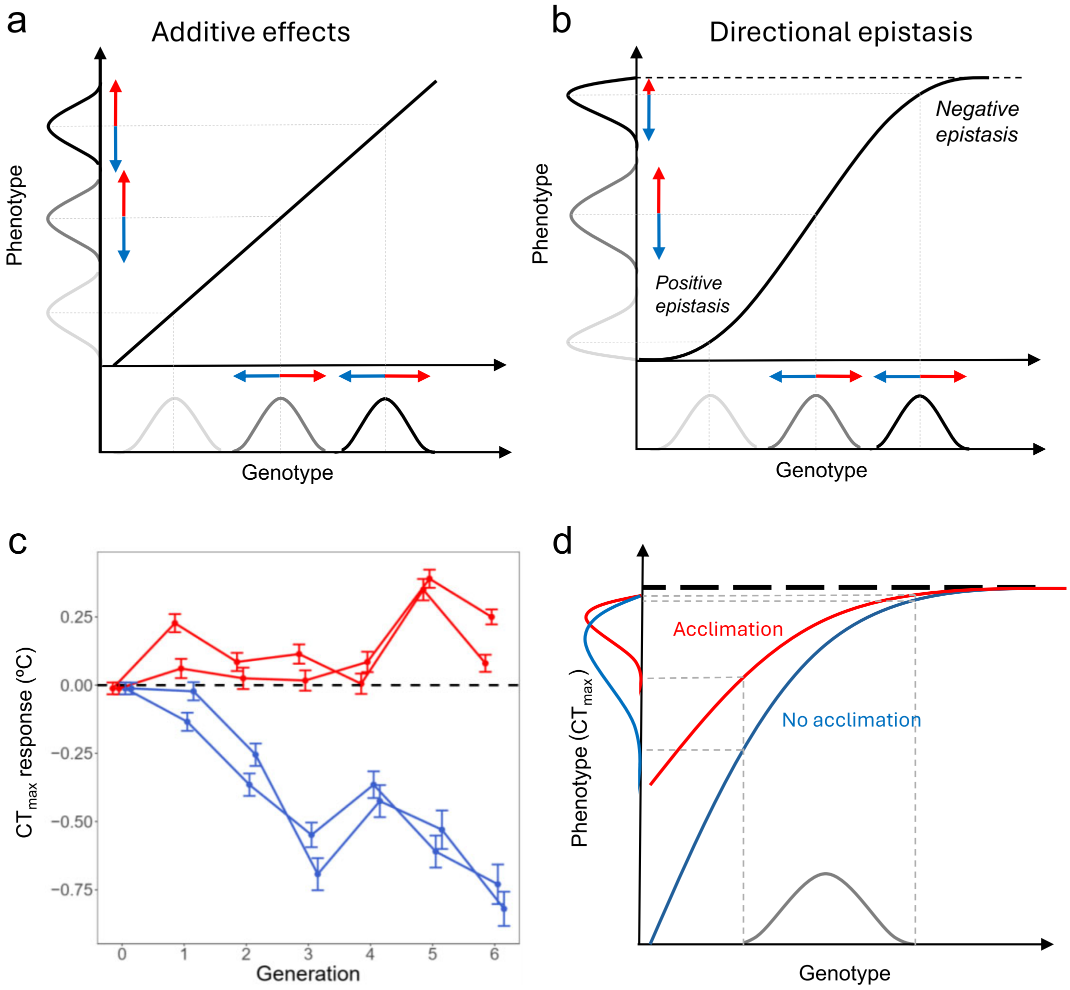


Figure 3. Linear and nonlinear genotype–phenotype maps (GP map), directional epistasis and evolvability. (a) A linear GP map where the black line represents the function that is mapping genetic variation, represented by bell curves on the **x**-axis, onto heritable phenotypic variation represented by bell curves on the **y**-axis. In this GP map, a genetic change in the DNA sequence that increases (the red arrows toward right) or decreases (the blue arrows toward left) the trait has always the same effect on the phenotype whatever the direction of the change and the genetic background in which it occurs (different genotypes on the **x**-axis correspond to different genetic background). With a such GP map, evolvability, which depends on heritable variation, remains constant when the trait evolves. (b) A nonlinear GP map where the phenotypic effect of a given genetic change depends on the direction of the change and the genetic background in which it occurs. For example, in the right half of the curve, the effect of a genetic change that increases the trait value diminishes when the trait increases (the red arrows on the **y**-axis decrease when the trait mean is moving toward its maximum value represented by the dashed line). This implies that genetic changes that increase the trait will decrease the effect of other genetic changes that also increase the trait, a mechanism referred to as negative directional epistasis. With directional epistasis, evolvability changes with the trait mean. (c) A possible example of negative directional epistasis in the artificial selection on maximum heat tolerance (CT_{max}) in zebrafish. The red lines and symbols (above the dash line) represent the response of the lines selected for an increase in CT_{max}, and the blue lines and symbols (below the dash line) represent the response of the lines to decrease CT_{max} (as compared with the control lines). The highly asymmetrical response to selection is possibly generated by biochemical limits at high temperature (Morgan et al. 2020). (d) Possible effect of environmental variation, represented by acclimation, on evolvability in the presence of negative directional epistasis. With acclimation, CT_{max} generally increases but shows less phenotypic and genetic variation. Source: Panels (c) and (d) were drawn from Morgan and colleagues (2020).

Causes of variation in evolvability

Understanding the causes of variation in evolvability requires identifying characteristics of underlying GP maps and their sources of variation. It then requires understanding how and how fast GP maps evolve and to what extent this evolution reflects structural properties of developmental systems versus the effects of natural selection on those systems.

Characteristics of the GP maps affecting evolvability and its variation: Differences in evolvability may stem from differences in the number of loci affecting the trait, in the effect sizes of alternative alleles, in the prevalence of pleiotropic effects that structure the GP map into developmental modules, and in the patterns of epistasis that confer specific properties to the GP map such as robustness (figure 2). The following questions address these issues.

Question 1: How are evolvability and molecular genetic variation related? Techniques such as next-generation sequencing, genome-wide association studies, gene knockdown and gene editing have improved our understanding of how sequence variation generates phenotypic variation. For phenotypes influenced by genes with large effect (e.g., age at maturation in salmon; Barson et al. 2015), identifying such genes may help explain evolvability and its variation within and among populations (e.g., Jensen et al. 2022). However, the amount of additive genetic variation that remains unexplained in many genome-wide association studies (e.g., Génin 2020, Wainschtein et al. 2022) indicates that genetic variants with large phenotypic effects are too rare to explain the amount of heritable variation responsible for microevolutionary changes of most quantitative traits. The difficulty in linking molecular genetic diversity to heritable phenotypic variation is further highlighted by studies of developmental processes that show how nonlinear GP maps obscure the relationships between DNA sequence variation and phenotypic variation (Hallgrímsson et al. 2009, 2023) and by increasing evidence that most traits are influenced by many loci (e.g., Yengo et al. 2022). Accordingly, measures of molecular genetic diversity and measures of heritable variation such as mean-scaled evolvability tend to be uncorrelated (Mittell et al. 2015).

Still, the absence of statistical correlation between these two types of variation does not mean that they are independent, and understanding the relationship between them remains necessary to comprehend how heritable phenotypic variation on which selection acts is generated. Furthermore, knowing when both types of variation could or should be correlated is of particular interest in conservation biology. Preserving evolutionary potential is crucial for facilitating evolutionary rescue—that is, when adaptive evolution restores positive growth of a population that declines because of environmental change and resulting maladaptation (Gomulkiewicz and Holt 1995). However, efforts to preserve the evolutionary potential in conservation programs are primarily focused on preserving molecular genetic diversity (e.g., Robuchon et al. 2023), possibly because molecular genetic data are now often cheaper and easier to obtain than quantitative genetic parameters, which are difficult to estimate in threatened species. Although such efforts can reduce extinction risks by reducing inbreeding depression (i.e., allowing genetic rescue; Frankham et al. 2017), the resulting presence of genetic diversity does not guarantee the evolvability of fitness and evolutionary rescue. Consequently, knowing when molecular data can or cannot predict evolvability may help conservation programs where evolutionary rescue is required.

Experimental evolution or artificial selection experiments combined with whole-genome sequencing (evolve and resequence; e.g., Wein and Dagan 2019 on bacteria) should contribute to our understanding of the mechanisms affecting the relationship between molecular genetic diversity and evolvability, but applying such knowledge in conservation biology will require general principles that could be broadly applied to a range of different traits and species. In the absence of such knowledge, overarching efforts to preserve genetic diversity remains the best options for preserving evolvability (Kardos et al. 2021, Willi et al. 2022).

Question 2: How are mutational variation and evolvability related? In principle, evolvability should increase with the magnitude of variation generated by new mutations (the *mutational variance*). Accordingly, positive correlations between mutational variance and mean-scaled evolvability have been observed in morphological and life-history traits of *Drosophila* (Houle 1998, Houle et al. 2017). However, a fundamental question is whether differences in mutational variation, and the resulting evolvability, stem from differences in locus-specific mutation rates, mutational effect sizes, or mutational target size (the number of loci with potential effects on the trait). Each mechanism has received empirical support (e.g., mutation rate, Chan et al. 2010; effect size, Estes et al. 2004; mutational target size, Besnard et al. 2020), and they all may nonexclusively contribute to variation in evolvability. However, evaluating their relative importance is fundamental for understanding evolvability and its evolution because mutation rates, effect sizes, and target sizes involve molecular processes occurring at different organizational levels (e.g., DNA repair fidelity, gene duplication, cooption of motives in gene-regulatory network) that evolve at different rates. Understanding the contribution of these mechanisms to evolvability is challenging, however, because the different processes are investigated via different methods involving different timescales and where selection is rarely considered (e.g., mutation accumulation, experiments, comparative genomics). However, recent experiments on *Arabidopsis thaliana*, revealing the covariation of within-genome mutation rates (locus and nucleotide-specific mutation rates) with within-species polymorphism and between-species substitution rates further suggest how mutations contribute to evolvability (Weng et al. 2019). Specific epigenetic features associated with these site-specific mutation rates in *A. thaliana* (Monroe et al. 2022) also provides a mechanism by which evolvability itself may evolve, such as through the evolution of protein–DNA epigenetic interactions.

Question 3: What is the relationship between pleiotropy, modularity and evolvability? It has become clear that evolvability of any trait depends on relationships with other traits and, more particularly, on the degree of underlying pleiotropy that leads to genetic correlations among traits alongside the alignment of selection (Etterson and Shaw 2001, Hansen 2003, Houle and Rossoni 2022). This issue is well known by breeders when they fail to increase multiple traits of interest that are negatively genetically correlated, such as the protein and oil content of soybean seeds (Bandillo et al. 2015). Consequently, univariate measures of additive genetic variation in single traits may often overestimate evolvability when the focal trait is genetically correlated with traits under opposing forms of selection.

Empirical estimates of conditional evolvability accounting for genetic correlations have confirmed the negative effect of pleiotropy on evolvability (e.g., Sztepanacz and Houle 2019, Opedal et al. 2023). However, such estimates generally include only few measured traits and neglect other unmeasured traits that are plausibly entangled with the focal trait. Because conditional evolvability may further decrease when additional traits are considered, conditional evolvability may still be overestimated for most traits. As automated and high-throughput phenotyping methods improve (Houle et al. 2010), we should aim to estimate G matrices (i.e., genetic variance–covariance matrices, $\mathbf{G}$) that encompass a large majority of potentially associated traits. Such studies would reveal the degree to which conditional evolvability decreases when the number of traits considered increases.

However, the constraining effects of genetic correlations among traits can be counteracted by the higher genetic variation that can emerge if many loci affect many traits (Hansen 2003). Furthermore, variation in pleiotropic effects across loci also reduces genetic correlations and opens the possibility of compensatory changes that can alleviate detrimental effects of correlated responses to selection. Some degree of modularity could ultimately emerge, whereby sets of traits become substantially genetically independent. Understanding the effects of modularity on evolvability therefore requires a population-genetics perspective incorporating the dynamics of the underlying genetic and developmental mechanisms. It also requires further efforts to relate the magnitudes and signs of genetic variances and covariances to the patterns of selection acting on different traits (e.g., Blows et al. 2004) or with the patterns of divergence among lineages, assuming that the divergence results from adaptation (e.g., Hohenlohe and Arnold 2008, Houle et al. 2017).

Question 4: What is the relationship between robustness and evolvability? By reducing the phenotypic expression of genetic changes, robustness is expected to decrease short-term evolvability (Ancel and Fontana 2000). However, robust phenotypes could ultimately be more evolvable if they accumulate conditionally neutral mutations that could create paths to novel phenotypes following either environmental or genetic changes (Gerhart and Kirschner 1997, Wagner 2008). This latter hypothesis, however, relies on specific assumptions about the structure of the GP map and the fitness landscape, and alternatives reasonable assumptions can equally generate a negative relationship between evolvability and robustness (Mayer and Hansen 2017). Ultimately, initial robustness may decrease evolvability over short timescales and under limited environmental variation, but it may increase evolvability over long timescales or when populations encounter rarer, more extreme and stressful environments. In an experiment on *Escherichia coli*, Zheng and colleagues (2019) observed that the rate of evolution of a fluorescent protein toward a new fitness optimum was faster in populations harboring cryptic genetic variation compared to populations without such variation. This study illustrates the type of approach that should help us assess the link between cryptic genetic variation and evolvability. However, a positive effect of robustness on the ability to respond to selection requires that the genetic variation accumulated under benign conditions is adaptive once expressed, a condition that is still debated, as is illustrated in the next question.

Question 5: Is cryptic genetic variation adaptive? Cryptic genetic variation can be adaptive if it is released by environmental changes to produce phenotypes that are beneficial in the new environmental conditions (Hoffmann and Parsons 1997, Rutherford and Linquist 1998, Hermisson and Wagner 2004). Waddington (1953, 1956) showed that selection on such environmentally induced phenotypes could lead to a process of genetic assimilation where trait expression shifts from being environmentally induced to being mostly genetically controlled. The hypothesis of adaptive cryptic genetic variation has been supported by theoretical (e.g., Hermisson and Wagner 2004, Masel 2005) and empirical studies (e.g., McGuigan et al. 2011, Zheng et al. 2019). However, novel traits or new genetic variation expressed under stressful conditions do not necessarily facilitate adaptation to such conditions. For example, despite observing an increase in additive genetic variance in desiccation resistance in *Drosophila* after a bottleneck event, van Heerwaarden and colleagues (2008) failed to observe the increased response to selection predicted by the new level of additive variance. Furthermore, the beneficial effect of cryptic genetic variation on fitness can be limited to specific novel environments possibly determined by the population's selection history. Accordingly, Grainger and colleagues (2021) found that the evolution of fecundity and developmental rates in *Drosophila melanogaster* populations exposed to cooling climate in the fall was contingent on the type of selection experienced by previous generations during the summer. Echoing the review by McGuigan and Sgro (2009), we emphasize that more studies are required like those discussed above and on an array of systems to understand the conditions under which potentially adaptive cryptic genetic variation can accumulate and be favourably expressed in nature. Such work would help clarifying the relationships between cryptic genetic variation and robustness and how these properties of the GP map affect evolvability.

Question 6: Do more plastic traits evolve faster? Phenotypic plasticity, when different phenotypes are produced by a genotype exposed to different environments, is often suggested to facilitate genetic adaptation, because it may produce variants that can increase fitness and allow persistence for long enough for adaptive evolution to occur via genetic accommodation. However, such a plasticity-first hypothesis (West-Eberhard 2003) is controversial and difficult to test, not the least because the effects of plasticity on evolution remain debated. If plasticity and evolvability are controlled by different mechanisms, adaptive phenotypic plasticity that shifts the phenotype toward the new fitness optimum should decrease the rate of evolution, because it decreases the strength of selection (e.g., Borenstein et al. 2006, but see Paenke et al. 2007). In contrast, phenotypic plasticity could accelerate evolution by increasing evolvability if selection for plastic genotypes that are more sensitive to environmental variation also selects genotypes that are more sensitive to mutations (Fierst 2011, Draghi and Whitlock 2012). This congruence hypothesis was initially suggested by Ancel and Fontana (2000).

Attempts to elucidate the effects of plasticity on evolution have considered the relative role of plasticity and genetic adaptation in populations differentiation. In a review of reciprocal transplant experiments, Stamp and Hadfield (2020) showed that genetic and plasticity-induced phenotypic differences among populations are generally positively correlated and that plasticity is the major contributor to population divergence for two thirds of the traits considered (see also Noble et al. 2019, Rohner et al. 2022, Rohner and Berger 2023). Together with the positive correlation observed between genetic and residual variation among traits (Hansen et al. 2011), these results give supports to the congruence hypothesis, although within-trait variation in heritability also implies some degree of independence between the different components of phenotypic variation (e.g., Ketola and Kronholm 2023). Correlation is not causation, however, and the correlation observed between plastic and genetic changes in population differentiation does not necessarily imply that plastic changes preceded genetic changes or even that both type of changes result from similar alteration of developmental pathways.

More studies are therefore needed to elucidate the relationship between phenotypic plasticity and evolvability. This can be achieved by comparing the phenotypic outcome of genetic or environmental perturbations on developmental pathways or by analyzing the consequences of artificial selection on variance (e.g., stabilizing, fluctuating, or disruptive selection) on the different components of phenotypic variation. For example, Pélabon and colleagues (2010) found that phenotypic variation among versus within individuals (i.e., developmental instability) responded differently to stabilizing and fluctuating selection, suggesting different genetic control of these sources of variation. Modular and clonal organisms are particularly useful in this context because they allow a better partitioning of the different components of the phenotypic variation. Similarly, animal-pollinated plants with different levels of phenotypic variation expected in vegetative versus reproductive organs may prove particularly useful to understand the evolution of the different components of phenotypic variation (Fenster and Galloway 1997).

Question 7: What is the strength and type of directional epistasis affecting phentoypic traits? Recent studies have highlighted that directional epistasis can be substantial and therefore must be considered in efforts to predict evolutionary responses to selection. For example, artificial selection on maximal heat tolerance (CT_{max}) in zebrafish showed that it is easier to generate an evolutionary decrease in CT_{max} than an evolutionary increase (figure 3c; Morgan et al. 2020). This may be because biochemical or physiological constraints prevent genetic changes that increase CT_{max} from being phenotypically expressed above certain temperatures. This implies that genetic or environmental changes that shift CT_{max} closer to these thermal limits decrease the effects size of mutations that should affect CT_{max}. This generates negative directional epistasis where genetic changes that increase CT_{max} interact with other such genetic changes and decrease their effect sizes. Consequently, additive genetic variation and therefore evolvability should decrease when CT_{max} evolves toward higher values (figure 3; Hansen 2013) or when acclimation to higher temperature increases CT_{max} (figure 3d). This example illustrates the expected effect of directional epistasis on the evolvability of quantitative traits and suggests that estimating additive genetic variance of such traits may not be sufficient to fully predict their evolvability in different (opposite) directions and over many generations of selection. One should keep in mind that it is not the presence of epistasis, as is classically estimated by the epistatic variance (e.g., Lynch and Walsh 1998), that is important for the evolutionary dynamics of quantitative traits but the directionality of epistasis, which affects evolvability in a nontransient manner (Hansen 2013).

Although changes in additive genetic variation alongside changes in the trait mean have long been acknowledged for *threshold traits*—that is, traits with discrete phenotypic states such as color polymorphisms, sex determination in reptiles, or partial migratory behavior (Dempster and Lerner 1950, Reid and Acker 2022)—empirical estimates of directional epistasis in continuously distributed phenotypic traits have been scarce (but see Pavlicev et al. 2010, Bourg et al. 2024, Le Rouzic et al. 2024). Consequently, it remains unclear how much directional epistasis could affect evolutionary predictions and at which timescale. However, a recent meta-analysis of line-cross data of size-related traits in animals shows that negative epistasis toward larger size is predominant for such traits and the median estimate predicts that evolvability would on average be halved when going from the small to the large parental lines used in the line crosses (Bourg et al. 2024). This could substantially constrain the evolution toward larger size in many organisms.

Estimating the type and strength of directional epistasis in different categories of traits could therefore improve our evolutionary predictions and help explain the differences in evolvability seen among different types of traits. This should be facilitated by newly developed statistical tools that allow estimating patterns of directional epistasis, either from artificial selection time series where patterns of directional epistasis can be inferred from their potential effects on the response to selection (Le Rouzic et al. 2011) or from line-cross data that allow building GP maps from which patterns of epistasis can be inferred (Bourg et al. 2024). Acquiring such broader knowledge about the patterns and strength of directional epistasis in different categories of trait may also help incorporate results of evolvability research into conservation biology. Indeed, estimating directional epistasis of specific key ecological traits in a threatened population for which evolutionary rescue is desirable may rarely be possible because of the difficulties of obtaining such genetic details. Using broad principles may remain the best way to improve our predictive models to determine whether this population is able to adapt to more extreme environment.

Evolution of evolvability: Beyond understanding the mechanistic causes of variation in evolvability, the next ambition is to understand how such mechanisms can themselves evolve. Many scenarios of adaptive and nonadaptive evolution of evolvability have been suggested. Lynch (2007, 2024) argued that the evolution of genetic architecture may be dominated by genetic drift and mutations, because the impacts of selection on genomic changes will typically be weak in multicellular organisms with long-term effective population sizes below 10,000 (the drift-barrier hypothesis, but see Whitney and Garland 2010, Monroe et al. 2022). Evolution of evolvability may also result from a tendency for developmental systems to become more robust against mutations when their complexity increases (Kauffmann 1993, Siegal and Leu 2014). In addition, with directional epistasis, additive genetic variance is affected by changes in the trait mean. Consequently, evolvability may evolve as an indirect consequence of directional selection on the trait mean (Carter et al. 2005, Hansen et al. 2006). Furthermore, if relaxed selection increases evolvability by allowing accumulation of genetic variation (Payne and Wagner 2019), evolution of traits that decrease the strength of selection, such as adaptive plasticity or key innovations allowing for example individuals to escape competition, may also increase evolvability (Galis 2001).

Alternatively, genetic architecture may have been selected to facilitate adaptive levels of evolvability, because more evolvable genotypes, populations, or species are better able to adapt and persist in changing environments (Lloyd and Gould 1993, Le Rouzic et al. 2013, Tufto 2015). Similar arguments have been developed to explain the evolution of genes promoting variation (Wagner 1981), sex, and recombination (Maynard Smith 1978, Bell 1982). Other adaptive hypotheses for the evolution of evolvability concern the generation of more localized or coordinated effects of mutations via developmental modularity and integration to reduce pleiotropic costs of phenotypic evolution (Raff 1996, Gerhart and Kirschner 1997) and the evolution of robustness and canalization when, as in conservative bet-hedging, short-term evolution causes a long-term decrease in fitness (Haaland et al. 2019). In addition, observations of lower mutation rates of genes subjected to purifying selection (e.g., Monroe et al. 2022) suggest that some feature of the genetic architecture affecting evolvability may respond to selection. The two following questions address this debate.

Question 8: Do changes in mutation rate under stressful conditions results from selection for evolvability? Some researchers have argued that the increase in mutation rate sometimes observed under stressful conditions is adaptive because it enhances evolvability (e.g., Metzgar and Wills 2000, Wei et al. 2022). However, no studies have yet convincingly demonstrated direct selection *on* evolvability instead of indirect selection *of* evolvability, and alternative hypotheses such as the drift-barrier hypothesis provide nonadaptive explanations for such changes (Lynch et al. 2023). Testing adaptive hypotheses about the evolution of mutation rate and evolvability is difficult, however, because natural selection can only favor traits that immediately benefit individuals, as opposed to potentially benefiting descendants. Consequently, adaptive hypotheses for the evolution of evolvability generally involve some components of group or lineage selection (Dawkins 1988, Lloyd and Gould 1993, Lynch 2007), as for any bet-hedging traits.

Empirical evidence of selection at these levels has been reported (e.g., Goldberg et al. 2010, Moreira et al. 2021), but rigorous tests of adaptive hypotheses concerning the evolution of evolvability at different levels (genome, population, or species) are still needed. Such tests should consider adaptive and nonadaptive scenarios at the different levels, as was recently done by Barnett and colleagues (2025). There, the rapid shift in natural selection on mat formation in the bacterium *Pseudomonas fluorescens* favoring cellulose-producing or non-cellulose-producing cells resulted in lineages evolving higher mutation rates and higher evolvability at the loci responsible for the shift in cellulose production.

Question 9: Does modularity result from constraints embedded in developmental systems or from the effect of natural selection on those systems? We cannot assume that modularity necessarily results from natural selection. Accordingly, several models of neutral evolution of modularity, where natural selection is either absent or plays a limited role, have been suggested (see Wagner et al. 2007 for a review). However, there are cases in which modularity and integration appear to have evolved as a result of natural selection. In the plant *Dalechampia scandens*, variation of involucral bracts that subtend the cluster of male and female flowers to form the blossom is decoupled from variation of the leaves from which they are developmentally derived (Armbruster 2023). Such variational modularity of the bracts seems adaptive given their role in the pollination process, as well as in the protection of the developing fruits (Pélabon et al. 2011). Inversely, fine-tuning of the pollination process is often achieved by *connation*, the fusion (integration) of floral parts, which may be a response to the stabilizing selection resulting from pollination accuracy (Armbruster et al. 2009). Eventually, whether modularity represents a constraint imposed by developmental systems or the effect of natural selection on those systems will depend on the rates at which pleiotropy and modularity evolve and whether such an evolution is a response to selection; that is, it coincides with changes in the patterns of multivariate selection. These considerations underline the relevance of studying the evolution of *G* matrices.

Theoretical studies that integrate some aspects of development suggest that *G* matrices can evolve rapidly under selection (e.g., Milocco and Salazar-Ciudad 2020, 2022). In addition, Pavlicev and colleagues (2008) reported genetic variation for pleiotropy that affects covariation among traits in mice. But on the other hand, artificial selection on correlated traits and experimental evolution studies modifying the orientation of the fitness landscape have provided inconclusive evidence about the adaptive evolution of genetic correlation and modularity (e.g., Bolstad et al. 2015, Sztepanacz and Blows 2017, Gomez et al. 2019). These experimental studies may suffer a lack of power to efficiently modify pleiotropic effects in a limited number of generations. Still, their results tend to be confirmed by comparative analyses of *G* matrices that often report a relative stability of **G** across populations and species (e.g., Delahaie et al. 2017, McGlothlin et al. 2022) and therefore suggest some possible constraints on the evolution of modularity. This interpretation remains contentious because relatively constant fitness landscapes could generate such consistency in **G** and information concerning the dynamics of fitness landscapes remains scarce. More studies are therefore necessary to understand whether and how selection can modify modularity, a conclusion shared by other properties of the GP map such as plasticity and robustness. Combining results on short-term evolution provided by comparative studies across populations and species with those of long-term evolution provided by historical data such as the fossil record, as in Uyeda and colleagues (2011), could provide valuable insight into the timeframe necessary to witness the evolution of these properties of the GP maps.

Consequences of variation in evolvability

Given our limited knowledge concerning the rate and causes of evolution of GP maps, it remains unclear over what timescales evolvability influences evolution. It is also often difficult to predict how such influences are manifested. The last three questions address these issues.

Question 10: Is the lack of evolvability responsible for macroevolutionary stasis? Many traits exhibit phenotypic stasis for millions of years (figure 1d; Gingerich 1993, Hansen and Houle 2004, Uyeda et al. 2011, Hunt et al. 2015), but rapid trait evolution is often observed on short timescales. In addition, contemporary estimates of population evolvability are too high to constrain evolution over timescales relevant for population and species divergence (Hansen and Houle 2004, Holstad et al. 2024). Several authors have therefore suggested that genetic correlations may substantially reduce evolvability and constrain evolution at macroevolutionary timescales (e.g., Hansen and Houle 2004, Galis and Metz 2007, 2008). This hypothesis makes two testable predictions. First, estimates of conditional evolvability should be small enough to constrain population or species divergence. Second, the constraining effect of evolvability should decrease over longer periods of time if pleiotropy and modularity evolve.

Testing the first prediction requires more complete G-matrices to fully account for the constraining effect of pleiotropy (see question 3). Concerning the second prediction, Holstad and colleagues (2024) observed a weaker relationship between measures of evolvability and species divergence compared with population divergence, which supports the idea of decreasing constraints at longer timescales. However, the relationship they observed between rates of evolution and the time interval over which those rates were measured was not compatible with an evolutionary scenario where evolvability gradually increased over time (see also Uyeda et al. 2011). To reconcile these observations, Holstad and colleagues (2024) suggested that trait stasis for up to one million years could be generated by fluctuating selection around stationary adaptive optima (i.e., no change of the long-term average optimum). Under this scenario, the divergence among populations tracking asynchronized fluctuating optima can be constrained by low evolvability. Testing this hypothesis requires further information concerning the long-term dynamics of fitness landscapes. This is the topic of our next question.

Question 11: Are contemporary measures of natural selection relevant to understand macroevolutionary consequences of evolvability? Natural selection has been shown to fluctuate on short timeframes (year to year; e.g., Siepielski et al. 2009, Reynolds et al. 2010, Acker et al. 2021), although some of these estimates are likely to be substantially inflated by sampling variance (Morrissey and Hadfield 2012). Increasing the number of rigorous estimates of temporal and spatial dynamics of fitness landscapes measured over longer time periods and using appropriate statistical methodologies will help resolve this issue. The increasing number of longitudinal studies of wild populations (e.g., Soay sheep on St Kilda, great tit populations in England and Netherlands) should make this possible, but such studies are still taxonomically restricted. We therefore require more long-term selection studies, while accepting that contemporary selection dynamics may not necessarily reflect patterns of selection that have shaped animal and plant species during the past thousands or millions of years. This is not least because of the increasing effects of global changes on contemporary populations, as pollution, habitat changes, and global warming may generate patterns of selection different from those experienced by plant and animal species in the last 10,000 years.

Question 12: Is evolvability relevant for macroevolutionary processes such as speciation and extinction? It has been repeatedly suggested that evolvability could influence speciation and extinction rates (Jablonski 2008). For example, Goldberg and colleagues (2010) suggested that reduced evolvability generated by self-compatibility in species with bisexual flowers causes the increased extinction rates in Solanaceae. Similarly, the scattered phylogenetic distribution of asexual taxa has long been interpreted to reflect elevated extinction rates because of low evolvability (e.g., Bell 1982, Moreira et al. 2021). In addition, Kolbe and colleagues (2011) found that survival of bivalve species through the Pliocene–Pleistocene extinction interval was correlated with greater morphometric variation, which can be broadly interpreted as evolvability (see also Liow 2007, Jablonski 2023). Yang (2001) also proposed that increased modularity between young and adult stages associated with holometabolous insect development, as compared with hemimetabolous development, increased evolvability and consequently species diversity among holometabolous insects.

These examples are suggestive but assessing whether evolvability causally affects species persistence and speciation rate is highly challenging. First, observed relationships between species persistence and morphological variation may be mediated by geographic and ecological breadth which influence patterns of selection (Love et al. 2022). Furthermore, the relationships between evolvability, speciation and species diversification are often complex. For example, in Goldberg and colleagues (2010), self-incompatibility was associated with higher species diversification. However, this pattern did not result from higher speciation rates of self-incompatible taxa (speciation rate was higher in self-compatible taxa) but from a lower extinction rate of those taxa, which may be better able to maintain adaptive potential (Clo et al. 2019 but see Sztepanacz et al. 2023). Similarly, if diversification and speciation are favored by the evolution of key innovations (Galis 2001, Maia et al. 2013), it remains unclear whether key innovations increase evolvability by generating new variation that results in further changes (e.g., Stroud and Losos 2016, Jablonski 2023) or whether increased evolvability generates novelties and key innovations—for example, because of the accumulation of new genetic variation under relaxed selection (Galis and Metz 2007). These possibilities may be resolved by comparing the evolutionary response of clades exposed to similar opportunities. A possible example concerns the comparison of the diversity in bill characteristics in the speciose Hawaiian honeycreepers versus their relatives, the Hawaiian thrushes, that colonized the archipelago at the same time. Lovette and colleagues (2002) concluded that the bill diversity associated with the higher number of honeycreeper species resulted from a clade-specific ability to evolve novel morphologies. Unfortunately, the number of clades where such comparisons can be made is limited, and the influence of contingency generated for example by different selection histories remains difficult to consider.

The effects of modularity on evolvability over macroevolutionary timescales have also been inferred from correlations between measures of modularity and measures of population or species divergence (e.g., Du et al. 2019). These studies remain mostly suggestive, however, because they lack well-defined models of evolution underpinning the quantitative relationships between measures of modularity and measures of evolutionary diversification such as the number of species (Houle and Pélabon 2023).

Jablonski (2023) argued that new methods for integrating fossil and present-day data should offer promising avenues to evaluate the role of evolvability in macroevolution (see also Love et al. 2022, Voje et al. 2023). Such approaches will need to overcome core difficulties, such as the fact that studies of evolvability of extant species typically concern specific traits, whereas macroevolutionary studies concern taxon- or clade-specific evolvability (Love et al. 2022). Similarly, the weak correlation often observed between speciation and morphological evolution (e.g., Hunt and Rabosky 2014) complicates the establishment of a link between contemporary measures of evolvability quantified as morphological divergence and macroevolutionary measures of evolvability quantified as number of species.

Conclusions

In recent years, evolvability has matured into a cohesive and cross-cutting research topic in evolutionary biology. Although the concept was originally developed independently in different disciplines, recent progress has established important bridges between research programs and agendas. This progress is evidenced by our highlighted questions, which often combine concepts, theories, and empirical approaches from multiple disciplines. Accordingly, efforts to answer these questions will necessarily further stimulate interdisciplinary and multifaceted research. This will, among other advances, require more fully integrating traditional quantitative genetics with modern genomic and phenomic capabilities among others.

Furthermore, the door is now open to more explicitly apply cutting edge insights stemming from the evolvability concept across more applied fields, including conservation biology and evolutionary medicine (e.g., Gatenby and Brown 2020, Mansur and Greaves 2023). The resulting insights regarding the causes, constraints, and implications of rapid evolution and the timeframes over which such processes act and evolve should reveal the potential for rapid desired evolution (e.g., in evolutionary rescue) and suggest new approaches to prevent rapid undesired evolution (e.g., in antibiotic resistance). The formal introduction of evolvability into such active fields should also generate reciprocal stimulation, because progress in such directions will prompt further developments to operationalize the evolvability concept.

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