Conceptual Roles of Evolvability across Evolutionary Biology: Between Diversity and Unification

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Abstract

A number of biologists and philosophers have noted the diversity of interpretations of evolvability in contemporary evolutionary research. Different clusters of research defined by co-citation patterns or shared methodological orientation sometimes concentrate on distinct conceptions of evolvability. We examine five different activities where the notion of evolvability plays conceptual roles in evolutionary biological investigation: setting a research agenda, characterization, explanation, prediction, and control. Our analysis of representative examples demonstrates how different conceptual roles of evolvability are quasi-independent and yet exhibit important relationships across scientific activities. It also provides us with the resources to detail two distinct strategies for how evolvability can help to synthesize disparate areas of research and thereby potentially serve as a unifying concept in evolutionary biology.

Keywords: characterization, concepts, control, evolvability, explanation, prediction, research agenda, unification

1 Introduction

Evolvability is a property of living systems that refers broadly to their capacity, ability, or potential to evolve. However, the property is conceptualized in different ways when being investigated by biologists (see also Chapter 3). For example, some researchers attribute evolvability to populations and construe it in terms of the ability to respond to selection (Flatt 2005), whereas others attribute evolvability to organisms and understand it as the capacity to generate heritable phenotypic variation (Kirschner and Gerhart 1998). A number of biologists and philosophers have noted the diverse interpretations of evolvability found in contemporary evolutionary research—at least one has called the evolvability literature a mess that needs to be cleaned up (Brown 2014).

One philosophical response to this situation is to identify a central or core meaning for the concept of evolvability. Differences in conceptualization are then understood as mere variations on this primary or basic meaning, such as "the joint causal influence of ... internal features [of populations] on the outcomes of evolution" (Brown 2014, 549). However, it quickly becomes difficult to specify what counts as an internal feature of a population (Love 2003). Similar difficulties arise when attempts are made to identify the essence of a scientific concept (e.g., "gene"; Griffiths and Stotz 2013). Another response is to argue that diverse interpretations correspond to distinct phenomena (Pigliucci 2008b), though this raises the question of why the same term "evolvability" is used.

A different response is to analyze what these different conceptualizations accomplish in scientific reasoning. It assumes that the variation in conceptualization is there for a reason and plays some functional *role*. Understanding these functional roles is potentially relevant to ongoing empirical inquiry because, once understood, they can be more actively marshaled to perform scientific tasks. Complementary possibilities for functional roles include: tracking distinct methodological approaches to a phenomenon of interest, representing distinct scientific

aims (either within or across disciplines), and locating different commitments about the significance of a concept within a set of theoretical assumptions (e.g., is it central or peripheral to a particular explanation?) or with respect to its range of application (e.g., is the concept intended to apply only under particular circumstances or be fully general?). The present analysis adopts this orientation and is motivated by empirical evidence that points toward these possible functional roles being operative across evolvability research.

A recent, large-scale citation analysis demonstrates that there are several co-citation clusters of research that concentrate on distinct conceptions of evolvability, either from a specific disciplinary or shared methodological orientation (Nuño de la Rosa 2017). These clusters map onto six broad disciplinary approaches: evo-devo, complex network analysis, molecular evolution, population genetics, quantitative genetics, and macroevolutionary studies. However, the clusters overlap and do not cleanly separate along disciplinary lines. This overlap is suggestive of links across different fields of evolutionary inquiry that might correspond to different functional roles. These links could help to synthesize associated theoretical commitments among conceptions of evolvability and their evidential underpinnings into a more general perspective on evolutionary processes.

This chapter takes as its starting point the different interpretations of evolvability and these intriguing patterns of usage within and across research clusters. We leverage this diversity to address the question of what *conceptual roles* evolvability plays across evolutionary biology. In particular, we identify and examine multiple scientific activities where the concept of evolvability plays a role in evolutionary biological investigation—setting a research agenda, characterization, explanation, prediction, and control. Our primary goal is to better grasp how the notion of evolvability is functioning in the investigative and explanatory practices of evolutionary biologists. The existence of different possible conceptual roles provides a rationale for why we might expect to find distinct interpretations of a central concept.[1] Additionally, an

understanding of differences in conceptual roles in distinct activities could yield resources to bridge different investigative approaches and thereby provide routes to synthesize findings about evolvability across disciplinary boundaries.

Our analysis of how scientists use the concept of evolvability to fulfill distinct roles in their various activities also can foster an understanding of its success or failure in accomplishing investigative work. Once we better understand *that* different conceptions can exhibit distinct roles in various scientific activities and *how* they do so, we are positioned to ask whether a particular conception *can or should* play a specific role in inquiry. This type of question can be elaborated to scrutinize how these distinct roles are related to one another and whether (and to what degree) these relations facilitate the successful investigation of evolvability. All of this takes on special significance because one or more of the roles that evolvability plays might serve to unify disparate areas of research in evolutionary biology.

We commence our analysis by distinguishing five different activities relevant to evolutionary biology where evolvability plays a role: setting a research agenda, characterization, explanation, prediction, and control (Section 2). Next, we turn to questions about how different activities can be related to one another or are jointly operative in evolvability research (Section 3). Finally, we argue that focusing on the role of evolvability in the research agenda setting activity could be strategic for unifying fields of study such as evo-devo, complex network analysis, population genetics, and macroevolutionary studies in contemporary evolutionary research (Section 4).

2 Conceptual Roles for Evolvability

There are many things to be said about conceptual roles in scientific practice. For the present discussion, we focus on how a concept can operate as a tool or a target in different scientific

activities, such as explanation, prediction, or control. A concept plays a role as a *tool* when it is used to accomplish a particular end in the context of a scientific activity. A concept plays a role as a *target* when it represents a particular aim for an activity of scientific inquiry. Concepts can play the same role in different activities, and different roles can operate in the same activity. In what follows, we range over research programs and disciplinary approaches to illuminate different instances of roles of evolvability in various scientific activities.

2.1 Setting a Research Agenda

Setting a research agenda functions to guide ongoing investigative efforts and motivate future research. One positive effect of the concept of evolvability emerging and increasing in prominence in the 1990s was that it encouraged investigation into the scope and generation of phenotypic variation independently of its selective value. Hendrikse et al. (2007) illustrate this vision of evolvability as establishing a research agenda, singling it out as a central problem in biology and the primary problem of evo-devo (see also Minelli 2010). Although this framing may foster neglect of other crucial questions in evo-devo (Müller 2021), it shows how an approach can set its own research agenda around evolvability questions that could not be answered or even articulated by either developmental biology or traditional evolutionary biology.

A research agenda not only highlights phenomena in need of investigation but also has an internal architecture that gives direction to scientific investigation and coordinates efforts across research groups (Love 2008, 2013). Such a *problem structure* consists in systematic relations between the individual component questions that make up the agenda. Evolutionary novelty is another example of a concept that functions to set an agenda, directing and coordinating attempts to account for the origin of characters (Brigandt and Love 2012). The problem structure of such a research agenda indicates how different explanatory contributions are to be synthesized, such as how modifications in lower-level traits (e.g., gene regulatory mechanisms) yield changes in

higher-level traits (e.g., cellular interactions and tissue formation). Likewise, paleontologists and taxonomists must establish a sequence of morphological changes and the phylogenetic junctures at which transitions took place. Only then can evo-devo biologists elucidate the relevant developmental mechanisms that underwent modification to yield the novelty.

The proposal by Hendrikse et al. (2007) already suggests some of the relevant problem structure for an evolvability research agenda. They articulate two related domains: "(i) Bias in the direction of variation generated" and "(ii) Modulation of the amount of variation generated" (396). From their evo-devo perspective, it is crucial to understand the interrelated developmental-genetic basis of both domains. Additional structure includes how investigations of contributing phenomena, such as modularity, heterochrony, morphological integration, and canalization can be coordinated.

Concepts that play roles in agenda setting can provide concrete guidance for a specific approach or field, such as evolvability research in evo-devo (Hendrikse et al. 2007). However, an agenda-setting concept also can be a tool for mapping out a landscape of research that is relevant to *multiple* biological fields. The landscape of such a research agenda can be described as a "trading zone" (Galison 1999): an interdisciplinary area of collaboration where members of different scientific communities exchange concepts, methods, and results that are then translated into the specific language of these different communities. Thus, evolvability need not only be a central problem for evo-devo; it may well function to set a research agenda across evolutionary biology, with a problem structure capable of coordinating interdisciplinary research and even uniting efforts from various fields (Brigandt 2015b; Nuño de la Rosa 2017). For example, theoretical insights about the relationship between modularity and evolvability have been shared across disciplines even though the notion of modularity is defined differently in terms of topological connections (computational evolution), developmental interactions (evo-devo), or constrained pleiotropic effects (quantitative genetics). The concept of evolvability's role as a *tool*

for setting a research agenda that coordinates interdisciplinary research makes it a natural candidate to consider when exploring how evolvability might serve as a unifying concept (see Section 4).

2.2 Characterization

Within a research agenda, it is crucial for scientists to adequately characterize the phenomenon of evolvability. Often this involves finding one or more working definitions. The way a phenomenon is characterized or defined "sets the frame" of an inquiry—it tells researchers what to attend to and what needs to be predicted, explained, or controlled (Colaço 2018). The activity of characterization involves distinguishing artifacts from genuine results or one phenomenon from another, identifying normal precipitating, inhibiting, and modulating conditions, and detailing the amount of variation possible for a phenomenon to exhibit (Craver and Darden 2013). In most of these situations, evolvability plays a role as the *target* of characterization by representing what the phenomenon is, the conditions that permit its manifestation, or how it differs from other biological phenomena. For example, characterizing evolvability as "the ability of a population to respond to directional selection" helps to distinguish a capacity for phenotypic change from the strength and direction of selection. An elaborated conception from quantitative genetics in terms of additive genetic variance provides a specific characterization of the causal basis of evolvability and details how it and directional selection operate as separate factors that result in phenotypic change (Hansen 2006).

A number of different characterizations of evolvability are present in the scientific literature (Nuño de la Rosa 2017; Pigliucci 2008a). These characterizations often focus on different features in need of investigation. A conception of evolvability as "the capacity of a developmental system to evolve" (Hendrikse et al. 2007, 394) points to the relevance of properties of development; a conception of evolvability as "the ability of a population to respond

to natural or artificial selection" (Houle 1992, 195) highlights the role of population and variational structure. A particular characterization can perform useful conceptual work by implying that research needs to pay specific attention to some feature, such as the generation of *novel* or *adaptive* phenotypic variation.

Evolvability as a target of characterization can involve specifying the conditions under which it can be precipitated or distinguishing alternative features that contribute to its occurrence. Different aspects of cellular processes and developmental mechanisms can contribute to evolvability, including weak regulatory linkage, compartmentation (modularity), and exploratory behavior (Kirschner and Gerhart 1998, 2005). For example, exploratory behavior can generate many potential phenotypic states and operate on many levels of organization, from the growing and shrinking of microtubules in a cell (permitting different cell shapes) to an initial overabundance of axons and synaptic connections during nerve growth followed by competitive axon pruning (resulting in functional innervation). Developmental processes exhibiting exploratory behavior permit the evolutionary generation of novel, functional phenotypes, such as muscles of a limb with a modified structure still being reliably innervated.

Theoretical and simulation approaches to evolvability also engage in characterization. The evolutionary roles of robustness and phenotypic plasticity have been investigated theoretically using computational models (Draghi 2019; Wagner 2005), which illuminates how these properties can contribute to evolvability. For example, theoretical analyses about the manifestation or maintenance of evolvability in hypothetical populations can ascertain whether the range of genetic variation within populations can be increased by phenotypic plasticity or if plasticity is maintained under repeated rounds of selection (Draghi and Whitlock 2012).

2.3 Explanation

Although evolvability seems to be an obvious candidate for playing a role as an explanatory *tool*

in evolutionary biology, it was largely treated as a background condition in the past because classical models presupposed the presence of variation responsive to natural selection. Research on evolvability moved to the foreground because researchers recognized that it was a non-trivial assumption—species and characters differ in their ability to respond to selection. Evolvability now plays a role as both target (*explanandum*) and tool (*explanans*) in evolutionary explanations (Wagner and Draghi 2010).

As the *target* of different explanatory projects, explaining evolvability might refer to identifying general properties of evolvable systems, such as their robustness or modularity, or unraveling the causal basis of the differential capacities of traits to evolve, such as additive genetic variance in quantitative genetics or developmental properties in evo-devo. For instance, pleiotropic relationships between floral and vegetative pigments account for the evolvability of floral color, resulting in diversification (Armbruster 2002). Alternatively, the goal can be to understand evolvability as a result of evolutionary principles, such as direct selection for a group-level adaptation, the accumulation of neutral changes in complex genomes, or indirect selection acting on phenotypic traits or their underlying developmental architecture (Hansen 2011).

Evolvability is used as a *tool* to explain a wide range of evolutionary phenomena, ranging from the plausibility of life (Vasas et al. 2012), the evolution of complexity (Wagner and Altenberg 1996), and metazoan diversification (Gerhart and Kirschner 2007), to specific evolutionary pathways. Evolvability is an explanatory tool for a variety of evolutionary trajectories in specific traits, including body shape (Bergmann et al. 2020), the stability of wing shape compared to the lability of life history traits in *Drosophila* (Houle et al. 2017), or differences between vegetative and floral traits (Pélabon et al. 2011).

These different situations can be understood in terms of distinct meanings for scientific explanation. Evolvability explanations found in quantitative genetics conform to the covering-

law model of scientific explanation (Hempel 1965), where phenomena (e.g., the evolution of a quantitative trait) are explained by subsuming them under law-like generalizations (e.g., the Lande equation; Lande 1979). In contrast, evolvability explanations in experimental approaches involve mechanistic reasoning, where explaining a phenomenon means breaking it down into interacting parts that are organized to produce, underlie, or maintain it (Craver and Darden 2013; Sterelny 2011). These evolvability explanations need not refer to actual mechanisms but can capture a space of possible and plausible changes and behaviors that arise from diverse causal processes (Austin and Nuño de la Rosa 2021; Brigandt 2015a; Nuño de la Rosa and Villegas 2019). For instance, robustness can facilitate evolvability by means of the accumulation of hidden variation, but this can be achieved by different mechanisms. Thus, using evolvability as an explanatory tool is relevant to both actual changes a trait underwent and changes it *could* potentially undergo (e.g., in response to various selection differentials or mutation rates; see Chapter 3).

This variety of legitimate conceptions of explanation helps to account for the existence of different approaches to explaining evolvability (target) or using evolvability to explain other evolutionary phenomena (tool). Scientific theories, concepts, and models are only explanatory in a context-dependent fashion (Woodward 2014). Explanations of evolvability take different forms depending on the investigative approach used and the type of question addressed, often in a discipline-dependent manner, just like scientific explanations in other domains.

2.4 Prediction

Researchers often want to predict the evolutionary trajectory of a biological system. The activity of prediction involves inferences from models, theories, and empirical knowledge about a phenomenon to some unobserved empirical fact. In some models of explanation, an explanation and a prediction have the same logical structure, but the ability to quantitatively predict need not

yield mechanistic explanations—explanation and prediction are often decoupled (Scriven 1959). This demands a separate treatment of prediction as a scientific activity where evolvability can play a role.

Inferring unobserved facts fulfills at least two distinct aims in scientific practice. First, predicting specific outcomes can serve as a basis for guiding future action, like intervening on a phenomenon to achieve different goals, such as designing artificial selection experiments or making policy recommendations with respect to environmental problems. Second, predictions are associated with the testability of hypotheses and models (e.g., Popper 2002 [1963]). A good scientific model is expected to make specific predictions that are empirically testable. If these fail, they point to difficulties with the model that require revision. Hypotheses and models about evolvability are often tested by comparing experimental results with specific predictions.

Evolvability can play a role as the *target* of predictions. Sometimes, rather than directly measuring evolvability, evolutionary biologists infer the evolutionary capacity of systems from prior knowledge. For example, robustness measures are a good proxy (and therefore predictive) of the evolutionary potential (i.e., evolvability) of the RNA virus φ6 under thermal stress in experimental studies (Ogbunugafor et al. 2009). In addition, scientists may want to predict changes in evolvability when some conditions of the system vary. For example, multilinear models of the G-P map predict changes in evolvability on the basis of the type of directional epistatic interactions, whether positive or negative (Carter et al. 2005; Hansen et al. 2011).

Evolvability is also an important *tool* for prediction as a part of a well-developed theoretical model that allows for precise measurement (see Chapter 10). There are at least two domains where evolvability measures fit this criterion: quantitative genetics and evolution on neutral networks. In quantitative genetics, a trait's evolvability is a measure of the capacity of that trait to change its phenotypic value in response to directional selection in a population. This enables researchers to predict mean phenotypic change of a trait under specific selective pressures, such

as wing shape divergence among *Drosophila* species under directional selection (Hansen and Houle 2008). Crucially, evolvability can be a tool in predictions that test evolutionary hypotheses, such as whether there are differences in the evolutionary potential of life history traits and morphology (Hillesheim and Stearns 1991; Houle 1992; Price and Schluter 1991). Similarly, it can play this role in guiding future action, such as the degree of resiliency and adaptability to drastic ecological changes within conservation biology (Gienapp et al. 2017) or the evolutionary dynamics of drug resistance in the context of medical research (e.g., Polster et al. 2016).

Neutral network approaches also have sufficiently developed theoretical models to facilitate evolvability playing a role in prediction. In this orientation, evolvability is a measure of the ability of a system to produce heritable phenotypic variation (Wagner 2008). From this measure, one can predict the ratio of evolutionary change provided that one explicitly models the structure of the genotypic space and mutation rates. Examples include making predictions about microbiome ecological interactions relevant to the development of medical treatments (Widder et al. 2016) or gene regulatory circuit evolution (Payne et al. 2014).

Sometimes predictions do not refer to future events but unobserved past ones and are distinguished as *retrodictions*. Retrodictions are important for reconstructing the evolutionary past, especially within macroevolutionary studies of evolvability, and can be an indicator of the predictive potential of a model. The quantitative genetics sense of evolvability can play a role in macroevolutionary retrodictions when phenotypic matrices are used as a proxy for genotypic matrices (Hunt 2007). This facilitates evaluating particular theoretical models of evolution using fossil record data (Love et al. 2021). However, the extrapolation of these measures to macroevolutionary retrodictions is contested because the parameters measured in extant populations over geological time spans can be unstable. For example, patterns of body size evolution in the fossil record diverge depending on different time scales used in analyses (Uyeda

et al. 2011). Yet there is growing evidence that evolvability can predict patterns of macroevolution at surprisingly long time scales, such as standing genetic variation within a population of *Drosophila melanogaster* being strongly correlated with phenotypic divergence across 40 million years of evolution in Drosophilidae (Houle et al. 2017).

2.5 Control

That evolvability can be used to make predictions suggests it might play a role in the activity of *control*, either to better understand natural systems or create novel artifacts, features, or processes. The former can be seen for studies of evolvability where aspects of its causal basis can be manipulated, either experimentally or in simulation, thereby playing a role as a *target* of control. In simulations, the manipulation of a G-matrix under the same selection gradient conditions can result in different kinds of evolutionary divergence (Jones et al. 2018). Similarly, perturbations of the connectivity of molecular networks in computational models facilitate the identification of network topology changes that confer increased evolvability on some genotypes (Ancel and Fontana 2000). The latter can involve limiting evolvability through genetically engineering pesticide resistance in crops or enhancing it by facilitating the spread of genetic variation in a population for purposes of conservation (Campbell et al. 2017). Additionally, when attempting to increase yield-related characteristics of wheat (Nadolska-Orczyk et al. 2017), the correlated change in traits connected by a pleiotropic genetic architecture can be subject to control during breeding.

Protein engineering is another locus for the activity of controlling evolvability (Bloom et al. 2006). This research deploys directed evolution on proteins to achieve particular properties (Bornscheuer et al. 2019). For example, enzymes used in industrial applications are subject to temperatures that often exceed (in both intensity and duration) those found in natural biological systems. Creating more thermostable enzymes via directed evolution permits more efficient and

widespread use of them in these applications (Rigoldi et al. 2018). This involves theoretical tools familiar to evolutionary biologists in order to identify trade-offs (e.g., fitness landscapes), such as between stability and solubility due to stabilizing mutations on the protein surface that increase hydrophobicity (Broom et al. 2017).

Evolvability can also be the target of control in conservation biology. One strategy for species preservation is to maintain the adaptive potential of populations for evolution through breeding protocols, either by mating genetically dissimilar individuals to increase genomic variation or stabilizing beneficial gene complexes through inbreeding (Allendorf et al. 2010). The overall effect is to maintain or increase levels of additive genetic variance. The manipulation of these forms of variation relevant to evolvability, rather than just variation *per se* (some of which might be neutral rather than adaptive), can lead to more effective conservation efforts and avoid unintended outcomes (Campbell et al. 2017).

3 Interrelationships between Conceptual Roles

Thus far we have treated each of the scientific activities where evolvability plays a conceptual role independently (see summary in Table 1). However, different conceptual roles are often present simultaneously across activities and, more importantly, bear significant relationships to one another. For example, in certain contexts a predictive model can be considered to explain the phenomena it predicts (see above, Section 2.4). Sometimes predictions may refer to already observed data that can be fit into a particular model or theory for explanatory purposes. Thus, predictive accuracy can be a measure of explanatory power, such as in quantitative genetics, where the ability of V_A to predict the response to selection is taken as evidence of additive variation explaining short-term evolvability. Similarly, failure of prediction also can guide the search for a better explanation. Problems with V_A predicting the evolvability of a population over longer time periods might indicate that mechanistic accounts of changes in the structure of G-P

maps are needed to complement statistical descriptions that typically figure in evolutionary genetics (Chapters 10 and 11; Hansen 2006).

[Insert Table 1 here]

Controlling evolvability through directed evolution increases understanding of what kinds of properties promote the ability to evolve and therefore can have an impact on characterization and explanation. For example, studies in protein engineering have demonstrated that the evolvability of proteins is facilitated by thermodynamic stability that engenders mutational robustness (Bloom et al. 2006; Tokuriki and Tawfik 2009). Even though the activity of control emphasizes what can be created or made experimentally, such as an enzyme with specific catalytic properties, researchers engaged in this manipulation are also concerned with prediction. Synthetic biologists aim to predict in order to control how biological artifacts will behave outside laboratory conditions or in unforeseen environments. Success in the manipulation of evolvability correlates with advances in prediction. Similarly, the manipulation of particular genetic aspects of a developing organism can lead to a more precise account of what evolvability is (i.e., its characterization), as well as to a better explanation of its causal basis (see Section 2.3).

Additionally, there are cases where characterizing evolvability more precisely increases the capacity of researchers to control it. A richer characterization of evolvability also provides a clearer conception of what is in need of explanation (i.e., evolvability as a target). It therefore has the potential to yield better resources for using evolvability to explain patterns of trait origination or distribution in a lineage (i.e., evolvability as a tool). Different characterizations of evolvability can lead to different preferred explanations. If we characterize evolvability as the robustness of a trait as represented by a neutral network, which confers a greater capacity for exploring phenotypic space, we may explain it in terms of the evolution of resistance to genetic perturbations (Wagner 2008). Different characterizations of evolvability also help to shape an investigative agenda, providing structure to the research questions that evolutionary biologists

ask (e.g., "can we predict how a trait will evolve under the manipulation of a particular genetic variable, which was determined to be a key contributor to modularity?").

Despite the existence of many connections among different conceptual roles of evolvability, these connections are not deductively necessary. A good prediction does not necessarily yield a good explanation and *vice versa*. First, one can make successful predictions without adequate explanations. Modularity might be a good predictor of evolvability, but this does not mean that it necessarily explains it in all circumstances (see Chapter 10). Speciation rates might be good indicators of evolvability (Rabosky et al. 2013), but they do not provide an explanation of why some lineages diversify at higher rates than others. Generally, predictions of an outcome based on a quantitative model often fall short of a mechanistic explanation that would capture all relevant components that causally generate the outcome. Second, one can explain without prediction. Evolutionary biology can provide good explanations of past evolutionary events, but be unable to offer good predictions of the evolutionary future due to unpredictability entailed by historical contingency (Blount et al. 2018; Scriven 1959). Manipulating a protein to increase evolvability does not automatically translate into more robust or precise predictions about population-level responses. Conversely, the ability to predict a trend under certain circumstances may not afford increased capacity to manipulate current conditions. The characterization of different contributors to evolvability (e.g., distinguishing modularity and phenotypic plasticity), whether through theoretical modeling or experimentation, does not immediately yield an explanation for *how* they make this contribution. Setting a research agenda shapes what counts as an explanation, organizing the lines of inquiry necessary to formulate an adequate account of evolvability, but it does not select from among the candidate explanatory factors or determine how they combine to provide an appropriate explanation. And having a good candidate explanation for evolvability with strong empirical and theoretical support does not mean the task of characterization is finished. Further exploration of the properties of developing organisms and

aspects of population structure has the potential to reveal hitherto unknown dimensions of what evolvability is.

We label the existence of natural but not necessary connections among conceptual roles *quasi-independence*. This quasi-*independence* of roles in different scientific activities makes it possible for progress to occur differentially across the diverse landscape of research into evolvability. Biologists can advance in understanding evolvability with respect to prediction but not necessarily with respect to explanation. Similarly, advances may occur in one approach to explaining evolvability but not others. *Quasi*-independence of conceptual roles means that different lines of research can sometimes exhibit correlative progress. Advances in our characterization of what evolvability consists of can be linked to advances in our abilities to predict or manipulate evolvability. Critically, quasi-independence makes it possible for different disciplinary approaches to favor or emphasize one or more roles or scientific activities over others. Evo-devo has tended to focus on the characterization and explanation of evolvability, largely leaving aside predictive and control aspects. This also implies that roles and their associated conceptions in different activities are not in direct competition and therefore can coexist in evolutionary biological research. Advances concerning explanation do not require a trade-off in progress with respect to prediction.

One final corollary of quasi-independence is that no role is necessarily more fundamental than another. As a consequence, there is not an expectation that a single scientific activity will predominate. If we achieve an adequate explanation of evolvability, this would not preempt evolvability's distinctive conceptual roles in prediction, characterization, or control. This is because what it means to explain a phenomenon varies across biological fields and research questions, and because the aims and means of prediction, characterization, or control cannot be reduced to those of explanation. The quasi-independence among roles and activities also suggests that no characteristic orientation (e.g., mechanistic explanation as an approach's central

aim) or preferred conception of evolvability is primary.

4 Implications for Unification

Evolvability is present in most, if not all, branches of evolutionary biology even if it appears in a scientific activity under the guise of different conceptions or roles. Thus, the extent to which evolvability might help to unify partially rests upon the extent to which evolutionary biology is a unified discipline. Although a potential synthesis across evolutionary approaches is being discussed in some contexts (e.g., Pigliucci and Müller 2010), the fields that compose evolutionary biology are diverse in their goals and methodologies. The evolvability concept also reflects this situation, with specific combinations of conceptions and roles falling along natural divisions among disciplinary or methodological approaches (Nuño de la Rosa 2017). A classical view of science identifies its progress with theory unification across domains. However, exploring the unificatory potential of conceptual roles across activities rather than aiming to reduce all of them to one fundamental theory seems a more promising avenue for understanding the relationships between these different approaches in evolutionary biology (Brigandt and Love 2012).

   Among the activities where evolvability plays a role, *prediction* stands out for its degree of theoretical development, especially within quantitative genetics. This follows from a precise mathematical characterization that can be obtained from measures in artificial and natural populations. For example, evolvability measures have been used to predict wing shape divergence in *Drosophila* species (Hansen and Houle 2008). However, this does not imply that evolvability should *primarily* play a role in the activity of prediction. The quasi-independence of conceptual roles for evolvability implies that success as a tool of prediction need not indicate or anchor achievements elsewhere across different disciplines.

Importantly, quasi-independence is not inconsistent with some scientific activity where evolvability plays a role serving as a basis for *unification* across different disciplinary approaches (without privileging any single approach). If one role can spur investigation by fostering organization among different approaches and research questions, then quasi-independence implies that this unifying capacity can manifest without making other roles that evolvability plays in different activities irrelevant. Although *prediction* is the activity where a role for evolvability is the most mathematized, we hypothesize that it does not have the most potential for unification across different disciplinary approaches. Instead, we hold that the activity of *setting a research agenda*, where evolvability plays a key role as a tool for structuring research, has the most unificatory promise.

When asking whether the concept of evolvability can play a unifying role, one needs to keep in view that there are different kinds of unification. One possibility is unifying the diverse *definitions* of evolvability. One fruitful attempt at such a *definitional unification* (Houle and Pélabon in Chapter 10) argues that all conceptions of evolvability assume it is "the disposition of a population (or higher-level entity) to evolve." Researchers are positioned to undertake meaningful measurements that estimate the disposition of evolvability in empirical cases when the relevant features that evolve (i.e., evolvability *of*) and the applicable conditions *under* and time scales *over* which evolution takes place are delineated.[2] This definitional unification shows one way in which evolvability could serve to unify evolutionary research; it yields an abstract scheme that encompasses many concrete definitions found in the literature (see Figure 1). Different conceptions simply focus on different, concrete "of-under-over" aspects: evolvability *of* a quantitative trait *under* directional selection *over* multiple generations versus evolvability *of* new phenotypic variants *under* mutation in a certain developmental architecture *over* millions of years. Although this framework offers a good strategy for measuring evolvability because it is characterized in a number of different disciplinary contexts, it does not provide a framework for

linking together different research questions (e.g., how explanations of short-term evolvability connect with explanations of long-term evolvability) or scientific activities (e.g., how the short-term prediction on the basis of V_A is related to the mechanistic explanation of evolvability).

[Insert Figure 1 here]

Independently of the success or failure of unification based on a common, abstract characterization of evolvability or the development of measures that predict both short term and long term phenotypic divergence, evolvability can unify in a different sense. The capacity to connect different scientific questions, fields, or approaches can be labeled *disciplinary unification*. The historical rise of scientific discourse about evolvability helped to synthesize investigations across research traditions that previously had been largely unrelated. This corresponds to the activity of setting a research agenda. A concept that sets a research agenda not only motivates further scientific efforts but also structures ongoing research and coordinates disciplinary contributions. This is because the agenda represented by the concept consists of many component questions, which are related in systematic ways (Section 2.1), such as the amount of phenotypic variation that can be generated and biases in the direction of variation (Hendrikse et al. 2007).

Figure 2 offers one illuminating (if incomplete) perspective on the structure of the problem agenda associated with evolvability. Although there are other ways of articulating the landscape of evolvability research (see Figure 1 in Houle and Pélabon Chapter 10), any account will have the agenda-setting benefit of mapping out some connections among fields and approaches. Figure 2 captures disciplines, phenomena, and clusters of questions in evolvability research. This makes it possible to display several patterns of existing research, such as evo-devo inquiry into developmental phenomena relevant to phenotypic variability (e.g., the modularity of the G-P map). At the same time, the figure not only includes phenotypic variability, phenotypic variation, and actual evolutionary change as phenomena directly germane to evolvability research, but it

also depicts how they are related to each other and other phenomena. Variation, including the covariation among different characters, can be measured in actual populations. Together with additional factors, such as selection, theoretical models can then predict the resulting microevolutionary change. However, if one wants to understand what leads to and accounts for patterns of phenotypic variation, further issues need to be investigated. In addition to the impact of population processes on variability (e.g., mating systems, population size), the potential for phenotypic variability has to be dissected in terms of the structure of the G-P map (e.g. modularity, robustness), all of which can be enriched by an investigation of epistatic patterns and the underlying developmental architecture. By foreshadowing how these different contributions from evolvability research can be connected, the concept of evolvability sets a research agenda that coordinates various scientific efforts.

[Insert Figure 2 here]

Perhaps most significantly, Figure 2 provides a map of the involvement of different *disciplines* and how these investigative approaches are related in evolvability research. Quantitative genetics focuses on the role of phenotypic variation, while population genetics and ecology are needed to understand how variability leads to realized evolutionary change. Evo-devo encompasses work on the developmental architecture that underlies phenotypic variability, whereas developmental evolution forges links with quantitative and population genetics. Comparative biology and paleontology are needed to investigate long-term trends and rates of actual evolutionary change; computational approaches have relevance across the whole loop of evolutionary phenomena relevant to evolvability (e.g., understanding the impact of neutral networks and robustness or simulating microevolutionary dynamics). This shows in rich detail how the agenda-setting role of the concept of evolvability can have a unifying effect by linking disciplines and mapping out connections among scientific contributions provided by different approaches.

The disciplinary landscape generated by evolvability research differs from those offered by other classical concepts, such as natural selection or developmental constraint. While the notion of selection synthesized a manifold of disciplines, it left out the role of development and physiology in structuring phenotypic variability (see Fig. 2, rectangle enclosed by a red dashed line). The concept of developmental constraint set a research agenda in the 1980s that involved biologists from several fields, including developmental biology and paleontology (Brigandt 2015b). At the same time, the notion of constraint had negative connotations for many evolutionary biologists (Arthur 2015). For example, constraint-based explanations were sometimes viewed as emphasizing the limiting aspects of development and as competing with or even excluding selection-based explanations (Amundson 1994). In contrast, the increasing prominence of the concept of evolvability in the 1990s had the advantage of setting a *positive* research agenda about the generation of variation and effecting evolutionary transformation, which included fields that rely on the notion of selection, such as quantitative genetics and population genetics. Indeed, the evolvability agenda has given rise to new research questions such as variational modularity or conditional evolvability (Hansen and Houle 2008).

It is crucial to see that Figure 2 also represents the ongoing nature of the evolutionary process, including how evolvability itself evolves (by means of a feedback loop). This suggests that there is no single, preferred starting point for evolvability research, where one discipline would have to conclude its research before others could initiate or contribute, or where one approach would be the most basic without needing explanatory resources from other disciplines. Although there may well be alternative and equally legitimate representations of how various components are structurally organized in evolvability research (e.g., mating systems are not represented in Figure 2), this does not detract from the fecundity of this version of disciplinary unification. In fact, the pursuit and construction of different representations of the research agenda of evolvability are likely to help establish more points of contact between the diversity of

approaches involved, thereby augmenting the role this agenda-setting strategy can play in unifying evolutionary biological investigations around the concept of evolvability.

*   *   *

We began our analysis with the observation that variation in the conceptualization of evolvability within research likely plays some functional *role* in the reasoning endeavors of scientists. To grapple with the significance of this observation, we examined evolvability in five different activities where a concept can play a role: setting a research agenda, characterization, explanation, prediction, and control (Section 2). Having canvassed a wide-ranging landscape of conceptual behavior for evolvability, we interrogated how different activities in combination with different roles and conceptions of evolvability can be related to one another or are jointly operative in diverse ways because of their quasi-independence (Section 3). In closing, we addressed the question of whether and how evolvability might play a unifying role in evolutionary biology by distinguishing different forms of unification and describing two candidate strategies: definitional unification and disciplinary unification (Section 4). Although we argued that the latter appears to harbor a more encompassing basis for unification across many fields and approaches in evolutionary biology (based on the research agenda setting role), the value of our analysis stands independent of this claim. Explicit scrutiny of the conceptual roles that evolvability plays in contemporary evolutionary biology helps to show how a rich and variegated space of possibilities can be utilized by researchers to facilitate fruitful interdisciplinary lines of investigation and thereby yield a deeper understanding of evolvability.

Acknowledgements

Notes

1. Many central concepts in biology have several interpretations and appear to display multiple roles across contexts; this is not a situation unique to evolvability. Most famous of these is "species" (Hey 2001), whose variations align with distinct activities and conceptual roles (Kitcher 1984), such as a phylogenetic species concept being used as a tool to characterize taxon boundaries, the biological species concept explaining how new species originate, or an ecological species concept acting as a tool for predicting distributions of taxa in a particular

biota. Similar patterns are observable for concepts outside of biology (e.g., "hardness" in material science; Wilson 2006).

2. Although this has some similarities to the philosophical response of providing a core meaning for the concept of evolvability noted in the introduction, it is different because the unification is done for a particular scientific aim: measurement. As a consequence, this definitional unification does not yield a characterization of what the evolvability concept could or must mean in any and all investigative contexts.

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Table 1

Examples of the concept of evolvability being used as a tool or

target in different scientific activities

	Setting a research agenda	Characterization	Explanation	Prediction	Control
Evolvability as a tool	Maps out the structure of collaborative research		Explains the evolution of complexity	Predicts evolutionary trends	
Evolvability as a target		Construing evolvability in terms of additive genetic variance	Exploratory behavior explains evolvability	Robustness measures as proxy for evolvability	Creating more thermostable enzymes

EVOLVABILITY
OF a trait mean,
UNDER directional selection,
OVER one generation

EVOLVABILITY
OF some entity,
UNDER a certain condition,
OVER a particular timescale

EVOLVABILITY
OF discrete states,
UNDER genetic drift,
OVER a hundred generations

EVOLVABILITY
OF a G-P map property,
UNDER fluctuating selection,
OVER thousands of generations

EVOLVABILITY
OF a novel trait,
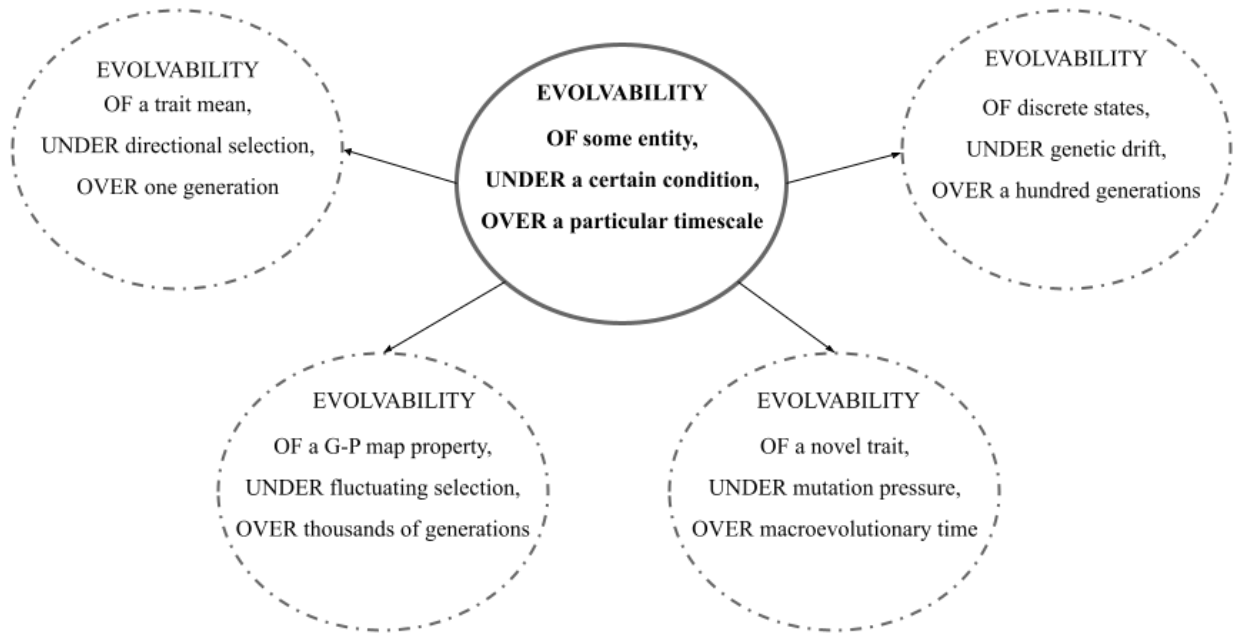UNDER mutation pressure,
OVER macroevolutionary time

Figure 1

Definitional unification. Understood as a measurable disposition, this schema

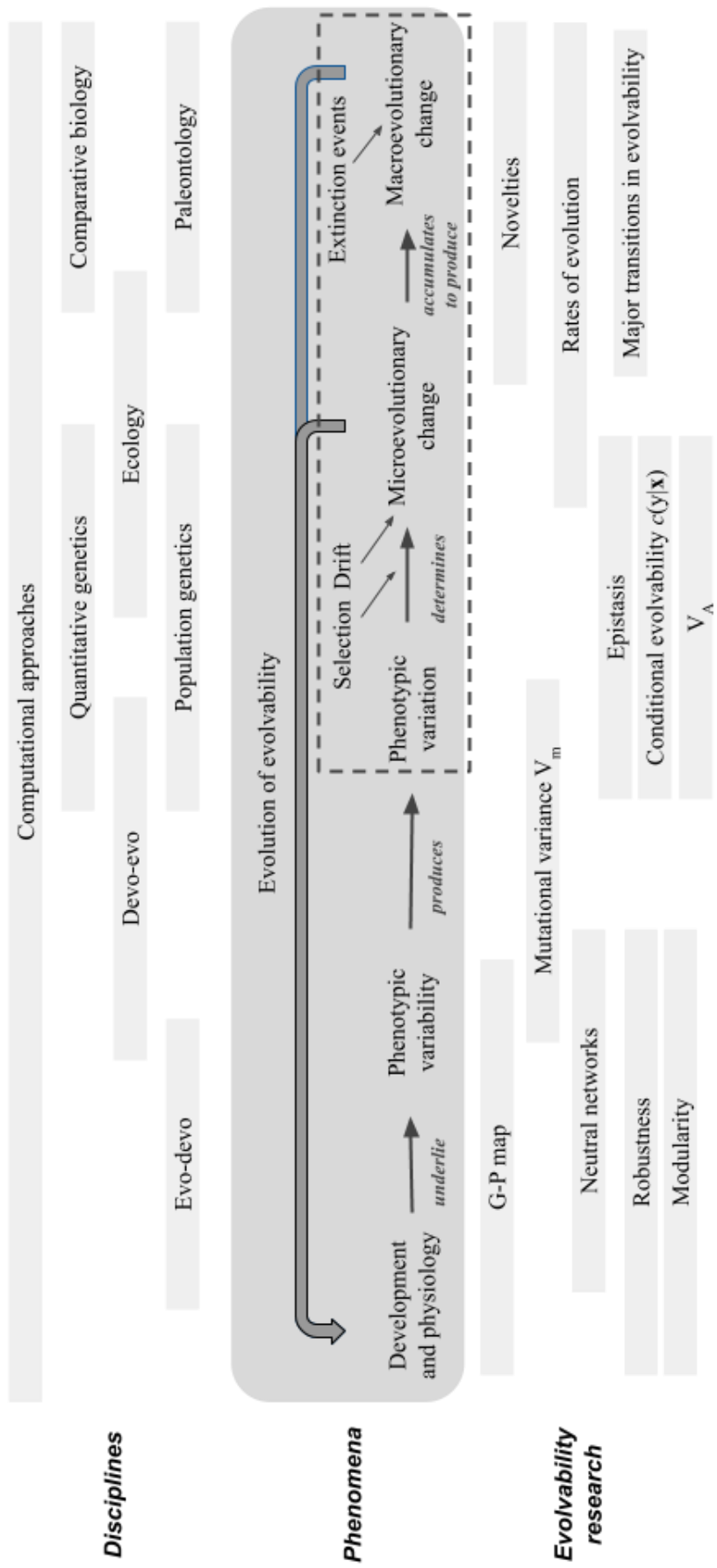intends to unify different conceptions of evolvability (see Chapter 10).

Disciplines

Computational approaches

Comparative biology

Quantitative genetics

Paleontology

Ecology

Devo-evo

Population genetics

Evo-devo

Phenomena

Evolution of evolvability

Development and physiology

underlie

Phenotypic variability

produces

Selection Drift

determines

Phenotypic variation

Microevolutionary change

accumulates to produce

Macroevolutionary change

Extinction events

Evolvability research

G-P map

Mutational variance V_m

Neutral networks

Robustness

Modularity

Epistasis

Conditional evolvability $c(y|\mathbf{x})$

V_A

Novelties

Rates of evolution

Major transitions in evolvability

Figure 2

Evolvability as a multidisciplinary research agenda. Different disciplines representing different approaches to evolvability are keyed to phenomena on different time scales that bear specific relationships to one another. These disciplines and phenomena also exhibit correspondence with questions found in evolvability research, such as the G-P map, conditional evolvability, or major transitions in evolvability. The dashed rectangle represents the classical picture of evolutionary research before the evolvability research agenda developed.