CellPress
REVIEWS

Opinion

# Evolvability Costs of Niche Expansion

Lisa M. Bono,[1] Jeremy A. Draghi,[2,3,4] and Paul E. Turner[5,6,*]

**What prevents generalists from displacing specialists, despite obvious competitive advantages of utilizing a broad niche? The classic genetic explanation is antagonistic pleiotropy: genes underlying the generalism produce 'jacks-of-all-trades' that are masters of none. However, experiments challenge this assumption that mutations enabling niche expansion must reduce fitness in other environments. Theory suggests an alternative cost of generalism: decreased evolvability, or the reduced capacity to adapt. Generalists using multiple environments experience relaxed selection in any one environment, producing greater relative lag load. Additionally, mutations fixed by generalist lineages early during their evolution that avoid or compensate for antagonistic pleiotropy may limit access to certain future evolutionary trajectories. Hypothesized evolvability costs of generalism warrant further exploration, and we suggest outstanding questions meriting attention.**

## Why Do Generalists Coexist Alongside Specialists?

Humans have long sought mechanisms to explain the teeming biodiversity on Earth. Prehistory abounds with creation myths, and ancient Greek philosophers proposed evolutionary explanations [1,2] long before Darwin articulated that natural selection was a process that could explain changes in population and species diversity over time. Today, mutations are understood as the raw variation fueling natural selection to explore phenotypes that best capitalize on limited resources. As this process unfolds across varied environments, populations may diverge sufficiently to become distinct species represented within the total biota on Earth.

However, it is unclear why this process should cause Earth to be speciose. Given the obvious benefit that should come from utilizing diverse resources, what prevents populations and communities from being dominated by **generalists** (see Glossary)? Rather, generalists (variants or species evolved to expansively occupy broad niche spaces) tend to coexist alongside **specialists** [competitors that specifically use few (or even single) resources] [3]. The observation that generalists do not universally outcompete specialists clearly suggests that generalists must suffer at least occasional fitness costs to counter the advantage of occupying a broad niche, otherwise generalists should dominate ecosystems [4–6].

The classic assumption is that a 'jack-of-all-trades is a master of none' [7], with costs of generalism emerging from genetic trade-offs. Specifically, this trade-off takes the form of **antagonistic pleiotropy**, which occurs when a mutation in a single gene controlling multiple traits improves fitness in one trait while simultaneously reducing fitness in another trait. In terms of generalism, antagonistic pleiotropy occurs when fitness gains in one environment are at the cost of lower fitness in another environment [8]. Such mutations can explain how a generalist 'ecotype' can evolve to occupy a broad niche space, while also performing worse than specialist ecotypes in the populations that excel in using specific portions of the niche. A familiar analogy is a Swiss Army knife that generally performs many tasks but may be outperformed in any one task by a specialized tool, such as a can opener. If antagonistic pleiotropy is an unavoidable consequence of constraints on performance, then this hypothesis could explain why generalists and specialists coexist within ecosystems. (We note that neutral mutations accumulated in one environment can also cause fitness to decline due to their deleterious effects in alternative environments; however, this process is not our focus because **evolvability** has more to do with evolutionary change driven by natural selection and less by genetic drift, whereas mutation accumulation tends to concern the relative importance of drift over selection.)

However, convincing evidence for the importance of antagonistic pleiotropy as a generic explanation for constraints on generalism has been difficult to detect empirically, suggesting (but not confirming) that the presumed costs are rare or do not universally account for the coexistence of generalists and

## Highlights

Given the obvious benefit from utilizing diverse resources, what prevents populations and communities from being dominated by generalists? Classical explanations hold that a 'jack-of-all-trades' is a master of none, meaning that niche-expanding mutations decrease fitness in the original environment (antagonistic pleiotropy).

We suggest an alternative cost to generalism: reduced evolvability. Generalists experience selection in multiple environments, relaxing the effects in any one environment, and forcing adaptive mutations through multiple environmental filters or compensatory mutations. These factors lead to generalists experiencing lag load, conceptualized as a more rugged fitness landscape.

Although this hypothesis has not been tested explicitly, we provide evidence for the elements of it from models of eco-evolutionary dynamics and experimental evolution.

[1]Department of Ecology, Evolution, and Natural Resources, Rutgers, the State University of New Jersey, New Brunswick, NJ 08901, USA

[2]Department of Biological Sciences, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA

[3]Department of Biology, Brooklyn College, City University of New York, Brooklyn, NY 11210, USA

[4]Program in Ecology, Evolutionary Biology and Behavior, Graduate Center, City University of New York, New York, NY 10016, USA

[5]Microbiology Program, Yale School of Medicine, New Haven, CT 06510, USA

[6]Yale University, Department of Ecology and Evolutionary Biology, New Haven, CT 06511, USA

*Correspondence: paul.turner@yale.edu

 https://doi.org/10.1016/j.tig.2019.10.003

specialists [9,10]. Furthermore, the underlying assumption of unavoidable trade-offs may be overly restrictive, ignoring the evidence that compensatory evolution may counter the fitness effects of antagonistic pleiotropy to produce 'no-cost' generalists [11–14]. Thus, even in systems where antagonistic pleiotropy has been detected early during generalist evolution, other genetic mechanisms may ameliorate this cost over time. If trade-offs only slow fitness gains, then why do generalists fail to dominate the ecosystems on Earth?

The 'jack-of-all-trades' hypothesis focuses on competition between species or ecotypes with static ecological properties, rather than emphasizing the process by which species acquire adaptations to their niches. However, ecology and evolution can occur on similar timescales, such that ecotypes can evolve rapidly in response to changing ecological conditions. Under conditions likely to produce eco-evolutionary dynamics, such as temporally fluctuating selection, frequency- and density-dependent selection, coevolution, and niche construction, the fitness of an ecotype reflects a shifting balance between the rates of environmental change and corresponding adaptation. In such a scenario, a broad niche might constrain fitness even in the absence of strong genetic trade-offs. Unlike antagonistic pleiotropy (a true genetically based cost of generalism that reduces fitness in a particular environment), these costs limit the capability of a generalist to keep pace with specialist adaptation. This is selection on evolvability, the capacity to generate variation useful for adaptive change [15–17].

Before summarizing theory and empirical data relating to the idea that generalism is limited by evolvability costs, we first connect this idea to more general explanations of the role of eco-evolutionary dynamics in ecological coexistence.

## Eco-evolutionary Dynamics and the Role of Evolvability in Coexistence

Evolvability has varied roles in theories of coexistence of multiple ecotypes or species, with the rate of adaptive change relative to ecological dynamics emerging as a key axis of this variation. Numerous studies have integrated evolution to model whether ecologically stable communities of multiple species are unsustainable in the face of trait evolution [6,18], unattainable as a result of adaptive evolution from simpler, ancestral communities [19], or unpredictable as a result of chance events during adaptation [20]. The rate of evolution in this type of eco-evolutionary model can be gradual, although some studies examine a continuum from slow to fast. For example, when the speed of adaptation was varied relative to ecological dynamics, faster rates of evolution were more likely to erode community stability in a two-species model with seasonal environmental changes [21].

When evolution is considered to be slow compared with ecological dynamics, then using phylogenetics to study long-term microevolutionary or even macroevolutionary patterns is the relevant framework for thinking about coexistence and evolvability. The balance of generalist and specialist species at the level of ecosystems or biomes depends on rates of extinction and speciation, and these might vary positively or negatively with the degree of specialization [22]. While the longstanding idea that specialist lineages suffer reduced persistence is supported in only a few systems [23], recent work in bacteria has found strong support for the idea that generalists more often give rise to specialists than the reverse [24]. More work will be needed to determine how niche breadth shapes persistence scale over macroevolutionary timeframes (e.g., perhaps maintaining genes that give an individual access to a broader array of niches is more critical for long-term evolutionary success), but we focus on microevolutionary timescales for the remainder of this paper.

Standing in contrast to macroevolution approaches are eco-evolutionary models that specifically invoke rapid adaptation on ecological timescales to predict distinct mechanisms driving coexistence. Eco-evolutionary feedbacks can arise as a key species reshapes its environment and alters selection on itself and other members of the community, provoking rapid evolution in competitive traits [25]. Similarly, models of eco-evolutionary dynamics focus on scenarios in which rapid evolution changes the traits or behavior of a species in the midst of its interactions with other players in an ecosystem [26]. One of the best-documented examples of this type is the evolution of prey defense traits in predator–prey systems. Here, rapid evolution is predicted to change the cyclic relationship between

### Glossary

**Antagonistic pleiotropy**: when a mutation in a gene controlling multiple traits improves fitness in one trait while simultaneously reducing fitness in another trait.
**Evolutionary rescue**: when a population escapes extinction due to genetic adaptation within that population, leading to a change from negative to positive population growth [61,62].
**Evolvability**: the capacity to generate variation useful for adaptive change [15,16].
**Experimental evolution**: direct observation of evolutionary processes in an evolving population, often conducted under controlled laboratory or field conditions [51].
**Generalist**: ecotype or species evolved to expansively occupy relatively broad niche space.
**Lag load**: the difference between the mean fitness of a population and the fitness of the best possible genotype in its current environment.
**Relaxed selection**: reduced or eliminated selection pressure, such that fixation (purging) of beneficial (deleterious) mutations occurs more slowly than expected.
**Specialist**: ecotype or species evolved to occupy relatively narrow niche space.

predator and prey population sizes, leading to phase shifts or instability [27,28]. These predictions have been validated in laboratory microcosms [29–32], inspiring reanalysis of field and laboratory time-series data and revealing a larger role of rapid evolution than previously appreciated [33]. Although competition among species at the same trophic level has received less attention than predator–prey models [26], recent theory also describes systems in which rapid adaptation is an essential stabilizing force enabling coexistence among competitors [34,35]. Coexistence based on purely ecological factors has not been rigorously assessed for most communities [36], leaving open the possibility that a significant role for rapid evolution is the norm.

The varied scales at which evolvability can impact coexistence arise because both the concept of 'evolvability' and of 'coexistence' can be applied to variants within a species, competing species within a community, or members of a broader ecosystem. At the microscale of competing genotypes within a species, differences in evolvability contribute to the fitness of lineages and determine the outcomes of competition between genotypes. At the macroscale, differences in evolvability can contribute to the relative persistence of species, although, at this scale, the concept of 'fitness' is less applicable. Connecting these disparate scales are perspectives such as **evolutionary rescue**, in which population genetics is harnessed to understand how evolvability at the level of a population contributes to the probability of extinction [37], as well as efforts to examine how best to extend the concept of 'fitness' over long timescales encompassing environmental change (e.g., [38]).

## Evolvability Costs of Niche Expansion

When confronted with changing environments, including those happening on pace with rates of evolution, specialists may be capable of faster evolution than generalists, hence preventing generalists from dominating (e.g., [39]). Evolvability can differ in characters that directly influence genetic variance. Evolvability concerns the ability of a population to generate variability, rather than the variability present within the population [40,41]. It can be promoted by individual traits that elevate mutation rate, increase propensity for gene flow with other lineages, and foster genetic robustness [15]. Genetic robustness is the degree of phenotypic constancy in the face of underlying mutations, and can influence evolvability by impacting the ability of the phenotype to access evolutionary innovations [42]. Thus, evolvability can be considered a trait moldable by selection. However, why might generalists be expected to be disadvantaged in evolvability (i.e., evolve slower) relative to specialist ecotypes?

Using the metaphor of fitness landscapes, evolvability can be conceptualized as the ability of a population to ascend pathways up a fitness peak: more evolvable phenotypes may have more trajectories available to them, or be able to climb peaks faster (Figure 1). Given that specialists can fix alleles benefiting performance in one environment regardless of costs elsewhere, their fitness landscapes should be relatively simpler than those traversed by generalists. Conversely, these relatively 'rugged' fitness landscapes of generalists may contain fewer fitness peaks, if generalists are unable to access beneficial mutations accessible to specialists. Alternatively, generalists may require longer evolutionary time to ascend fewer fitness peaks, if compensatory mutations are required to achieve fitness improvement. Thus, some models predict that generalists may suffer reduced evolvability (on average) compared to specialists, but is there evidence of this?

Here, we synthesize modeling results from a variety of approaches to emphasize that generalists and specialists can coexist without having to invoke antagonistic pleiotropy as the driving genetic force. Also, we describe how **relaxed selection** and **lag load** (Box 1) experienced by generalists are consistent with the theoretically predicted disadvantages for a population evolving in a complex environment. Last, we discuss evidence for the idea drawn from **experimental evolution**, but highlight that abundant possibilities exist to further explore the hypothesis.

## Modeling the Effect of Niche Breadth on Selection

All else being equal, adaptive evolution should generally occur faster for populations experiencing relatively stronger selection to adapt to an environmental challenge. Several models, which we

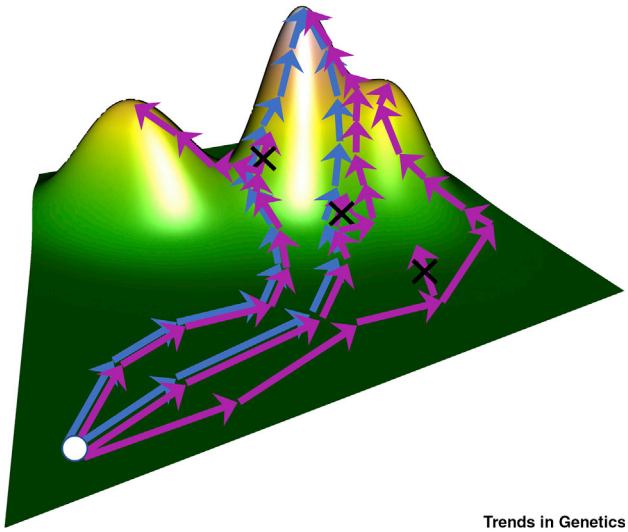


**Figure 1. Comparison between Generalist and Specialist Lineages Derived from a Common Ancestor (White Circle), Evolving on an Adaptive Landscape**

Arrows represent distances traversed on the landscape by evolving lineages, due to individual beneficial mutations. Blue arrows represent hypothetical evolutionary trajectories available to specialists, whereas purple arrows represent those available to generalists. Black 'X' represents a mutation inaccessible to a generalist. Note that some generalist trajectories reach local peaks of lower fitness, rather than ascending the global fitness peak on the landscape. If a generalist successfully reaches the global fitness peak, the path is more circuitous and the trajectory requires fixation of relatively more mutations than those fixed by a specialist (i.e., lag load).

discuss later, have taken a population-genetics approach to explore how distinct ecotypes can experience selection differently and, therefore, achieve differing mean fitnesses in responses to the same environments. Consider a mutation that is beneficial in only one environment within the niche of a species and neutral in other environments; selection will favor this mutation only weakly [43], and its effective selection coefficient will be reduced in proportion to the amount that reproduction in the 'neutral' environments contributes to the next generation [44]. Therefore, generalists can experience relaxed selection on key loci with environment-specific effects. As a consequence of this relaxed selection, generalists may lag behind specialist competitors in their adaptive match to present circumstances [43,45,46], reflecting a deficit in evolvability relative to specialists. While generalists experience relaxed selection, specialists can benefit from stronger selection resulting from positive feedback loops. The strength of selection for a particular environment increases as organisms more frequently experience selection in that environment [46], creating a positive feedback loop. This can arise through organismal preference for a particular environment. When an ecotype is more fit in a specific environment, it will tend to reproduce more often in that environment, reinforcing the ability of selection to operate there [45]. This is particularly pronounced when the environment constitutes a biotic interaction (e.g., associations between hosts and parasites, and host plants and phytophagous insects). Here, the possibility for coevolution (i.e., reciprocal evolution) can cause generalist parasites to suffer lag load (Box 1) in response to the complex selection exerted by interacting with multiple hosts. By contrast, specialists are able to more rapidly respond to changes in host resistance [46]. Similarly, source–sink dynamics can lead to positive feedback loops that reinforce selection in favor of specialists. If a source population of specialists expands its niche into a novel environment, generalists in the novel environment can act as a sink population (deaths exceed births) because of their poor initial levels of adaptation. In this scenario, selection tends to favor improvement in the environment experienced by the greatest number of individuals [44], meaning the specialist source population. These ecological examples illustrate how selection can favor specialists, due to stronger selection relative to that experienced by generalists.

**Box 1. Using Phage φ6 to Explore Evolvability Costs of Generalism**

Key empirical evidence for the hypothesized evolvability costs of generalism stems from studies of niche expansion in dsRNA phage φ6. In the laboratory, this virus typically infects *Pseudomonas syringae* pathovar *phaseolicola* bacteria, whereas host-range mutations can readily expand the niche to include other pseudomonad species. The niche expansion affords competitive benefits via broader resource use, but may be costly for fitness (i.e., worse growth) on the typical host. Many mutations allowing niche expansion show this antagonistic pleiotropy, and experimental evolution of one such mutant led to novel-host specialism, an extreme consequence of inability to infect the original host [63]. However, a subset of host-range mutations led to neutral or even improved fitness on the typical host [54,55]. Overall, these studies show that some (but not all) host-range generalists suffer antagonistic pleiotropy, a departure from theory that assumes generalism causes performance trade-offs.

Further studies examined whether niche expansion in phage φ6 affected evolvability, the capacity to adapt to a novel environment. Both generalist and specialist ecotypes showed ability to adapt to a novel bacterial host (a homogeneous environment), but specialists did so via a greater breadth of mutations [60]. This outcome suggested a relatively larger universe of beneficial mutations was accessible by the specialists, such that prior niche expansion (generalism) constrained future evolution.

Similar experiments involving increased environmental complexity impacted the evolvability costs of generalism and ability for generalists and specialists to coexist. In a heterogeneous environment (both typical and novel hosts present), generalists might evolve compensatory mutations that ameliorate antagonistic pleiotropy, fostering improvement on both hosts [64,65]. Instead, studies showed that generalists suffered an adaptability cost: specialists evolved relatively faster on the typical host [65]. Furthermore, generalists showed lower genetic diversity when evolving in a heterogeneous environment compared with a homogeneous one [59]. During selection to overcome fitness effects of antagonistic pleiotropy in a heterogeneous environment, generalists experienced reduced genetic diversity, thus hampering future adaptive potential.

Taken together, these studies show that even when most niche-expanding mutations incur antagonistic pleiotropy, the nature of the selective environment critically influences evolvability costs of generalism. When considering a broad host range, selection under environmental heterogeneity helps ameliorate antagonistic pleiotropy, but causes fewer mutations to pass through this environmental filter, thus limiting genetic diversity potentially useful for further adaptation. Ultimately, generalists can adapt to a broader niche by overcoming antagonistic pleiotropy, but in doing so, they may suffer restricted access to evolutionary trajectories (reduced evolvability).

One premise of the relaxed selection argument is that mutations are frequently adaptive in one environment but silent in other environments within the range of a species. One way that mutations might have such specific effects is through plasticity in their regulation, such that environmental cues influence the expression of genes and traits, producing one phenotype in a particular environment but another in a different environment. In circumstances where generalists and specialists differ in plasticity, several other effects on evolvability come into play. Plasticity has not only been correlated with evolvability both within populations [47] and at the level of the divergence and persistence of species [48,49], but has also been speculated to slow adaptive responses in some circumstances (reviewed in [50]). These contrasting predictions highlight the difficulties in synthesizing the many perspectives on plasticity (genetic, developmental, population genetic, and macroevolutionary) into a coherent picture of evolvability.

## Evidence from Microbial Experimental Evolution

Empiricists have had a longstanding interest in measuring evolution on ecological timescales, and there has been a tradition of performing such experiments in rapidly evolving microbial systems. Microbes can be evolved experimentally in the laboratory under carefully controlled ecological conditions, while allowing the storage of ancestral and evolved samples for future analysis and sequencing [51–53]. While the effect of niche breadth on evolvability has yet to be explicitly tested, elements of this framework have been studied using experimental evolution. We use examples from microbial systems, because they have several features that enhance measurement of evolvability:

large population sizes, rapid generation times, and indefinite freezer storage. The latter allows microbial genotypes and populations to be conveniently reanimated at any stage of their evolutionary trajectories and to be directly compared in terms of evolved potential, an approach that is more cumbersome or simply absent in other study systems.

## Pleiotropy and Adaptation to Novel Environments

Examining costs associated with niche expansion often begins by assessing the initial mutations that allow a new ecotype to evolve. The classic formulation of the 'jack-of-all-trades' hypothesis assumes that the environment is relatively simple, and that antagonistic pleiotropy is ubiquitous [7]. However, if even a single mutation avoids antagonistic pleiotropy, no-cost generalists can evolve [13]. Thus, a logical first test of this hypothesis is to evolve generalists to assess what portion of the mutations have antagonistic versus synergistic pleiotropy, or are neutral. Such studies found that, while many niche-expanding mutations do have antagonistic pleiotropy, such costs are not universal. For instance, most spontaneous mutations allowing host (niche) range expansion of phage ϕ6 onto additional bacterial host species were costly on the original host (antagonistic pleiotropy). However, a few mutations were nearly neutral or even beneficial on the original host [54,55], indicating that no-cost generalists were possible (Box 1). However, the distribution of mutational fitness effects can vary greatly by novel host with a larger proportion of beneficial mutations in more distantly related hosts (e.g., [56,57]).

Pleiotropic costs are only relevant when an ecotype undergoes selection in multiple environments [10]. Selection can filter mutations only if they are costly in that environment, because selection is blind to costs not faced in the current environment. When an ecotype experiences selection in multiple environments, that filter becomes less porous, allowing fewer mutations to pass through to the next generation (Figure 2). A meta-analysis found that the costs associated with niche-expanding mutations are more likely to be detected when a generalist evolves in a homogeneous rather than heterogeneous environment [58] (see Box 2 for an in-depth discussion). Consequently, when generalists adapt via maintaining a broad niche, selection in a homogeneous environment allows more genetic diversity to be maintained within the generalist population. For instance, when a generalist variant of ϕ6 was evolved on a single host (homogeneous environment), the resulting population harbored greater genetic diversity than when the same generalist evolved in multiple, temporally

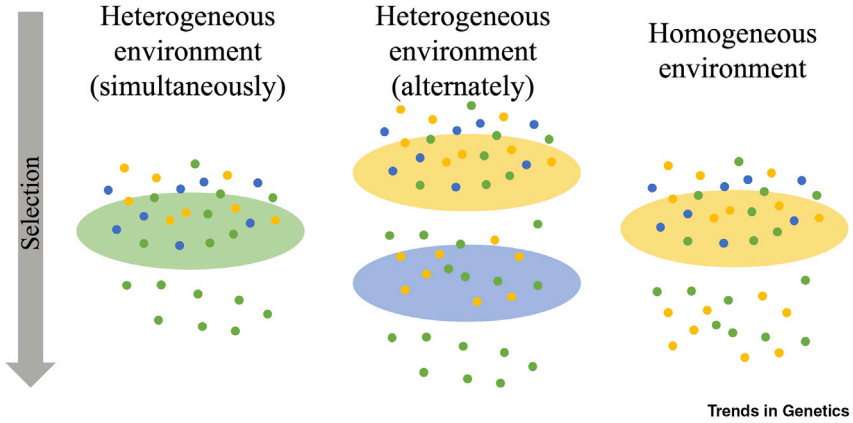


**Figure 2. Selection Only Filters Mutations that Are Costly for a Population in the Current Environment.** Ovals represent the differently labeled selective environments. Yellow circles represent mutations advantageous (or neutral) for the population in the yellow environment but costly in the blue environment, while blue mutations are advantageous (or neutral) in the blue environment but costly in the yellow one. Green mutations are advantageous (or neutral) in both yellow and blue environments. Note that a population undergoing selection in a homogeneous environment has greater genetic diversity (larger number of circles transiting the selective filter) than populations experiencing selection in a constant or temporally changing (e.g., seasonal) heterogenous environment.

**Box 2. How Environmental Heterogeneity Influences Genetic Diversity of Populations**

Generalists can adapt to heterogeneous environments either by adapting to particular aspects of a niche, potentially leading to niche partitioning or local adaptation, or by adapting to all of the environments, maintaining a broad niche [10] (this latter scenario is our main focus throughout this paper). When generalists take the former route, more genetic diversity may amass within the generalist population. As generalists spend more time in a particular environment, mutations with antagonistic pleiotropy are more likely to be fixed rather than purged. Frequency-dependent selection can maintain diversity among populations of generalists in heterogeneous environments [10]. This outcome is more likely in a spatially heterogenous environment, because patchiness may allow generalists to take refuge in favorable environmental conditions in which they have higher fitness while avoiding others where they have lower fitness. Regardless of the type of heterogeneity, generalists that adapt by maintaining a broad niche experience selection in multiple environments, meaning that antagonistic pleiotropy is more likely to be purged, leading to reduced genetic diversity. Given that all phenotypes in temporally heterogeneous environments are exposed to selection in multiple environments, the likelihood that generalists will evolve to a broad niche is increased, although generalists in spatially heterogeneous environments may also adapt by maintaining a broad niche. (We note that these patterns of diversity are not expected to hold when considering neutral mutations that are unlinked from adaptive loci; e.g., [66].)

heterogeneous host environments [59]. This outcome suggests that a generalist experiencing selection in multiple environments has fewer beneficial mutations and more deleterious ones than a specialist experiencing selection in only one of those environments. Alternatively, generalists can fix mutations with antagonistic pleiotropy and later ameliorate the cost via compensatory mutations (Box 3) [58]. Either way, generalists experience greater lag load (Box 1). Ultimately, these early mutations may also constrain potential evolutionary trajectories available to generalists, decreasing their evolvability.

## Evolutionary Trajectories in Microbial Experimental Evolution

While the impact of early mutations on subsequent evolvability has not been examined specifically in the context of generalism, it has been studied broadly over the course of adaptation to novel resources. Since multiple mutations typically allow adaptation, evolution experiments can track replicate lineages that fix different mutations early to assess how those mutations influence long-term

**Box 3. Generalists Experience Lag Load Relative to Specialists**

The lag load experienced by generalists is akin to slower adaptation as a cost to complexity [67]. Orr argued that, even without trade-offs, a higher degree of pleiotropy makes a mutation less likely to be beneficial in a more complex organism. One parallel mechanism by which generalists and complex organisms experience lag load relates to their abilities to fix beneficial mutations. Even in the absence of trade-offs, when specialists and generalists experience mutations of equal size and equivalent strengths of selection, it should be relatively more difficult for generalists to fix beneficial mutations because of relaxed selection when adapting to a broad niche (see main text). First, the beneficial mutations available to generalists may be numerically fewer; within the universe of possible mutations, those of benefit in both the original and alternative environments should be rarer than mutations beneficial in one or none. Thus, specialists only contend with costs in a single environment and face fewer constraints on which mutations are beneficial. By contrast, generalists have to contend with mutational costs in multiple environments and, therefore, experience relatively fewer beneficial mutations and greater deleterious mutations that can fix via drift. Random mutations are less likely to be beneficial in complex genotypes for similar reasons [67–69]. Second, generalists take more time to fix beneficial mutations. The time to fixation for an environment-specific beneficial mutation is related to the proportion of time individuals experience that environment: the longer time occupied in the focal environment, the faster the mutation will fix. Similarly, the probability that a mutation fixes declines as the genotype increases in complexity [67]. Thus, both increased niche breadth and increased complexity intensify lag load. In turn, this lag load also affects evolvability: genotypes with greater lag load have decreased adaptability (by definition) and take longer to climb an adaptive peak (see [70] for further discussion of complexity and evolvability).

**Outstanding Questions**

Does no-cost generalism exist in the wild? Trade-offs may be subtle and high-dimensional, meaning that trade-offs (or a lack thereof) measured in the relatively static laboratory may not translate to the complex conditions experienced in the wild. Factors that may mask critical trade-offs include complex or changing biotic and abiotic environments, leading to eco-evolutionary dynamics and coevolution.

Which species show continual adaptation on ecological timescales? Many studies of eco-evolutionary dynamics have focused on parasites of hosts with adaptive immune systems. While these studies have shown exceptional rates of change, these dynamics have not been documented more broadly and deserve greater attention.

What are the relative contributions of mutational load versus lag load to costs of niche breadth expansion? Small populations may suffer reduced fitness due to the accumulation of deleterious mutations under relaxed selection, but larger populations with coevolving hosts, prey, or competitors may suffer even greater costs by adapting slower than specialists.

How does niche breadth interact with sex and demography? Burdens to adaptation that are intrinsic to broad niches may be partially compensated by beneficial effects of recombination, a large population size, or other boosts to evolvability.

How relevant are results of microbial experimental evolution studies to processes occurring in natural populations? Experimental evolution studies discussed here were designed to maximize rates of adaptation by utilizing large populations and high mutation rates. It is unclear whether these results should extend to parameter spaces where populations are smaller in size, have lower mutation rates, and sample fewer mutations.

How well do the predictions from the theoretical models play out

evolutionary success. During a long-term evolution experiment in *Escherichia coli*, the fitness of mutations present in populations after 500 generations was compared with mutations that eventually swept to a high frequency in the population after an additional 883 generations of evolution. Interestingly, the two mutations that would eventually sweep (the eventual winners) had lower competitive fitness than other mutations present early in adaptation (the eventual losers). Despite having lower fitness initially, the eventual winning mutations were able to evolve to outcompete the eventual losing mutations. The success of the eventual winners was replicated by repeated evolution experiments that demonstrated that they were more evolvable. In particular, the eventual winners fixed a specific mutation (*topA*), whereas the eventual losers fix a mutation that is immediately adjacent (*topA1*). Only *topA* enabled specific, subsequent adaptive mutations that were inaccessible to lineages with *topA1*. Even when these key mutations were inserted into the *topA1* genetic background, the eventual losers did not significantly increase in fitness as the *topA* lineages did. Therefore, the *topA* mutation conveyed higher evolvability than did the *topA1* mutation because of epistatic interactions with subsequent, potentially beneficial mutations. Ultimately, the winning lineages were able to follow a trajectory in the fitness landscape that other lineages could not [17]. Furthermore, mutations fixed during a niche expansion may impact the ability of an ecotype to adapt to another novel environment. When compared with their specialist ancestor, evolved generalist ϕ6 viruses had fewer mutations enabling niche expansion to a novel host. When generalist and specialist ϕ6 viruses were exposed to a novel host, the specialist was able to jump into the novel host via at least nine different mutations occurring across several genes. The generalists were only able to do so via one or two mutations in a single gene [60], suggesting that generalists in this system have fewer potential evolutionary trajectories available to them. Thus, mutations that fix early in evolution can have long-term fitness consequences, altering the trade-offs experienced by the evolving ecotype as well as their niche breadth.

empirically? While some results of theoretical models concerning lag load have parallels to existing studies in experimental evolution, some predictions from models have yet to be tested thoroughly.

## Concluding Remarks

The maintenance of generalist and specialist ecotypes within a population has long intrigued evolutionary biologists and ecologists [4–7]. The 'jack-of-all-trades' model is overly restrictive and has consistently not borne out empirically. Instead, we hypothesize that generalists experience reduced evolvability relative to specialists. Generalists and specialists are embedded in a complex interaction of ecological and evolutionary dynamics, and differences in niche breadth alter the ability of ecotypes to adapt. Since this hypothesis has not been tested directly, we have presented evidence from models and experimental evolution that generalists experience lag load when subjected to selection in multiple environments (see Outstanding Questions). Consequently, generalists are unable to adapt as quickly as specialists, providing a mechanism to explain the maintenance of generalists within a population. We hope to stimulate discussion about how the field can move beyond the classic models and integrate concepts across fields.

## Acknowledgments

We would like to thank two anonymous reviewers for their helpful comments. L.M.B. acknowledges partial support from Brown Endowed Postdoctoral Fellowship from Yale University. J.A.D. acknowledges partial support from the US National Science Foundation's Systems and Synthetic Biology program under award number 1714550. P.E.T. acknowledges support from the NSF BEACON Center for the Study of Evolution in Action (NSF Cooperative Agreement DBI-0939454).

## References

1. Lovejoy, A.O. (1936) *The Great Chain of Being: A Study of the History of an Idea*, Harvard University Press
2. Osborn, H.F. (1894) *From the Greeks to Darwin; An Outline of the Development of the Evolution Idea*, Macmillian Magazines and Co
3. Schluter, D. (2000) *The Ecology of Adaptive Radiation*, Oxford University Press
4. Wilson, D.S. and Yoshimura, J. (1994) On the coexistence of specialists and generalists. *Am. Nat.* 144, 692–707
5. Chesson, P. (2000) Mechanisms of maintenance of species diversity. *Annu. Rev. Ecol. Syst.* 31, 343–366
6. Abrams, P.A. (2006) The prerequisites for and likelihood of generalist-specialist coexistence. *Am. Nat.* 167, 329–342
7. MacArthur, R.H. (1972) *Geographical Ecology: Patterns in the Distribution of Species*, Princeton University Press
8. Falconer, D.S. (1981) *Introduction to Quantitative Genetics*, 2nd edn, Longman

9. Futuyma, D.J. and Moreno, G. (1988) *The evolution of ecological specialization* 19, 207–233
10. Kassen, R. (2002) The experimental evolution of specialists, generalists, and the maintenance of diversity. *J. Evol. Biol.* 15, 173–190
11. Turner, P.E. and Elena, S.F. (2000) Cost of host radiation in an RNA virus. *Genetics* 156, 1465–1470
12. Remold, S.K. *et al.* (2008) Evolutionary genomics of host adaptation in vesicular stomatitis virus. *Mol. Biol. Evol.* 25, 1138–1147
13. Remold, S. (2012) Understanding specialism when the jack of all trades can be the master of all. *Proc. R. Soc. B Biol. Sci.* 279, 4861–4869
14. Alto, B.W. *et al.* (2013) Stochastic temperatures impede RNA virus adaptation. *Evolution (N. Y).* 67, 969–979
15. Colegrave, N. and Collins, S. (2008) Experimental evolution: experimental evolution and evolvability. *Heredity (Edinb)* 100, 464–470
16. Burch, C.L. and Chao, L. (2000) Evolvability of an RNA virus is determined by its mutational neighbourhood. *Nature* 406, 625–628
17. Woods, R.J. *et al.* (2011) Second-order selection for evolvability in a large *Escherichia coli* population. *Science* 331, 1433–1436
18. Shoresh, N. *et al.* (2008) Evolution exacerbates the paradox of the plankton. *Proc. Natl. Acad. Sci. U. S. A.* 105, 12365–12369
19. Egas, M. *et al.* (2004) Evolution restricts the coexistence of specialists and generalists: the role of trade-off structure. *Am. Nat.* 163, 518–531
20. Kremer, C.T. and Klausmeier, C.A. (2017) Species packing in eco-evolutionary models of seasonally fluctuating environments. *Ecol. Lett.* 20, 1158–1168
21. Kremer, C.T. and Klausmeier, C.A. (2013) Coexistence in a variable environment: eco-evolutionary perspectives. *J. Theor. Biol.* 339, 14–25
22. Vamosi, J.C. *et al.* (2014) Evolutionary ecology of specialization: insights from phylogenetic analysis. *Proc. R. Soc. B Biol. Sci.* 281, 20142004
23. Day, E.H. *et al.* (2016) Is specialization an evolutionary dead end? Testing for differences in speciation, extinction and trait transition rates across diverse phylogenies of specialists and generalists. *J. Evol. Biol.* 29, 1257–1267
24. Sriswasdi, S. *et al.* (2017) Generalist species drive microbial dispersion and evolution. *Nat. Commun.* 8, 1162
25. Post, D.M. and Palkovacs, E.P. (2009) Eco-evolutionary feedbacks in community and ecosystem ecology: interactions between the ecological theatre and the evolutionary play. *Philos. Trans. R. Soc. B Biol. Sci.* 364, 1629–1640
26. Fussmann, G.F. *et al.* (2007) Eco-evolutionary dynamics of communities and ecosystems. *Funct. Ecol.* 21, 465–477
27. Cortez, M.H. and Weitz, J.S. (2014) Coevolution can reverse predator-prey cycles. *Proc. Natl. Acad. Sci. U. S. A.* 111, 7486–7491
28. Abrams, P.A. and Matsuda, H. (1997) Prey adaptation as a cause of predator-prey cycles. *Evolution (N. Y).* 51, 1742–1750
29. Yoshida, T. *et al.* (2007) Cryptic population dynamics: rapid evolution masks trophic interactions. *PLoS Biol* 5, 1868–1879
30. Yoshida, T. *et al.* (2003) Rapid evolution drives ecological dynamics in a predator-prey system. *Nature* 424, 303–306
31. Becks, L. *et al.* (2012) The functional genomics of an eco-evolutionary feedback loop: linking gene expression, trait evolution, and community dynamics. *Ecol. Lett.* 15, 492–501
32. Hiltunen, T. and Becks, L. (2014) Consumer co-evolution as an important component of the eco-evolutionary feedback. *Nat. Commun.* 5, 1–8
33. Hiltunen, T. *et al.* (2014) A newly discovered role of evolution in previously published consumer-resource dynamics. *Ecol. Lett.* 17, 915–923
34. Lankau, R.A. (2009) Genetic variation promotes long-term coexistence of *Brassica nigra* and its competitors. *Am. Nat.* 174, E40–E53
35. Vasseur, D.A. *et al.* (2011) Eco-evolutionary dynamics enable coexistence via neighbor-dependent selection. *Am. Nat.* 178, E96–E109
36. Siepielski, A.M. and McPeek, M.A. (2010) On the evidence for species coexistence: a critique of the coexistence program. *Ecology* 91, 3153–3164
37. Bell, G. (2017) Evolutionary rescue. *Annu. Rev. Ecol. Evol. Syst* 48, 605–627
38. Graves, C.J. and Weinreich, D.M. (2017) Variability in fitness effects can preclude selection of the fittest. *Annu. Rev. Ecol. Evol. Syst.* 48, 399–417
39. Bono, L.M. *et al.* (2015) Evolutionary rescue and the coexistence of generalist and specialist competitors: an experimental test. *Proc. R. Soc. B Biol. Sci.* 282, 20151932
40. Wagner, G.P. and Altenberg, L. (1996) Complex adaptations and the evolution of evolvability. *Evolution (N. Y).* 50, 967–976
41. Levinton, J. (1988) *Genetics, Paleontology, and Macroevolution*, Cambridge University Press
42. McBride, R.C. *et al.* (2008) Robustness promotes evolvability of thermotolerance in an RNA virus. *BMC Evol. Biol.* 8, 231
43. Whitlock, M.C. (1996) The red queen beats the jack-of-all-trades: the limitations on the evolution of phenotypic plasticity and niche breadth. *Am. Nat.* 148, S65–S77
44. Holt, R.D. (1996) Adaptive evolution in source-sink environments: direct and indirect effects of density-dependence on niche evolution. *Oikos* 75, 182–192
45. Fry, J.D. (1996) The evolution of host specialization: are trade-offs overrated? *Am. Nat.* 148, S84–S107
46. Kawecki, T.J. (1998) Red queen meets Santa Rosalia: arms races and the evolution of host specialization in organisms with parasitic lifestyles. *Am. Nat.* 152, 635–651
47. Noble, D.W.A. *et al.* (2019) Plastic responses to novel environments are biased towards phenotype dimensions with high additive genetic variation. *Proc. Natl. Acad. Sci. U. S. A.* 116, 13452–13461
48. Pfennig, D.W. *et al.* (2010) Phenotypic plasticity's impacts on diversification and speciation. *Trends Ecol. Evol.* 25, 459–467
49. Pfennig, D.W. and Murphy, P.J. (2003) A test of alternative hypotheses for character divergence between coexisting species. *Ecology* 84, 1288–1297
50. Ghalambor, C.K. *et al.* (2007) Adaptive versus non-adaptive phenotypic plasticity and the potential for contemporary adaptation in new environments. *Funct. Ecol.* 21, 394–407
51. Kawecki, T.J. *et al.* (2012) Experimental evolution. *Trends Ecol. Evol.* 27, 547–560
52. Jessup, C.M. *et al.* (2004) Big questions, small worlds: microbial model systems in ecology. *Trends Ecol. Evol.* 19, 189–197
53. Jerison, E.R. and Desai, M.M. (2015) Genomic investigations of evolutionary dynamics and epistasis in microbial evolution experiments. *Curr. Opin. Genet. Dev.* 35, 33–39
54. Duffy, S. *et al.* (2006) Pleiotropic costs of niche expansion in the RNA bacteriophage phi 6. *Genetics* 172, 751–757
55. Ferris, M.T. *et al.* (2007) High frequency of mutations that expand the host range of an RNA virus. *Genetics* 176, 1013–1022
56. Lalić, J. *et al.* (2011) Effect of host species on the distribution of mutational fitness effects for an RNA virus. *PLoS Genet* 7, e1002378

57. Carrasco, P. *et al.* (2007) Distribution of fitness and virulence effects caused by single-nucleotide substitutions in Tobacco Etch Virus. *J. Virol.* 81, 12979–12984
58. Bono, L.M. *et al.* (2017) The emergence of performance trade-offs during local adaptation: insights from experimental evolution. *Mol. Ecol.* 26, 1720–1733
59. Zhao, L. and Duffy, S. (2019) Gauging genetic diversity of generalists: a test of genetic and ecological generalism with RNA virus experimental evolution. *Virus Evol* 5, vez019
60. Zhao, L. *et al.* (2019) Existing host range mutations constrain further emergence of RNA viruses. *J. Virol.* 93, e01385-18.
61. Carlson, S.M. *et al.* (2014) Evolutionary rescue in a changing world. *Trends Ecol. Evol.* 29, 521–530
62. Gonzalez, A. *et al.* (2013) Evolutionary rescue: an emerging focus at the intersection between ecology and evolution. *Philos. Trans. R. Soc. B Biol. Sci.* 368, 20120404
63. Duffy, S. *et al.* (2007) Evolution of host specificity drives reproductive isolation among RNA viruses. *Evolution (N. Y).* 61, 2614–2622
64. Bono, L.M. *et al.* (2013) Competition and the origins of novelty: experimental evolution of niche-width expansion in a virus. *Biol. Lett.* 9, 20120616
65. Bono, L.L.M. *et al.* (2015) Evolutionary rescue and the coexistence of generalist and specialist competitors: an experimental test. *Proc. R. Soc. B* 282, 20151932
66. Huang, Y. *et al.* (2014) Genome-wide patterns of genetic variation within and among alternative selective regimes. *PLoS Genet* 10, e1004527
67. Orr, H.A. (2000) Adaptation and the cost of complexity. *Evolution* 54, 13–20
68. Fisher, R.A. (1930) *The Genetical Theory of Natural Selection*, Oxford University Pres
69. Maynard Smith, J. (1978) *The Evolution of Sex*, Cambridge University Press
70. Wagner, G.P. and Zhang, J. (2011) The pleiotropic structure of the genotype-phenotype map: the evolvability of complex organisms. *Nat. Rev. Genet.* 12, 204–213