Trends in Parasitology

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Opinion

Evolution of generalism under Muller's ratchet

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Host-range expansion in parasites is usually framed as an adaptive response to heterogeneous environments and trade-offs. In this opinion article, I propose Ratchet-Driven Generalism (RDG): in some parasites, broad host range may instead arise non-adaptively after the loss of sexual recombination. Under Muller's ratchet, deleterious mutations accumulate in asexual or rarely recombining lineages. Over time, genomic erosion can degrade host-specific adaptations, including host-interaction genes. In parallel, reduced competitive filtering among parasite genotypes can weaken selection for host-specific performance. Consequently, genotypes that are merely viable across hosts may persist. RDG predicts genomic signatures of functional decay and reduced efficacy of selection. It also suggests that such generalism may be transient, because continued genomic erosion can increase extinction risk. I outline comparative genomic tests to examine RDG.

Highlights

Host-range expansion is usually framed as an adaptive process shaped by trade-offs, spatiotemporal heterogeneity, and gene flow, which affects local adaptation.

A recent genomic study of *Giardia duodenalis* reports host-range expansion coincident with a loss of sexual recombination.

Ratchet-Driven Generalism proposes that host-range expansion can be a non-adaptive by-product of Muller's ratchet eroding host-specific adaptations.

Loss of recombination can weaken soft selection by reducing recombinant diversity and increasing reliance on viability filtering by hard selection.

Ratchet-Driven Generalism predicts genome-wide signatures of functional decay, elevated mutational load, and reduced Red Queen-type signals.

Non-adaptive evolution of generalism

Broad host range in parasites is usually interpreted as an adaptive outcome of selection in heterogeneous environments, mediated by trade-offs, plasticity, gene flow, and frequency-dependent interactions. These mechanisms are well-established and probably explain most cases of parasite generalism. However, they do not exclude the possibility that some forms of host-range expansion arise through non-adaptive processes.

This Opinion was motivated by our recent genomic analysis of *Giardia duodenalis* [1]. We showed that a derived, predominantly asexual lineage of this typically human-associated parasite has a broader host range than its sexual relatives, while also exhibiting elevated deleterious mutation accumulation and reduced signatures of selection and **Red Queen coevolution** (see Glossary). That combination suggests that a broader host range need not always reflect adaptive optimisation across hosts [1].

In this section, I refer to this as the **Ratchet-Driven Generalism (RDG)** hypothesis. RDG proposes that host-range expansion can emerge as a by-product of two linked consequences of **clonality**. First, reduced recombination increases vulnerability to **Muller's ratchet** [1–3]. Over time, this can lead to the accumulation of deleterious mutations and increased **genetic load**, including loss-of-function changes at **host-interaction loci** that contribute to efficient host exploitation. Such genomic erosion can weaken finely tuned host-specific interactions, including antigenic and immune-interface features, potentially facilitating infection of previously incompatible **non-hosts** [1,4–6]. Second, the loss of sex reduces the diversity of recombinant genotypes competing within hosts. **Soft selection** still operates, but it has less variation to act on, reducing genotype-level **competitive filtering** (Box 1) [1].

Together, these processes provide a route by which host-range expansion can occur without adaptive optimisation across hosts. Under RDG, weakened competitive filtering under soft selection allows viable genotypes carrying deleterious or loss-of-function variants to persist. The resulting genomic erosion of host-specific adaptations can increase permissiveness on alternative hosts by weakening host-interaction barriers. In this Opinion, I position the RDG hypothesis

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Box 1. Hard selection, soft selection, and Muller's ratchet in asexual parasites

Hard and soft selection act as distinct filters

Hard selection imposes an absolute viability threshold: genotypes below this threshold cannot persist (Figure IA). Soft selection acts additionally on relative performance within a local competitive setting, so genotype success also depends on the performance of competing genotypes rather than on absolute viability alone. Its efficacy therefore depends on recombinant variation among competing genotypes, which is reduced or absent in asexuals (Figure IB).

Why this matters under RDG

In predominantly clonal populations, hard viability filtering still operates, but reduced recombinant variation leaves soft selection with less variation to discriminate among viable genotypes. This weakens genotype-level competitive filtering and increases vulnerability to Muller's ratchet (Figure IB,C). Under RDG, loss-of-function variants at host-interaction loci can then accumulate, weakening host-specific barriers and permitting transient host-range expansion.

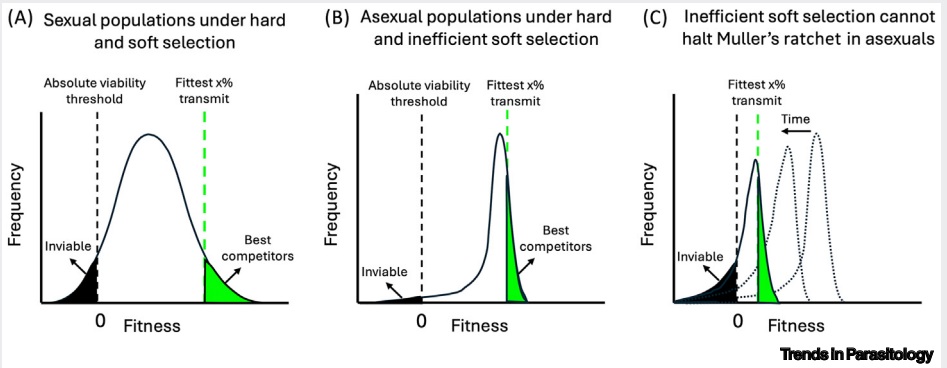

Figure I. Hard selection, soft selection, and Muller's ratchet under RDG. (A) Hard selection imposes an absolute viability threshold: genotypes below this threshold are inviable. In sexual populations, recombination generates broad fitness variation among viable genotypes, allowing soft selection to impose an additional competitive filter in which the fittest subset transmits. (B) In asexual populations, hard selection still removes inviable genotypes, but reduced recombinational variation narrows the fitness distribution among viable competitors. Soft selection, therefore, has less variation to act on, reducing genotype-level competitive filtering. (C) In the absence of recombination and with reduced efficacy of soft selection, Muller's ratchet continues to reduce fitness in asexual populations. Deleterious mutations accumulate over generations until an increasing fraction of genotypes falls below the absolute viability threshold, ultimately causing mutation meltdown and extinction. RDG: Ratchet-Driven Generalism.

within the broader literature on the evolution of generalism, discuss which systems are most likely to exhibit RDG, and outline testable predictions.

The evolution of generalism—How does existing theory explain generalism?

A substantial body of theory has already identified multiple routes by which broad niche breadth (i.e., 'generalism') can evolve (reviewed in [7,8]). These models typically treat generalism as an emergent outcome of (i) the form and curvature of performance trade-offs across resources/hosts, (ii) how environmental heterogeneity is experienced across space or time (fine-grained vs. coarse-grained exposure), (iii) spatial structure and gene flow that constrain or permit local adaptation, and (iv) **phenotypic plasticity** and habitat or host choice. Finally, (v) **frequency dependence** can modify the outcomes of (i)–(iv) by affecting whether competing strategies are able to coexist. In this section, I briefly review these models.

Performance trade-offs

Performance trade-offs arise because improving exploitation of one host typically requires host-specific molecular and life-history tuning, such as receptor binding and entry, immune evasion,

Glossary

Avirulence factor: a pathogen molecule (often an effector) that can be recognised by a host immune receptor, triggering defence. Loss or alteration can permit infection of otherwise resistant host genotypes or non-hosts.
Clonality: predominant reproduction through mitotic replication with little or no recombination, resulting in genetically near-identical lineages.
Competitive filtering: the removal of poorly performing genotypes through within-host or within-patch competition. Under soft selection, even small performance differences can determine which genotypes contribute to transmission.
Effector gene: a pathogen gene encoding a secreted or delivered molecule that alters host cell processes to promote infection. Effectors can contribute to host specificity; if an effector is recognised by a host immune receptor, it can function as an avirulence factor.
Frequency dependence: selection in which the fitness of a genotype depends on its frequency. Negative frequency dependence (rare-type advantage) can maintain polymorphism and stabilise coexistence.
Generalist: a genotype, lineage, or population that can exploit a broad range of hosts or resources. 'True' generalists are individual genotypes or lineages with broad host use, not mixtures of specialised ecotypes.
Genetic load: the proportional reduction in mean population fitness relative to that of the optimal genotype, caused by deleterious genetic variation (this is the fitness definition). Also, the sum of selection coefficients of harmful mutations in a genome (genetic definition).
Hard selection: selection based on absolute viability or performance thresholds, such that individuals or genotypes survive if they exceed a minimum standard, irrespective of the fitness or density of other genotypes ('survival of the sufficiently fit').
Host-interaction loci: genes affecting attachment, invasion, immune evasion, or resource exploitation in a host. Changes at these loci can alter host specificity and infection success.
Muller's ratchet: the irreversible accumulation of deleterious mutations in asexual populations due to genetic drift and the inability to recreate the least-

and resource acquisition. Consequently, alleles that increase performance on host A tend to have antagonistic (pleiotropic) effects on performance on host B [9]. However, such trade-offs are not universal and can be weak or context-dependent [8]. Under performance trade-offs, adaptive-dynamics models show that **generalists** can be evolutionarily stable and that the outcome hinges on the curvature of the performance trade-off between exploiting alternative hosts [10,11] (Figure 1). If the trade-off is concave (weak), the loss in fitness on either host is only mild, and an intermediate 'compromise' phenotype performs reasonably well. Under these conditions, selection can favour stable generalist genotypes [10,11]. If the trade-off is convex (strong), intermediate strategies are disproportionately penalised because they perform poorly on both hosts. Consequently, selection tends to favour diversification and the emergence of coexisting specialists [10,11]. Depending on trade-off curvature and ecological feedbacks, the same ecological setting can yield either a stable generalist optimum or evolutionary branching into coexisting specialist types [10,12,13].

Heterogeneity

Spatial and temporal heterogeneity is a classic driver of niche breadth [7,14]. In fine-grained heterogeneity, individuals (or infection lineages) repeatedly experience multiple environments (e.g., hosts) within a lifetime or across short time scales (Figure 2). In this case, selection tends to favour generalists (or plastic phenotypes) that maintain reasonable performance across conditions [14,15]. In coarse-grained heterogeneity, individuals experience only one environment (or one host), and conditions differ among patches or generations. In such an environment, selection tends to favour local specialists, resulting in spatial (or temporal) structure with local adaptation [7,16]. The exact outcome depends on the frequency of switching and the costs/constraints of breadth [14]. Broad tolerance is most likely when trade-offs are weak, whereas strong trade-offs tend to penalise compromise phenotypes and favour specialists rather than generalists [9] (as discussed earlier). Generalism can also be favoured by temporal environmental variation when long-term success depends on performance across fluctuating conditions rather than

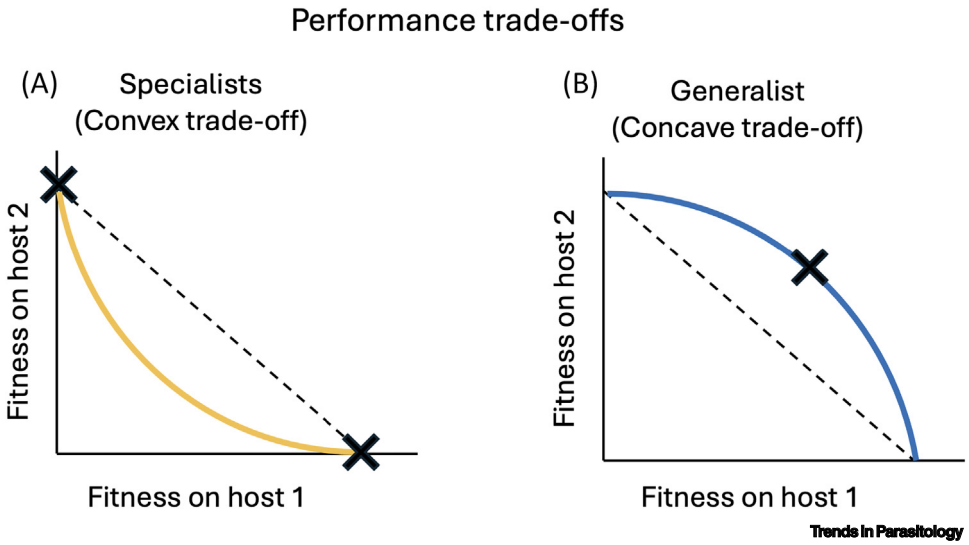

Figure 1. Performance trade-offs can favour specialists or generalists depending on curvature. (A) Performance across two hosts constrains attainable fitness combinations (solid trade-off curve). Under a convex trade-off (strong costs of breadth), intermediate phenotypes perform poorly on both hosts, and selection favours specialists at the extremes (crosses). (B) Under a concave trade-off (shallow costs of breadth), an intermediate phenotype achieves relatively high performance on both hosts, favouring a generalist (cross). Dashed lines show a linear (no-curvature) reference.

loaded genotypes through recombination.

Mutation meltdown: a feedback process in which accumulating deleterious mutations reduce population fitness and size, strengthen genetic drift, and accelerate further mutation accumulation, potentially leading to extinction.

Non-host: a species that does not normally permit parasite infection because of compatibility barriers, such as host defences, that prevent successful exploitation.

Phenotypic plasticity: the capacity of a single genotype to produce different phenotypes across environments (e.g., hosts) via changes in gene expression, physiology, morphology, or life-history. Plasticity can broaden apparent host use without genetic change.

Ratchet-Driven Generalism (RDG): a hypothesis proposing that, in some predominantly clonal parasite lineages, host-range expansion can arise as a non-adaptive by-product of recombination loss. Reduced recombinant variation weakens genotype-level competitive filtering, while Muller's ratchet erodes host-specific adaptations and increases permissiveness on alternative hosts.

Red Queen coevolution: ongoing reciprocal adaptation between hosts and parasites, driven by antagonistic interactions and soft selection, resulting in the evolution of new immune escape and counter-defence variants.

Soft selection: selection based on relative performance within local patches (e.g., within-host competition), so fitness depends on ranking among competitors ('survival of the fittest').

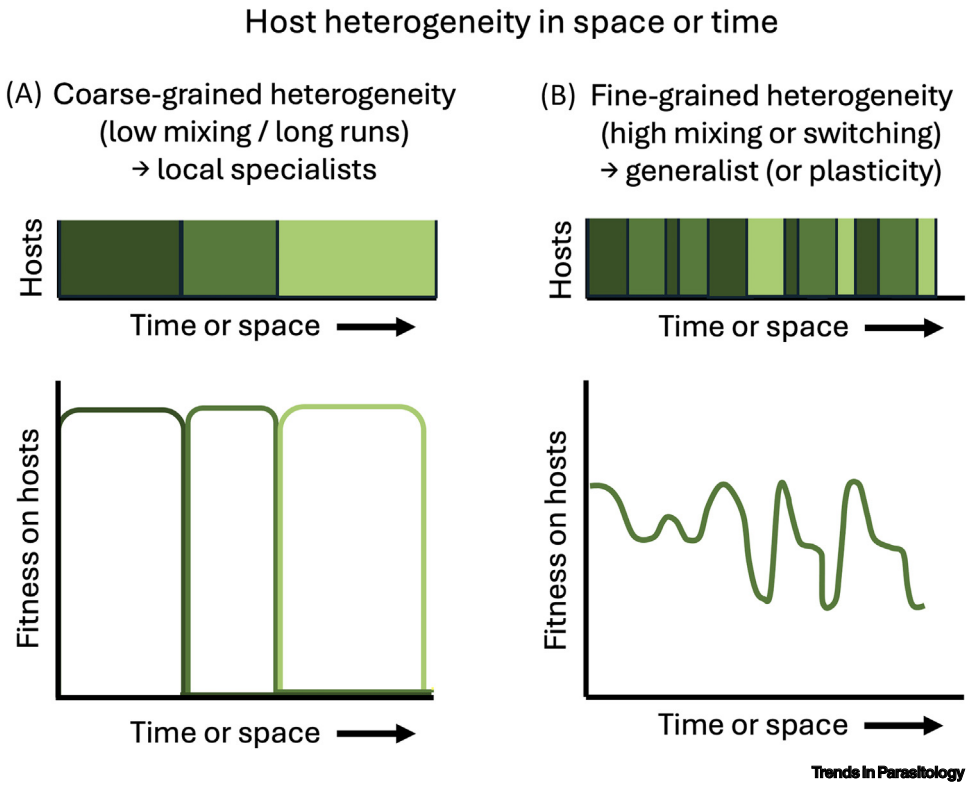

Figure 2. Host heterogeneity in space or time (grain) shapes selection for niche breadth. (A) Schematic of a patchy host environment experienced across time or space (colours denote host types). Under coarse-grained heterogeneity (low mixing/long runs), infection lineages experience one host type for extended periods, enabling host-specific adaptation and favouring specialists. (B) Under fine-grained heterogeneity (high mixing/frequent switching), lineages repeatedly encounter multiple host types within the relevant evolutionary timescale, favouring generalists and/or phenotypic plasticity. Fitness consequences: in coarse-grained environments, host specialists achieve high fitness on their matched host but low fitness elsewhere; in fine-grained environments, a broad-tolerance (generalist/plastic) strategy yields moderate but more consistent fitness across changing hosts.

maximising fitness in any single state (Figure 2). In such settings, selection can favour strategies that maximise geometric mean fitness [17–19]. This can occur via conservative bet-hedging, where a robust, generalist-like phenotype possesses a modest amount of variance in fitness [17–20]. It can also occur via diversified bet-hedging, where risk is spread across alternative phenotypes or life-history states [19,20]. For parasites, seasonal host availability, shifting community composition, or episodic transmission opportunities can generate precisely such temporal uncertainty, making 'broad-enough' host use advantageous even if it is not optimal on any given host at any given time [21].

Gene flow and local adaptation

Whether specialists can evolve is also affected by the impact of dispersal or the amount of gene flow. Limited gene flow permits patch-specific adaptation and niche segregation, whereas high gene flow can homogenise populations and constrain local adaptation [22,23]. This class of models is particularly relevant to host-associated organisms because hosts can be treated as discrete habitat patches connected by transmission. In host–parasite metapopulations, the key prediction is that the relative dispersal rates of hosts and parasites shape whether parasites evolve local adaptation/specialisation versus broader host ranges [24,25].

Plasticity and host or habitat choice

A further route to apparent generalism is phenotypic plasticity, where a single genotype expresses different phenotypes across environments or hosts [26]. For example, *Myzus persicae* can colonise distantly related plant species via rapid, host-induced transcriptional shifts. This can be accomplished even in clonal lineages of genetically identical individuals. These shifts include coordinated regulation of duplicated gene clusters that are detectable within days after a host switch [26]. More broadly, comparative syntheses of pest aphids highlight that some widely distributed 'superclones' exhibit genuinely broad host use and invasion success [27]. Such clone-level generalism illustrates that plasticity and regulatory flexibility can facilitate local adaptation without the need for genetic change. Plasticity can therefore reduce the need for a fixed 'compromise' strategy by enabling context-dependent exploitation. Over longer timescales, plastic responses can become genetically stabilised via genetic accommodation or genetic assimilation [28]. In host-associated systems, plasticity in traits that mediate host exploitation or immune evasion can thus widen host use without requiring uniformly high performance across hosts. At the same time, plasticity often interacts with host or habitat choice. When organisms can choose where to feed, infect, or reproduce, selection can favour behavioural matching that concentrates individuals on the environment where they perform best [29].

Frequency dependence as modifier

Competition and antagonistic interactions (e.g., host–parasite, predator–prey) often generate frequency dependence, meaning the advantage of a strategy depends on how common it is. Rather than being a standalone driver of generalism versus specialism, frequency dependence modifies the outcomes of (i) performance trade-offs, (ii) spatiotemporal heterogeneity, (iii) gene flow, and (iv) levels of plasticity. It determines the extent to which alternative strategies can be maintained in dynamic coexistence or whether they are excluded. As a phenotype becomes common, its marginal fitness often declines because it competes more with similar types for limiting resources. Lewontin captured this succinctly as, 'a genotype is its own worst enemy' [30]. Additionally, in host–parasite systems, this effect can be reinforced because common parasite genotypes are more likely to be countered by host defences. Negative frequency dependence can thus stabilise polymorphism, and when strategies map onto different hosts or niches (see i–iv), a stronger rare-type advantage makes the coexistence of multiple specialists more robust.

The RDG hypothesis

Broad niche breadth at the species or population level can reflect among-genotype variation, where taxa labelled 'generalist' comprise multiple specialised ecotypes, pathotypes, or lineages ('generalist paradox'; [31–33]). Conversely, 'true' generalists are those in which individual genotypes (or lineages) themselves exploit a broad range of hosts [34]. In this paper, RDG is framed as a mechanism to explain the evolution of 'true' generalism after the loss of sex.

Soft selection, competitive filtering, and Red Queen coevolution

Competition among conspecific genotypes exploiting a finite resource is a key driver of adaptive evolution that can generate strong frequency- and density-dependent selection [30,35]. Under soft selection, fitness is determined by relative performance within local populations or patches [35–38]. As such, soft selection is true 'survival of the fittest'. Under **hard selection**, by contrast, fitness depends primarily on whether genotypes exceed an absolute viability threshold, rather than on their competitive rank relative to other conspecific genotypes within a patch. Hard selection can thus be considered 'survival of the sufficiently fit'. Consequently, under soft selection, even small differences in infection efficiency can have fitness consequences, and inferior genotypes can be eliminated despite remaining viable in absolute terms. Soft selection can therefore promote ecological specialisation and fine-tuned adaptations that optimise performance in

antagonistic interactions, including host–parasite, predator–prey, and plant–herbivore systems [7,39]. In this sense, soft selection provides a mechanistic basis for Red Queen coevolution, where continuing biotic conflict sustains selection for ever more specific counter-adaptations [39–42]. Furthermore, it helps explain why and how specialists evolve [7,35,38], because soft selection exposes host-specific performance trade-offs and thereby favours specialist genotypes over 'compromise' generalists. A similar pattern is observed in insect–plant datasets, which show that stronger defences are associated with narrower diets [43]. This pattern, too, is consistent with arms-race dynamics favouring tighter host association and specialisation.

RDG as a modifier of the selection regime after the loss of sex

Against this background, generalism can evolve under a range of eco-evolutionary conditions. Even so, why it emerges in some systems but not others remains an intriguing biological puzzle, captured in the so-called 'paradox of generalism'. This paradox has been the subject of recent synthesis and debate [44]. RDG proposes a non-adaptive explanation, complementing the theory on how generalism can evolve. Specifically, when sexual reproduction breaks down, competitive filtering among recombinant genotypes is reduced [35,38]. Although absolute viability filtering by hard selection continues to operate, reduced variation among recombinant genotypes leaves soft selection with less discriminatory power, weakening genotype-level competitive filtering [1] (Box 1). In parallel, the absence of recombination makes lineages more vulnerable to the irreversible accumulation of deleterious mutations through Muller's ratchet [1].

Adaptive routes to host-range expansion through acquisition

Host-range expansion and host switches are often framed as adaptive processes that require the acquisition or modification of virulence functions, including **effector genes** and host-interaction traits. Novel virulence activities can arise *de novo* by mutation, as well as through processes that involve gene flow and recombination, including introgression after hybridisation, horizontal gene transfer, or horizontal chromosome transfer in fungi [32,45–47]. For example, host-range expansion in *Albugo candida* races has been linked to mosaic genomes shaped by introgression, consistent with gene flow delivering host-interaction variants that facilitate infection on additional hosts [32,33].

Adaptive routes to host-range expansion through loss

Host-range shifts can also be achieved by the loss or inactivation of virulence determinants, particularly when effectors function as **avirulence factors** that trigger host recognition. For example, McMullan *et al.* [32] suggested that recognised effector alleles could be lost through segregation in hybrid progeny via loss of heterozygosity, thereby enabling infection of non-hosts that would otherwise recognise the effector. Indeed, in plant pathogens, loss, truncation, or mutation of recognised effectors is a common route to evade immunity and thereby expand the set of hosts or genotypes that a lineage can infect [45,48]. RDG differs in that it treats host-range widening as a non-adaptive by-product of genome-wide mutational erosion under clonality, rather than as selection-driven gain/reshuffling of virulence functions or selection-driven loss of recognised effectors.

The RDG mechanism

Clonality can erode the molecular specificity that underpins the tight host adaptation of parasites, including genes involved in immune manipulation or host-specific exploitation [1,4–6]. When absolute viability remains above a persistence threshold, such losses may be only weakly selected against, allowing deleterious and loss-of-function changes to accumulate [3]. Erosion of finely tuned host-interaction features can then reduce host specificity and increase permissiveness on alternative hosts, enabling transient host-range expansion [1]. Generalism, therefore, arises not through broad adaptive optimisation across hosts but as a consequence of mutational erosion when competitive

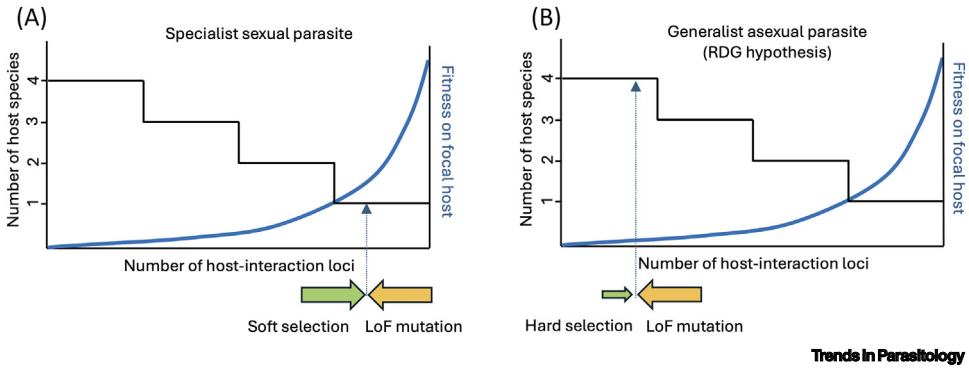

Figure 3. Conceptual model of Ratchet-Driven Generalism in asexual parasites. (A) In a sexual specialist parasite, host specificity is maintained by many host-interaction loci and by strong competitive filtering under soft selection ('survival of the fittest'). Loss-of-function (LoF) mutations at host-interaction loci are therefore strongly selected against because they reduce competitive performance on the focal host. As a result, the lineage remains highly fit on one host species but is unable to infect many others. (B) Under the Ratchet-Driven Generalism (RDG) hypothesis, an asexual lineage still experiences hard viability filtering, but reduced recombinant variation weakens genotype-level competitive filtering under soft selection. In this setting, LoF mutations at host-interaction loci accumulate by drift under Muller's ratchet. Loss of host-specific virulence factors that trigger immune recognition in non-hosts can allow infection of additional host species and promote the evolution of generalism. In both panels, the black step function shows the number of host species that can be infected as the number of functional host-interaction loci decreases, and the blue curve shows fitness on the original focal host. The green arrow indicates selection favouring higher fitness on the focal host, whereas the yellow arrow indicates mutational pressure toward LoF. Adapted from Tichkule *et al.* [1].

filtering among conspecific genotypes is relaxed (Figure 3) [1,35,38]. This mechanism is exemplified by a recent genomic analysis of the human-associated parasite *G. duodenalis*, which identified a derived, recently evolved asexual lineage with a broader host range than its sexual relatives, elevated accumulation of deleterious mutations, and reduced signatures of selection and Red Queen coevolution [1]. The RDG hypothesis proposes that such ratchet-driven loss of adaptations can permit transient host-range expansion, but that continued mutation accumulation ultimately predisposes the asexual lineage to **mutation meltdown** and extinction [1,3]. By contrast, in sexual populations, recombination sustains genotypic diversity and facilitates efficient soft selection, enabling the purging of low-performing, loss-of-function-laden genotypes before they contribute to host-range expansion [1,35,38].

Positioning RDG relative to existing theory and non-adaptive change

The standard determinants of the niche breadth of generalists, reviewed in an earlier section are likely to explain most cases of generalism evolution [7,8]. In this Opinion, I propose RDG as a distinct, non-adaptive explanation for broad host range in predominantly clonal lineages, arising through the loss of host-specific adaptations rather than adaptive optimisation across hosts. After the loss of sexual reproduction, competitive filtering among conspecific genotypes becomes relaxed, which increases vulnerability to Muller's ratchet and loss-of-function accumulation at host-interaction loci [1,3,35,38]. More broadly, not all evolutionary change is adaptive: at the molecular level, substantial change can reflect neutral or nearly neutral processes shaped by drift and purifying selection rather than optimisation [49]. RDG adds a distinct, testable non-adaptive hypothesis (Table 1): transient host-range expansion can arise as a by-product of mutational erosion rather than optimisation across hosts [1].

When does RDG occur in nature?

Whether RDG is common in nature remains an open question, and the likelihood depends on the biology of the species and the demography of the population. Matched sexual–asexual

Table 1. Conditions favouring Ratchet-Driven Generalism, expected empirical signals, and methods for testing them

Condition favouring RDG	Why it should favour RDG?	Expected signal	How to test?
Expanded host range in a low recombination or asexual lineage relative to sexual sister lineages	This is the core comparative prediction of RDG	Host-range broadening coupled to genomic erosion rather than clear signatures of adaptive gain	Compare host breadth, genetic load, LoF at host-interaction loci, demography, recombination, and signatures of selection and Red Queen coevolution across recombination contrasts
Low effective population size (N_e) through recurrent transmission bottlenecks	Strong drift weakens purifying selection and speeds up Muller's ratchet	Reduced diversity, shallow coalescence, and elevated genetic load	Demographic inference from genome-wide diversity, site-frequency spectra, temporal sampling, and transmission data
Predominant clonality with little recombination or admixture	Least-loaded genotypes cannot be reconstituted efficiently, allowing deleterious variants to accumulate	Strong linkage disequilibrium, stable clonal structure, and lineage-specific accumulation of deleterious variants	Population structure and admixture analyses, haplotype network analyses, recombination tests
High deleterious mutation input and/or a large mutational target of host-interaction loci	Increases the supply of LoF variants that leads to Muller's ratchet	Enrichment of gene truncations, pseudogenisation, transposon insertions, or LoF variants in host-interaction genes	Annotation of host-interaction loci, LoF analysis, genetic load tests, transposable element analysis, and gene-family comparisons
Strong host-specific immune recognition of parasite avirulence factors	Loss of recognisable host-interaction molecules can relax host restriction and permit infection of additional hosts	Loss, truncation, or absence of candidate avirulence-like loci in broader-host-range lineages	Comparative genomics and transcriptomics linked to infection assays, and gene knockout experiments
Reduced genotype-level competitive filtering under soft selection	Hard selection can tolerate viable genotypes carrying loss-of-function mutations	Broader host permissiveness despite reduced performance on the focal host	Compare within-host competition, absolute fitness (e.g., pathogen load), across sexual and asexual lineages
Reduced recognition in non-host	Loss or erosion of host-interaction factors weakens host detection	Weaker host immune activation and higher permissiveness in novel hosts	Cross-host infection trials measuring pathogen load, transmission, and host immune responses
Ecological isolation of transmission chains	Limits rescue by gene flow and amplifies founder effects, genetic drift, and Muller's ratchet	Strong population subdivision, repeated local drift signatures, and parallel erosion across lineages	Combine host landscape structure, epidemiological data, and parasite population genomics
Low-recombination genomic regions, such as chromosomal inversions	Reduced recombination locally limits the reconstitution of low-load haplotypes and can weaken purging of deleterious variants	Elevated deleterious or loss-of-function burden within low-recombination regions, especially at host-interaction loci	Compare variant burden, linkage disequilibrium, and host-interaction gene content inside versus outside low-recombination regions, while controlling for gene density and demography

sister-lineage comparisons would provide the cleanest tests of RDG, but other comparisons are also informative. In particular, comparative datasets could exploit variation in effective recombination rates, contrasting predominantly clonal, occasionally recombining, and frequently recombining lineages. Promising starting points include *Giardia* assemblages, apomictic root-knot nematodes (*Meloidogyne* spp.), the *Thrips tabaci* cryptic species complex, and parasite or pathogen groups with genomic evidence for contrasting clonality, admixture, or recombination, such as *Cryptosporidium*, *Leishmania*, *A. candida*, and *Magnaporthe oryzae*. These systems should be treated as candidates for testing RDG-like predictions, not as established examples of RDG.

Among candidate species, apomictic root-knot nematodes and parthenogenetic pest lineages in scale insects and thrips are particularly relevant because some asexual lineages show unusually broad host ranges [50,51]. Generalism in these taxa has been explained by hybrid/polyploid origins or general-purpose genotypes [50,51]. Predominantly clonal oomycete and fungal pathogens with large repertoires of effectors create a substantial mutational target for loss-of-function changes, which makes them candidates for RDG. For example, lineages of the generalist oomycete *A. candida* show clonal expansion and host-range change linked to immune

suppression and effector variation, while clonal lineages of the rice blast fungus *M. oryzae* differ in effector repertoires [32,33,52]. However, these systems are also shaped by hybridisation and genetic introgression [32,33].

RDG depends on Muller's ratchet and drift, which are weak when the effective population size (N_e) is large [3,53,54]. Muller's ratchet can nevertheless proceed rapidly during population bottlenecks or when background selection reduces the N_e of the least-loaded class [3,53,54]. RDG should therefore be most likely in systems with recurrent strong transmission bottlenecks, for example, through isolated hosts and in fragmented host populations. RDG should also be more likely when the deleterious mutation rate is high and when the mutational target for host-interaction functions is large, because both increase the supply of loss-of-function variants on which Muller's ratchet can act. The same logic may also apply locally within genomes: low-recombination regions, such as chromosomal inversions, are prone to the accumulation of deleterious mutations. Linked variants cannot recombine freely, reducing the recombinant variation available to soft selection (Box 1). If such regions include host-interaction loci, locally accumulated loss-of-function variants could weaken host-specific barriers and contribute to host-range expansion under RDG (Table 1).

Many parasites will not meet these conditions because they retain some recombination and gene flow through mixed infections and sexual stages, which can restore variation and slow or halt ratchet-driven erosion [55]. In *Giardia*, the life cycle is direct; infections are initiated by ingestion of environmentally robust cysts, and trophozoites then expand clonally by binary fission in the host [56]. Because the infectious dose can be very low (~10 cysts in humans, with ID_{50} estimates in the tens of cysts) [57], transmission can impose strong founder events, providing a plausible route to recurrent transmission bottlenecks, strong drift, and Muller's ratchet [3,57]. The genome is also compact (~12 Mb), implying limited redundancy in some cellular systems, so loss-of-function changes at host-interaction loci can have immediate phenotypic consequences even if they are not adaptively favoured [1,58].

Concluding remarks and future perspectives

RDG makes a set of tractable, genome-scale predictions that can be evaluated with comparative datasets (see Table 1 and Outstanding questions). Because generic signatures of relaxed selection are not sufficient to diagnose Muller's ratchet, RDG requires a combined signal: reduced recombination, demographic evidence for drift or bottlenecks, and lineage-specific accumulation of deleterious or loss-of-function variants. Future population-genetic modelling is needed to characterise the parameter space in which RDG operates and distinguish it quantitatively from relaxed selection, demographic bottlenecks, and adaptive host-range expansion. The predicted erosion under RDG should be detectable genome-wide, including within host-interaction and immune-interface gene families that contribute to host specificity. Asexual generalists are also expected to show reduced signatures of Red Queen-type frequency-dependent selection at these loci. Finally, Muller's ratchet and the absence of recombination are expected to elevate extinction risk in RDG lineages and thus to increase lineage turnover, yielding shallow divergence times [1]. These predictions can be tested using matched phylogenomic comparisons that quantify the distribution of fitness effects and genetic load, compare rates of protein-changing versus silent substitutions (d_N/d_S), and assess gene-family turnover in host-interaction genes. Genome data can also be used to date phylogenies and estimate offshoot age and persistence. A demography-controlled association linking broader host range with reduced recombination, elevated genetic load, recent emergence, erosion of host-interaction loci, and reduced Red Queen signatures would provide a strong comparative test of RDG.

Outstanding questions

In which parasite systems is RDG most plausible, given the life cycle, transmission mode, bottleneck frequency and severity, mutation rate, recombination rate, and the mutational target size of host-interaction loci?

Across sexual–asexual sister lineages, when does broadened host use coincide with genome-wide signals of reduced efficacy of selection and functional decay at host-interaction loci?

To what extent does the loss of recombination weaken genotype-level competitive filtering, reduce the efficacy of soft selection, and increase reliance on threshold-like viability filtering under hard selection?

Is RDG evolutionarily transient and restricted to small parasite populations, or can it be evolutionarily stable?

Which genomic readouts are most diagnostic for RDG (e.g., burden of deleterious variants, loss-of-function variants, gene-family turnover in host-interaction loci, and weakened frequency-dependent signatures)?

How do occasional recombination, mixed infections, or admixture events alter RDG trajectories and prevent the extinction of RDG lineages?

Can matched comparative datasets (host-range data, genomes, and demography) be assembled to test RDG predictions across multiple independent transitions to predominant clonality?

Can loss-of-function variants in asexual, host-range-expanded parasites help identify avirulence factors that trigger host defences in non-hosts?

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Declaration of interests

The author declares no competing interests.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author used ChatGPT (OpenAI) to assist with language editing and manuscript revision. After using this tool, the author reviewed and edited the content as needed and takes full responsibility for the content of the publication.

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