Intrinsic emergence and modulation of sex-specific dominance reversals in threshold traits

Running title: Sex-specific dominance and thresholds

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Abstract

Sex-specific dominance reversals (SSDRs) in fitness-related traits, where heterozygotes' phenotypes resemble those of alternative homozygotes in females versus males, can simultaneously maintain genetic variation in fitness and resolve sexual conflict and thereby shape key evolutionary outcomes. Yet, the full implications of SSDRs will depend on how they arise and the resulting potential for evolutionary, ecological and environmental modulation. Recent field and laboratory studies demonstrate SSDRs in threshold(-like) traits with dichotomous or competitive phenotypic outcomes, implying that such traits could promote emergence of SSDRs. But, such possibilities have not been explicitly examined. I show how phenotypic SSDRs can readily emerge in threshold traits given genetic architectures involving large-effect loci alongside sexual dimorphism in the mean and variance in polygenic liability. I also show how multi-locus SSDRs can arise in line-cross experiments, especially given competitive reproductive systems that generate non-linear fitness outcomes. SSDRs can consequently emerge in threshold(-like) traits, as functions of sexual antagonism, sexual dimorphism and reproductive systems, even with purely additive underlying genetic effects. Accordingly, I identify theoretical and empirical advances that are now required to discern the basis and occurrence of SSDRs in nature, probe forms of (co-)evolutionary, ecological and environmental modulation, and evaluate net impacts on sexual conflict.

Keywords: Liability; sex-specific dominance reversal; sexual antagonism; sexual conflict; sexual dimorphism; threshold trait.

Introduction

Core ambitions in evolutionary biology are to identify key processes that maintain genetic variation in fitness and that shape the outcome of evolutionary sexual conflict (Johnson and Barton 2005; Bonduriansky and Chenoweth 2009; Arnqvist 2011; Connallon and Clark 2010, 2014; Connallon 2015; Hendry et al. 2018; Plesnar-Bielak and Łukasiewicz 2021). Observations that magnitudes of standing genetic variation in fitness (and major fitness components) can substantially exceed those expected solely due to mutation-selection balance imply that some forms of balancing selection must act to maintain polymorphisms (Johnson and Barton 2005; Charlesworth 2015; Connallon and Chenoweth 2019). While sexual conflict resulting from sexually antagonistic selection can in principle be resolved through evolution of sexual dimorphism, such outcomes depend on genetic architectures of focal traits, including sex-specific additive and non-additive genetic effects and (co)variances (Lande 1980; Connallon and Clark 2010; Arnqvist et al. 2014; Wyman and Rowe 2014). Accordingly, overarching objectives are to identify interacting processes and architectures that can jointly generate balancing selection and facilitate emergence of sexual dimorphism, and to understand how such processes and architectures can themselves arise or be constrained (Bonduriansky and Chenoweth 2009; Connallon and Clark 2010, 2014; Connallon 2015; Llaurens et al. 2017; Grieshop and Arnqvist 2018; Ruzicka et al. 2019; Kaufmann et al. 2021; van der Bijl and Mank 2021).

In this context, sex-specific dominance reversals (SSDRs) are of direct interest because they constitute one key mechanism that could both maintain genetic variation and ameliorate sexual conflict (Fry 2010; Arnqvist 2011; Arnqvist et al. 2014; Grieshop and Arnqvist 2018; Connallon and Chenoweth 2019; Ruzicka et al. 2019; Grieshop et al. 2021). SSDRs are defined as occurring when heterozygotes' phenotypes resemble the phenotypes of alternative

homozygotes in females versus males (Figure 1). Such SSDRs allow expression of differing sex-specific optimal phenotypes given the same heterozygous genotype at a focal locus (Figure 1). This can in turn generate net heterozygote advantage at the population level, which can contribute to maintaining genetic variation (i.e. through net balancing selection, Figure 1). Such SSDRs could therefore both defuse sexual antagonism and maintain potential for future evolution (Fry 2010; Arnqvist 2011; reviewed by Connallon and Chenoweth 2019; Grieshop et al. 2021). However, in general, such impacts will depend on the frequency of occurrence and magnitude of effect of SSDRs and hence on the circumstances under which SSDRs can actually arise, evolve and be modulated in nature (as with dominance relationships more generally, Billiard et al. 2021).

Fundamental questions of whether dominance of beneficial versus detrimental alleles can directly evolve, and/or simply arises as an intrinsic property of non-linear genotype-phenotype (or genotype-fitness) maps, have been widely considered and historically generated considerable controversy. One key contention was that, since dominance manifests in heterozygotes, a relatively high frequency of heterozygosity is required to generate appreciable selection on dominance and hence any possible dominance evolution, yet sufficient heterozygosity may not generally arise (arguments summarised by Otto and Bourguet 1999; Manna et al. 2011; Spencer and Priest 2016; Connallon and Chenoweth 2019; Billiard et al. 2021). Yet, recent population genetic theory shows that dominance can in principle evolve in circumstances where some additional process generates or maintains heterozygosity (Otto and Bourguet 1999; Billiard et al. 2021). This includes evolution of SSDRs given sexually antagonistic selection (Spencer and Priest 2016). Here, sexual antagonism can initially maintain sufficient genetic variation (and hence heterozygosity) at focal large-effect

loci to allow invasion of sex-specific dominance modifiers, which effectively reduce sexual conflict and further maintain genetic variation (Spencer and Priest 2016).

Meanwhile, it has also been highlighted that intrinsic SSDRs can emerge if genotype-fitness maps for both sexes are non-linear and, specifically, concave around each sex's optimum. Given strong sexually antagonistic selection at a focal locus such that opposite homozygotes have higher fitness in females versus males, sex-specific fitness values for heterozygotes can then be geometrically closer to each sex-specific maximum even given purely additive underlying allelic effects (Fry 2010; reviewed and illustrated by Connallon and Chenoweth 2019). This scenario concurs with the general points that any non-linear genotype-phenotype map can generate intrinsic dominance (Gilchrist and Nijhout 2001; Vasseur et al. 2019), and that recessivity in detrimental small-effect mutations can arise given smooth non-linear fitness landscapes (e.g. given stabilising selection across underlying traits, Manna et al. 2011). Hence, overall, the points that evolved and/or intrinsic SSDRs could in principle exist are now well substantiated (Grieshop and Arnqvist 2018; Connallon and Chenoweth 2019; Grieshop et al. 2021).

Indeed, four major empirical studies have now demonstrated SSDRs in key fitness-related traits in disparate systems. These four studies concern maturation in Atlantic salmon (*Salmo salar*, Barson et al. 2015); occurrence of anadromy (i.e. sea migration) in rainbow trout (*Oncorhynchus mykiss*, Pearse et al. 2019); survival through bacterial exposure in *Drosophila melanogaster* (Geeta Arun et al. 2021); and competitive reproductive success in seed beetles (*Callosobruchus maculatus*, Grieshop and Arnqvist 2018). They provide striking evidence of SSDRs involving heterozygosity at known large-effect loci or genomic inversions (Barson et al. 2015; Pearse et al. 2019), or given polygenic heterozygosity generated through heroic efforts

with experimental evolution and/or line-crosses (Grieshop and Arnqvist 2018; Geeta Arun et al. 2021).

Yet, while these four studies demonstrate manifestations of SSDRs, they do not focus on investigating how such SSDRs could or do arise. This is reasonable; simply demonstrating SSDRs in fitness-related traits in wild or wild-derived systems represents a notable advance, while probing their basis requires further challenging investigations (Pearse et al. 2019; Geeta Arun et al. 2021; Grieshop et al. 2021). However, some insights into underlying mechanisms, and specifically the degrees to which observed phenotypic SSDRs represent explicit genetic dominance reversals versus intrinsic properties of non-linear genotype-phenotype or genotype-fitness maps, will ultimately be required to fully understand key forces that maintain genetic variation in fitness and resolve sexual conflict in nature. This is especially true when SSDRs are revealed by experimental evolution and/or line crosses; such approaches may be highly effective in demonstrating potential for SSDRs, but may not necessarily imply that observed effect sizes routinely arise or hence substantively shape evolutionary outcomes in the wild.

Here, jointly considering the four empirical studies (Barson et al. 2015; Grieshop and Arnqvist 2018; Pearse et al. 2019; Geeta Arun et al. 2021) can help develop conceptual frameworks and hypotheses. In particular, all four studies concern threshold or threshold-like traits, defined here as focal phenotypes that are manifested as dichotomous or competitive outcomes (further explained below). This is notable because threshold(-like) traits (as opposed to traits that are directly expressed and continuously distributed on observed phenotypic scales) are not typically the predominant focus of work in quantitative genetics or experimental evolution, or of explicit theory on (sex-specific) dominance evolution. The observation that all four empirical studies that demonstrate SSDRs concern threshold(-like)

traits consequently raises interesting questions of whether such traits have properties that foster evolution and/or expression of SSDRs involving large-effect loci and/or polygenic variation, and hence how such traits could play key roles in maintaining genetic variation and resolving sexual conflict in nature.

To address these questions, I first summarise pertinent properties of threshold(-like) traits. I then demonstrate how these properties can readily generate phenotypic SSDRs that arise as intrinsic consequences of sexual dimorphism and/or competition, without necessarily requiring either direct SSDRs in underlying allelic effects or directly concave genotype-fitness maps. I achieve these objectives using illustrative caricatures of traits, quantitative genetic architectures and study designs reported in the four recent empirical studies (Barson et al. 2015; Grieshop and Arnqvist 2018; Pearse et al. 2019; Geeta Arun et al. 2021). I thereby use these studies as inspiration to consider how SSDRs could arise, but do not imply that outlined scenarios necessarily apply in the focal systems. Finally, I highlight how explicitly considering the properties of threshold(-like) traits opens new theoretical and empirical routes to examining the dynamics of SSDRs and their impacts on evolutionary outcomes in nature.

Fundamental properties of threshold traits

The threshold trait concept is long established in quantitative genetics as a route to rationalising and predicting the dynamics of dichotomous phenotypes underpinned by highly polygenic genetic architectures. In brief, individuals are envisaged to have latent 'liabilities', which can comprise additive and/or non-additive genetic and environmental effects, and are assumed to be continuously distributed across individuals. Individuals' liability values translate into expression of alternative discrete phenotypes when above versus below some threshold (Figure 2, Falconer and Mackay 1996, Ch. 18; Roff 1996; Lynch and Walsh 1998, Ch.

25; Reid and Acker 2022). The threshold trait concept therefore explicitly invokes a highly non-linear genotype-phenotype map, and hence a non-linear genotype-fitness map if resulting dichotomous phenotypes substantively impact fitness.

While the basic threshold trait construction envisages a steep fixed threshold that generates entirely discrete phenotypes (Figure 2, Falconer and Mackay 1996; Lynch and Walsh 1998), the concept can be broadened to encompass shallower threshold slopes which could yield partial trait expression and which could themselves evolve (Chevin and Lande 2013). Broadly threshold-like properties can consequently arise for fitness components that are not intrinsically phenotypically dichotomous but that emerge from competitive interactions with some degree of 'winner takes all'. For example, competition for reproductive resources, matings or fertilisations can result in substantial variance in outcomes, even with relatively little variance in underlying trait values, if 'winning' individuals monopolise disproportionate shares (as observed in numerous systems, e.g. Dodson et al. 2013; Laturney et al. 2018; Parker 2020; see *Discussion*). Values of competing individuals must then be exceeded to achieve substantial reproductive success.

Since non-linear genotype-phenotype maps generally generate intrinsic dominance (Billiard et al. 2021), it is immediately plausible that threshold(-like) traits could induce such effects. Indeed, it is well established that threshold traits transform effects that are strictly additive on underlying liability scales into non-additive effects on observed phenotypic scales (Gianola 1982; Lynch and Walsh 1998; de Villemereuil 2018). There can therefore be substantial 'cryptic' genetic variation in liability, which has little or no immediate effect on phenotype, on either side of the threshold (Roff 1996, 1998; Reid and Acker 2022). However despite these properties, intrinsic dominance, and SSDRs more specifically, have predominantly been formally theoretically considered in the context of smooth fitness

surfaces, with little explicit consideration of threshold(-like) traits (Fry 2010; Manna et al. 2011; Connallon and Chenoweth 2019; Vasseur et al. 2019; but see Gilchrist and Nijhout 2001 for treatments of diffusion-gradient-threshold models). This omission is perhaps surprising since Wright (1934) originally postulated the threshold trait concept as a parsimonious explanation for otherwise puzzling and inconsistent patterns of apparent inheritance and dominance (as observed for guinea pig digit numbers).

Further, the threshold trait construction also fundamentally implies that mean observed phenotype depends not only on mean liability (relative to the threshold) but also on the variance in liability. This is because the mean and variance jointly define the proportion of individuals whose liabilities exceed the threshold and hence express the alternative phenotype (Figure 2, Supporting Information S1, Falconer and Mackay 1996). Hence, in the context of sex-specific effects, the observed degree of phenotypic sexual dimorphism in a threshold trait jointly depends on the degrees of sexual dimorphism in the mean and the variance in liability. Accordingly, sexual dimorphism in mean liability might or might not translate into sexual dimorphism in phenotype, depending on the degree of sexual dimorphism in the variance and on the distances of the sex-specific mean liabilities from the threshold (Figure 2, Supporting Information S1).

Given these well-established properties, the potential for threshold(-like) traits to generate SSDRs on observed phenotypic scales, with or without explicit genetic SSDRs acting on underlying liability scales, can be outlined with broad reference to the four recent empirical studies.

Linking from empirical studies to concepts of SSDRs in threshold(-like) traits

SSDRs involving large-effect loci: scenarios based on salmonids

Theory on SSDRs, involving either evolution of direct dominance modifiers or intrinsic effects of non-linear fitness landscapes, primarily envisages large-effect loci that detectably affect fitness (Fry 2010; Spencer and Priest 2016). Correspondingly, Barson et al. (2015) and Pearse et al. (2019) demonstrate SSDRs involving large-effect loci that affect related life-history traits in salmonids: maturation in Atlantic salmon and anadromy in rainbow trout. Both traits are commonly sexually dimorphic; males mature earlier and are less anadromous than females on average. Such dimorphisms likely result from sexually antagonistic selection arising because reproductive success is more strongly positively related to body size in females than males. This drives female-specific selection for prolonged growth, anadromy and later maturation, which trades off against increased probability of pre-reproductive mortality (Barson et al. 2015; Czorlich et al. 2018; Pearse et al. 2019). Meanwhile, the relatively undifferentiated sex chromosomes of salmonids have been suggested to inhibit sequestration of sexually antagonistic genes through sex linkage, generating interest in identifying additional mechanisms that could resolve sexual conflict (Pearse et al. 2019).

In salmon, genome-wide association studies using relatively high-density SNP data revealed a large-effect locus, VGLL3, where alternative alleles substantially affect the occurrence of maturation, and hence resulting maturation age, in both sexes (Barson et al. 2015). Genome construction and SNP-based interrogation in trout then revealed a double-inversion supergene that affects occurrence of anadromy (Pearse et al. 2019). In both cases, field data yielded evidence of SSDRs where heterozygotes show mean maturation ages or probabilities of anadromy that are to some degree closer to the alternative homozygotes in females versus males (e.g. Figure 1; Barson et al. 2015; Pearse et al. 2019). Yet, maturation

238 and anadromy in salmonids are also highly polygenic heritable traits, affected by numerous
239 loci of medium or small effect (e.g. Hecht et al. 2013; Weinstein et al. 2019; Sinclair-Waters
240 et al. 2020). Hence, they can be appropriately conceptualised as sexually dimorphic threshold
241 traits (Dodson et al. 2013; Debes et al. 2021), where substantial standing polygenic variation
242 in liability can exist alongside polymorphic large-effect loci.

243 Simple illustrations then show how such genetic architectures could readily generate
244 phenotypic SSDRs. To see this, first consider that females have relatively low mean baseline
245 liabilities to mature at a particular timepoint, with a population-wide distribution that scarcely
246 spans the threshold (e.g. blue curve on Figure 3A). Meanwhile, males have higher mean
247 baseline liabilities with identical variance, meaning that the population-wide distribution
248 substantially spans the threshold (e.g. blue curve on Figure 3B). Consequently, some males
249 will mature now but most females will not, meaning that sexual dimorphism in mean liability
250 translates into partial phenotypic sexual dimorphism (Figure 3).

251 Then, we can consider an alternative allele at a large-effect locus that increases mean
252 liability equally in both sexes. Population-wide distributions of liabilities of homozygotes for
253 the alternative allele (i.e. genotype AA instead of baseline aa) could then substantially exceed
254 the threshold in both sexes, meaning that most males and females will mature now,
255 potentially still with some phenotypic sexual dimorphism (e.g. grey curves on Figure 3).

256 Regarding SSDRs, the key question then concerns the locations of the sex-specific
257 distributions of liabilities of heterozygotes (i.e. genotype Aa) at the large-effect locus relative
258 to the threshold, and the resulting sex-specific frequencies of the alternative phenotypes.
259 Here, Figure 3 illustrates how SSDRs can readily emerge, even given purely additive effects
260 (i.e. co-dominance) of the large-effect alleles on the liability scale. This scenario occurs when
261 the increase in mean liability due to one copy of the alternative allele is sufficient to cause

most of the population-wide liability distribution to exceed the threshold in males but not females (e.g. red curves on Figure 3B versus 3A). Mean heterozygote phenotype (i.e. the proportion of Aa individuals that express the alternative phenotype) is then closer to that for the baseline (late maturing or anadromous) homozygote in females and the alternative (early maturing) homozygote in males, representing phenotypic SSDR (e.g. inset panels on Figure 3).

Given this scenario, Figure 3 illustrates how phenotypic SSDRs emerge from the combination of three properties: the deviations of the two sex-specific mean baseline liabilities from the threshold (shown by the two black horizontal lines) which together define the degree of sexual dimorphism in baseline liability (blue horizontal line) and its translation into sexual dimorphism in phenotype; and the additive effect size of the alternative allele at the large-effect locus (red horizontal lines). Diverse forms of symmetrical or asymmetrical partial or complete SSDR can consequently emerge, depending on the degree to which the three properties cause the mean liabilities for the heterozygotes and alternative homozygotes to lie on opposite sides of the threshold in the two sexes (mathematical derivations in Supporting Information S1).

Such SSDRs can then be further modulated by the variance in liability, and by the degree of sexual dimorphism in the variance (Supporting Information S1). For example, the scenario illustrated in Figure 3 can easily generate almost complete rather than partial SSDR given smaller variance in liability in both sexes (Figure 4A,B versus Figure 3). This is because the liability distributions for the heterozygotes (red curves) then lie almost completely on opposite sides of the threshold in females versus males (Figure 4A,B). Sexual dimorphism in the variance in liability could then generate partial phenotypic dominance in one sex and complete dominance in the other.

These scenarios imply that ongoing evolution of the degree of sexual dimorphism in mean and/or variance in liability, or simply environmental effects on the mean and/or variance and resulting phenotypic sexual dimorphism, could alter the emerging degree of phenotypic SSDR. For example, if there were less sexual dimorphism in mean baseline liability than illustrated in Figure 3, or the same degree of dimorphism but shifted relative to the threshold, then SSDR can readily disappear (e.g. Figure 4C,D). Hence, the forms of sexual dimorphism in the mean and variance in baseline liability, and in resulting phenotypes, can effectively act as dominance modifiers on the large-effect locus.

Indeed, temporal and/or spatial variation in sexual dimorphism in liability could readily arise in nature if the form of (sex-specific) selection varies among environments, potentially driving evolution of (sex-specific) plasticity and resulting phenotypic outcomes. For example, mean salmonid maturation ages and degrees of anadromy and sexual dimorphism commonly vary among populations, and even among cohorts (e.g. Dodson et al. 2013; Barson et al. 2015; Pearse et al. 2019; Weinstein et al. 2019). Observed degrees of SSDR could consequently vary among populations or cohorts, even with substantial gene flow and hence likely very similar genetic architectures. Indeed, the degree of phenotypic SSDR associated with VGLL3 genotype differed markedly between two Atlantic salmon populations despite low genetic divergence (low F_{ST}, Czorlich et al. 2018). Meanwhile, the genomic inversion that showed SSDR in anadromy in a Californian trout population (Pearse et al. 2019) had no detected effect in an Alaskan population (Weinstein et al. 2019). SSDRs can consequently be environment- and population-specific rather than a fixed intrinsic property of any particular large-effect locus or biological system, and the intrinsic properties of threshold traits can readily foster such modulations. Phenotypic dominance modification can

309 then be straightforward; it can simply result from additional genetic and/or environmental
310 effects on liability for any threshold trait.

311 Yet, while threshold traits can readily generate phenotypic SSDRs given purely additive
312 allelic effects on liability (Figures 3 and 4), there could in principle be direct SSDRs at the large-
313 effect locus that act on the liability scale (i.e. *liabilities* of heterozygotes could be closer to
314 opposite homozygotes in the two sexes, Figure 5, Supporting Information S1). Such liability-
315 scale SSDRs could translate into strong phenotypic SSDRs (Figure 5A,B), but will not
316 necessarily do so. Indeed, they could in principle even appear as purely additive phenotypic
317 effects (Figure 5C,D). This could occur if sex-specific dominance coefficients shift the liability
318 distributions for the heterozygotes so that the proportions of values exceeding the threshold
319 in each sex equal the means across the two homozygotes (Figure 5C,D). Consequently, the
320 degree of liability-scale SSDR cannot necessarily be directly inferred by quantifying the degree
321 of phenotypic SSDR, or vice versa.

322 Nevertheless, an alternative conceptual model for evolution of sex-specific
323 dominance modifiers on large-effect loci can be postulated. Current population genetic
324 models envisage that a focal large-effect locus already exists, and consider whether mutant
325 (sex-specific) dominance modifiers can invade (given some process that maintains
326 appreciable heterozygosity at the focal locus, e.g. Otto and Bourguet 1999; Spencer and Priest
327 2016). Yet, the threshold trait scenario implies that this logic could potentially be reversed:
328 we could assume that a potential dominance modifier (e.g. sexual dimorphism in mean
329 liability) already exists, and consider whether a large-effect mutation (or genomic inversion)
330 can invade. This scenario could remove the initial requirement for appreciable heterozygosity
331 at the large-effect locus. Since sexual dimorphism in mean trait values can clearly evolve and
332 show plasticity, and there can also be sexual dimorphism in additive genetic and phenotypic

variances (Lande 1980; Wyman and Rowe 2014), the background conditions for effective invasion of genetic variants that show SSDRs may be commonplace. Such scenarios for evolution of SSDRs can in future be further examined (see *Discussion*).

In the scenarios depicted in Figures 3-5, population-wide distributions of liabilities are Gaussian, as is typically assumed in quantitative genetic analyses of threshold traits and is plausible given manifold genetic and environmental effects (Wright 1934; Falconer and Mackay 1996; Lynch and Walsh 1998; Moorad and Promislow 2011; Supporting Information S1). However, in principle, SSDRs in threshold traits could also readily emerge given different distributions of liabilities (even given uniform distributions, Supporting Information S3); the same principles as for Gaussian distributions still apply. Consequently, to generate SSDRs in threshold traits, there is no necessary condition that distributions of liabilities must be Gaussian or concave around the mean, as is required for genotype-fitness maps to generate intrinsic SSDRs in sexually dimorphic traits that are directly expressed on observed phenotypic scales (Fry 2010; Connallon and Chenoweth 2019). Hence, overall, polygenic threshold traits involving large-effect loci could readily generate substantial and dynamic SSDRs without requiring any specific or tightly restrictive underlying distributions of liabilities.

Genome-wide SSDRs: scenarios based on experimental evolution in *Drosophila*

While the above scenarios and salmonid examples concern SSDRs involving large-effect loci, evidence of SSDRs that effectively involve highly polygenic variation, without any known loci of detectably large individual effect, has also emerged. Geeta Arun et al. (2021) undertook a major experiment that revealed polygenic SSDR for survival through exposure to bacteria (*Pseudomonas entomophila*) in *Drosophila melanogaster*. Such survival is clearly a key fitness component, implying selection for increased immunity. However, increased immunity may

trade-off against reduced mating success, particularly in males (Geeta Arun et al. 2021). Fitness may consequently be higher in less resistant individuals in the absence of bacterial exposure. Such trade-offs may be weaker in females, which compete less strongly for mates. Immunity, and hence survival, can consequently experience sexually antagonistic selection of a magnitude that depends on bacterial exposure. Further, in general, survival can often be reasonably envisaged as a highly polygenic threshold trait (Lynch and Walsh 1998; Moorad and Promislow 2011).

Geeta Arun et al.'s (2021) stock *Drosophila* showed low survival rates when experimentally challenged with *Pseudomonas*, with only slight (not statistically significant) phenotypic sexual dimorphism. Then, 65+ generations of experimental evolution, where parents in each generation comprised individuals that survived bacterial challenge, successfully generated lines that were more resistant, with much higher survival rates and still little phenotypic sexual dimorphism. This evolutionary response indicates substantial additive genetic variation underlying survival, with no evidence of sex-linkage (Geeta Arun et al. 2021).

Geeta Arun et al. (2021) then crossed the evolved resistant lines back to the original stock, and assayed survival of resulting 'hybrid' offspring through further experimental challenge with *Pseudomonas*. Sexual dimorphism then emerged, where female hybrids showed relatively high survival rates (closer to the resistant lines than the stock), while male hybrids showed relatively low survival rates (closer to the stock than the resistant lines). These patterns imply (partial) polygenic SSDR, at least assuming the hybrids are relatively heterozygous at numerous loci compared to the stock and resistant lines (Geeta Arun et al. 2021).

The question then is whether such SSDRs, with phenotypic sexual dimorphism in hybrid offspring without substantial phenotypic sexual dimorphism in either the stock or evolved parental lines, can potentially emerge in a threshold trait even without any explicit genetic dominance reversal (i.e. with purely additive genetic effects on liability). Simple scenarios suggest that they potentially can, due to the key property that mean phenotypic values of threshold traits depend on both the mean and variance in liability (Figure 2).

For example, consider that survival through bacterial challenge constitutes a threshold trait where the *Drosophila* stock population has some sexual dimorphism in both mean and variance in liability, such that males have lower mean and higher variance than females (e.g. blue curves on Figure 6). This is broadly consistent with a stronger trade-off between immunity and mating success in males than females, which could stabilise a lower mean yet maintain more (cryptic) genetic variation. Yet, despite such dual sexual dimorphism in baseline liability (i.e. in mean and variance), there may be little sexual dimorphism in observed phenotypic survival rate (Figure 6). Most liability values in both sexes lie below the threshold, implying relatively low survival rates (as observed by Geeta Arun et al. 2021).

Then, following experimental evolution, mean liabilities for both sexes lie above the threshold, with little or no sexual dimorphism in either mean or variance, or hence in mean phenotype (e.g. grey curves on Figure 6). This outcome reflects that the experimental environment imposes consistent strong selection for increased immunity, potentially altering the balance of sex-specific trade-offs with mating success and decreasing the degree of sexual antagonism (as commonly postulated in harsher environments, Berger et al. 2014; Punzalan et al. 2014; Connallon and Hall 2016; Plesnar-Bielak and Łukasiewicz 2021). Consequently, following evolution, most individuals of both sexes now survive (as observed by Geeta Arun et al. 2021).

Now, given crosses to create hybrid offspring and assuming purely additive genetic effects, mean liabilities for female and male hybrids could lie above and below the threshold respectively with some asymmetry (e.g. red curves on Figure 6). Majorities of females and males consequently survive and die respectively. Mean phenotypic survival for the two sexes is therefore closer to the evolved versus stock parental lines respectively, constituting (partial) SSDR (e.g. inset panels on Figure 6, as observed by Geeta Arun et al. 2021).

This simple example illustrates how initial sexual dimorphism in the mean and variance in liability underlying a threshold trait can potentially generate apparent SSDRs following experimental evolution and backcrossing, even with purely additive genetic effects on the liability scale and without substantial phenotypic sexual dimorphism in either the stock or evolved populations. Such scenarios can be formally conceptualised in analogous ways as given a large-effect locus, where the shift in mean breeding value generated by experimental evolution is analogous to the liability-scale effect size of the alternative large-effect allele (Supporting Information S1). Emergence of SSDRs therefore depends on the sex-specific means and variances in liability in the baseline and evolved lines. Additional complexities could arise, for example because variances in liabilities could more plausibly differ between lines than between groups of individuals that simply differ in genotype at a large-effect locus (e.g. Figure 6, Supporting Information S1).

But, scenarios such as that sketched in Figure 6 raise questions regarding the implications of such experimentally-induced SSDRs for the maintenance of genetic variation and/or resolution of sexual conflict within focal populations in nature, which are key reasons why SSDRs are of interest. One immediate implication is that widespread expression of substantial net SSDRs for highly polygenic traits may require frequent introgression among diverged lines to generate relatively high degrees of genome-wide heterozygosity in offspring

428 of parents whose mean liabilities lie on opposite sides of the threshold. Such introgression
429 could be relatively common in spatially structured systems where locally adapted populations
430 are linked by dispersal. However, this is not the primary circumstance where additional
431 explanations for the maintenance of genetic variation are required. Rather, dispersal and
432 resulting gene flow can directly maintain standing genetic variation exceeding that expected
433 solely due to mutation-selection balance (McDonald and Yeaman 2018). Further, persistence
434 of local adaptation despite frequent introgression implies low fitness of hybrid offspring (or
435 subsequent descendants). This in turn implies epistatic effects resulting in outbreeding
436 depression or hybrid breakdown, which could eliminate phenotypic SSDRs. Consequently, it
437 is not yet clear to what degree capacity for SSDRs as observed through experimental evolution
438 and backcrossing among diverged lines will actually translate into substantial SSDRs in fitness
439 in nature.

440 Increased genome-wide heterozygosity within populations, and hence increased
441 opportunity for SSDRs in highly polygenic traits, could also potentially be generated by
442 disassortative mating for focal traits given positive cross-sex genetic covariances in allelic
443 effects. Such disassortative mating is conceivable in systems such as Geeta Arun et al.'s (2021)
444 *Drosophila*, for example if high-immunity females are most likely to survive to reproduce
445 while low-immunity males are most attractive (given the postulated trade-off, Geeta Arun et
446 al. 2021). This would effectively represent positive assortative mating for fitness, given
447 sexually antagonistic genetic effects (e.g. Arnqvist 2011). Some substantive degree of SSDR in
448 fitness may then emerge in resulting offspring. However, more generally, some additional
449 mechanism may be required to generate divergent sex-specific phenotypic outcomes given
450 continuously distributed underlying genetic variation. Such mechanisms could potentially

include evolution of direct liability-scale SSDRs, or further non-linearities resulting from competitive interactions.

Genome-wide SSDRs: scenarios based on line-crosses in seed beetles

The potential for competitive interactions to generate phenotypic SSDRs underpinned by polygenic variation can be considered with reference to Grieshop and Arnqvist's (2018) line-cross experiment in seed beetles. Here, strong sexually antagonistic selection occurs in the stock population, with a negative cross-sex genetic correlation for fitness evident at standard temperatures (Berger et al. 2014). Grieshop and Arnqvist (2018) crossed 16 isogenic (inbred) lines representing the spectrum of female-beneficial (male-detrimental) versus male-beneficial (female-detrimental) variants in a full-diallel design (i.e. all 16 lines mated with all 16 lines). Lifetime reproductive success (i.e. fitness) of resulting F1 offspring was assayed through competitive trials. Then, for each of the 16 lines, the covariance between the mean competitive fitness of F1 offspring resulting from crosses between the focal line and each other line versus inbred F1s from the other line, was calculated (Grieshop and Arnqvist 2018). Here, small covariance implies that the focal line contains many dominant alleles, such that genetic effects of the other lines are effectively irrelevant. Conversely, large covariance implies that the focal line contains many recessive alleles, such that genetic effects of the other lines dominate. These covariances were calculated for females and males separately, and the cross-sex correlation in covariances across the 16 lines was computed, giving a strongly negative value. Consequently, lines with small covariance across line crosses for males (implying genome-wide dominance) had large covariance for females (implying genome-wide recessivity), and vice versa. This implies genome-wide SSDR for fitness (Grieshop and Arnqvist 2018, reviewed by Connallon and Chenoweth 2019).

Of interest here is the assay used to quantify individual fitness. To approximate natural conditions, Grieshop and Arnqvist (2018) staged competitive mating trials, where focal individuals competed against (sterilised) reference stock individuals for resources and fertilisations (females) or paternity (males). Such approximations of natural conditions are valuable since simple environments can strongly affect outcomes of sexual selection and associated experiments in model systems (Yun et al. 2017; Plesnar-Bielak and Łukasiewicz 2021; Matzke et al. 2022). Indeed, the form of fitness assay could potentially shape the manifestation of SSDRs, by turning fitness into a threshold-like trait.

Specifically, if there is a negative cross-sex genetic correlation in underlying additive genetic value and some degree of non-linear or 'winner takes all' fitness outcome in both sexes, then females and males from female-beneficial (i.e. male-detrimental) lines will have disproportionately high and low success respectively, while females and males from male-beneficial (i.e. female-detrimental) lines will have disproportionately low and high success respectively. Simple simulations show how opposite non-additive effects on fitness can then emerge in females versus males, readily generating a negative cross-sex correlation in line cross covariance and hence apparent phenotypic SSDR (Figure 7, Supporting Information S4, as observed by Grieshop and Arnqvist 2018). Indeed Grieshop and Arnqvist (2018) report some evidence of epistatic variance, which is consistent with a non-linear fitness function.

Such outcomes depend on the shapes of the relationships between genetic value and competitive reproductive success in each sex, and on the relative mean value of the reference population against which competitive reproductive success is assayed (which effectively defines the threshold for disproportionately high or low success, Figure 7A, Supporting Information S4). Intrinsic emergence of SSDRs can consequently be shaped by details of the mating and reproductive systems, which therefore effectively act as dominance modifiers.

499 Ongoing evolution of, or ecological or environmental effects on, the mating system and forms
500 of pre- and post-copulatory sexual selection could consequently shape the manifestation of
501 SSDRs in fitness.

502 Yet, the evolutionary implications of outcomes such as those observed in the seed
503 beetle experiments (Grieshop and Arnqvist 2018) will again also depend on the degree to
504 which heterozygosity across numerous loci affecting fitness actually arises in nature, and the
505 resulting degree to which the full intrinsic potential for SSDRs is actually expressed. Genome-
506 wide heterozygosity of magnitudes analogous to those resulting from inbred line crosses
507 could plausibly arise in invertebrates and plants that can produce inbred or selfed generations
508 on ephemeral or isolated resources followed by episodes of dispersal and outcrossing,
509 generating cycles of inbreeding and outbreeding (e.g. Goodwillie et al. 2005; Cornell and
510 Tregenza 2007; Whitehead et al. 2018), but will typically be more restricted otherwise.
511 Intrinsic potential for genome-wide SSDRs is therefore intertwined with mating system
512 dynamics.

513

514 ## *Discussion*

515 SSDRs could, in principle, contribute substantially to maintaining genetic variation and
516 resolving sexual conflict in nature (Fry 2010; Barson et al. 2015; Spencer and Priest 2016;
517 Grieshop and Arnqvist 2018; Connallon and Chenoweth 2019; Grieshop et al. 2021). But, the
518 prevalence, magnitudes and implications of such effects depend on how SSDRs in fitness and
519 fitness components actually arise in wild populations, and hence on their potential for
520 evolutionary, ecological and environmental modulation. I highlight how phenotypic SSDRs
521 could in principle readily arise in threshold(-like) traits characterised by dichotomous and/or
522 competitive outcomes, potentially allowing rapid modulations that are intertwined with the

evolutionary dynamics and plasticity of sexually antagonistic selection, sexual dimorphism and reproductive systems. New theoretical and empirical efforts are now required to examine dynamics of locus-specific and genome-wide SSDRs arising in the contexts of natural genetic, ecological and environmental variation, and to infer short-term and longer-term impacts on standing genetic variation and sexual conflict.

Emergence and modulation of SSDRs in threshold(-like) traits

The presented illustrative scenarios show how threshold(-like) traits can readily generate phenotypic SSDRs that broadly caricature those observed in recent empirical studies, even given purely additive genetic effects on underlying scales. Given polygenic quantitative genetic architectures that include large-effect loci, simply the presence of sexual dimorphism in mean baseline liability relative to the threshold (and potentially also in the variance) can generate phenotypic SSDRs (e.g. Figures 3 and 4, Supporting Information S1). Given genome-wide effects, substantial phenotypic SSDRs can emerge given crosses among diverged lines, and/or given a negative cross-sex genetic correlation and a reproductive system that generates some non-linear or disproportionate outcome (e.g. Figures 6 and 7, Supporting Information S4). Explicit SSDRs acting directly on underlying scales, for example involving some form of direct sex-specific genetic dominance modification, could exist but are not necessarily required, and could conceivably even eliminate rather than generate phenotypic SSDRs (e.g. Figure 5).

These scenarios show how forms of genetic and phenotypic sexual dimorphism and reproductive systems, which in turn shape and are shaped by the degrees of sexually antagonistic selection, can effectively act as broad-sense dominance modifiers that could modulate the degree of phenotypic SSDR in threshold(-like) traits. While the occurrence of

sexual dimorphism in trait means is widespread and very well known, the possibility that there can be sexual dimorphism in genetic and/or environmental trait variances is also embedded in core aspects of evolutionary quantitative genetic theory and increasingly evidenced in diverse empirical systems, resulting from some degree of sex-specific autosomal as well as sex-linked genetic effects (e.g. Lande 1980; Brommer et al. 2007; Ober et al. 2008; Wyman and Rowe 2014; Janicke et al. 2016; Wolak et al. 2018; Kaufmann et al. 2021; van der Bijl and Mank 2021). Furthermore, degrees of sexual dimorphism, mating and reproductive systems and magnitudes of sexually antagonistic selection and sexual conflict can commonly vary markedly with ecological and environmental conditions (e.g. Post et al. 1999; Punzalan et al. 2014; Taylor et al. 2014; Connallon 2015; Connallon and Hall 2016; de Lisle et al. 2018; Perry and Rowe 2018; Whitehead et al. 2018; Zhou et al. 2019; Chelini et al. 2021; Plesnar-Bielak and Łukasiewicz 2021; Matzke et al. 2022). Indeed, numerous threshold traits, including alternative reproductive tactics, can show rapid environmentally-induced expression of alternative phenotypes, implying environmental modulation (i.e. plasticity) on both liability and phenotypic scales (Roff 1996; Dodson et al. 2013; Neff and Svensson 2013; Reid and Acker 2022).

Taken together, these well-established forms of sexual dimorphism and ecological variation imply that SSDRs in threshold(-like) traits should not necessarily be viewed as fixed properties that could act as alternatives to evolved sexual dimorphism in resolving sexual conflict. Rather, they can be viewed as evolutionarily, ecologically and environmentally labile outcomes that could emerge from, and potentially co-evolve with, degrees of sexual dimorphism and reproductive systems. While it is long-established that dominance relationships emerge as intrinsic properties of non-linear biological systems, such systems are often considered to be relatively fixed or stable (e.g. involving enzymatic and biochemical

571 pathways and overall fitness landscapes generated by stabilising selection, Otto and Bourguet
572 1999; Fry 2010; Manna et al. 2011; Connallon and Chenoweth 2019; Billiard et al. 2021, but
573 see Gilchrist and Nijhout 2001). Considering the properties of threshold traits shows how
574 biological systems that tune the degree of intrinsic SSDR could potentially be highly dynamic,
575 readily evolve, and be subject to ecological and environmental modulation.

576 Such possibilities are pertinent because many key life-history traits that affect fitness
577 in wild, domesticated and human populations can be reasonably conceptualised as polygenic
578 threshold(-like) traits. Obvious examples include occurrences of maturation, seasonal
579 migration, diapause, resistance to disease, survival, alternative reproductive tactics and
580 development of alternative morphologies (Roff 1996; Moorad and Promislow 2011; Pulido
581 2011; Dodson et al. 2013; Neff and Svensson 2013; Wray and Visscher 2015; Debes et al. 2021;
582 Reid and Acker 2022). Forms of mate choice, competition and resulting sexual selection can
583 also readily generate non-linear relationships between phenotypic trait values (and hence
584 underlying additive genetic effects) and fitness. Such non-linearities arise where single
585 individuals dominate mating or reproduction (i.e. strongly skewed outcomes of intra-sexual
586 competition); where all or most individuals preferentially mate with the same chosen mate(s)
587 (i.e. strongly directional pre- or post-copulatory mate choice); and/or single males achieve
588 disproportionate fertilisation success through post-copulatory processes (e.g. 'loaded raffle'
589 outcomes of sperm competition and/or strong first- or last-mating precedence). Some degree
590 of 'winner takes all' is consequently commonplace across diverse taxa and reproductive
591 systems (e.g. Nonacs and Hager 2011; Dodson et al. 2013; Laturney et al. 2018; Parker 2020;
592 Matzke et al. 2022), including in the seed beetles that generated evidence of genome-wide
593 SSDRs (Yamane et al. 2015). Fitness will therefore typically be affected by at least one
594 threshold(-like) trait in many, or most, species.

595 Accordingly, the potential for threshold(-like) traits to generate strong phenotypic
596 SSDRs, including through co-evolutionary feedbacks involving genetic architectures, forms of
597 sexual dimorphism and reproductive systems, should now be more explicitly examined, both
598 theoretically and empirically. Such work can aim to more clearly distinguish key points: the
599 degrees to which SSDRs can in principle arise through combinations of intrinsically non-linear
600 genotype-phenotype maps and/or explicit genetic dominance modification, and the degrees
601 to which such SSDRs are actually likely to be expressed, to be dynamic, and to act as
602 predominant forces that could widely maintain genetic variation and resolve sexual conflict
603 given forms and impacts of heterozygosity arising in nature.
604
605 **Opportunities for theoretical advances**
606 Multiple opportunities for theoretical advances are evident. First, we can examine whether,
607 by facilitating emergence of phenotypic SSDRs, threshold traits with sexual dimorphisms in
608 liability could actually facilitate invasion and maintenance of stable polymorphisms for large-
609 effect mutations or complexes of linked genes with sexually antagonistic phenotypic effects.
610 We can then examine whether such invasions can feed back to shape the form and plasticity
611 of underlying sexual dimorphism. To date, dynamics of genetic architectures involving large-
612 effect loci or gene clusters have been examined in the context of local adaptation and
613 migration-selection-drift balance (e.g. Yeaman and Whitlock 2011; Yeaman 2013), but
614 scarcely explicitly considered in the context of threshold traits or SSDRs (or more widely in
615 the context of balancing selection, Llaurens et al. 2017). Such work would encompass the key
616 point that, since phenotypic dominance of any large-effect allele effectively depends on
617 (polygenic) genetic values for baseline liabilities, SSDRs in threshold traits can substantially
618 reflect epistasis. While it has been highlighted that forms of additive-by-additive epistasis can

shape the maintenance of sexually antagonistic genetic variation given SSDRs (Arnqvist et al. 2014), the reciprocal point that intrinsic SSDRs in threshold(-like) traits can effectively result from epistasis given underlying sexual dimorphism has not been emphasised.

Second, we can examine whether, given initial sexual conflict manifested as negative cross-sex genetic correlations for fitness, reproductive systems can actually evolve to shape fitness functions that generate some degree of disproportionate competitive outcome and thereby generate SSDRs that in turn ameliorate sexual conflict. Such evolution could, for example, conceivably involve diverse mechanisms that shape the occurrence and outcome of competition for reproduction, including degrees of directional mate choice, first- or last-mating precedence, and even polyandry itself. Expression of substantial genome-wide SSDRs shaped by numerous loci of small effect also requires some degree of genome-wide heterozygosity, which could be fostered by evolution of some degree of disassortative mating for traits (and resulting assortative mating for fitness given sexual antagonism, Arnqvist 2011). Yet, by imposing sexual selection for opposite sex-specific phenotypes, evolution of disassortative mating could potentially exacerbate net sexually antagonistic selection on target phenotypes, and resulting sexual conflict. Evolution of mechanisms that generate heterozygosity and thereby foster SSDRs could therefore conceivably strengthen rather than necessarily reduce conflict, potentially undermining any evolutionary benefit of SSDRs. Any such joint dynamics of SSDRs and reproductive systems could also usefully be placed in the context of population structure and environmental variation and change, which can alter the degrees of heterozygosity and sexual conflict and shape sex-specific evolutionary outcomes (e.g. Berger et al. 2014; Punzalan et al. 2014; Connallon and Hall 2016; de Lisle et al. 2018; Perry and Rowe 2018; Chelini et al. 2021; Plesnar-Bielak and Łukasiewicz 2021; Tschol et al. 2022).

643 Third, we can examine the plausibility of evolution of explicit dominance modifiers
644 that act directly on underlying liability scales. In general, loci affecting liabilities could
645 potentially show relatively high heterozygosity, which is generally required for evolution of
646 dominance modifiers (e.g. Otto and Bourguet 1999; Spencer and Priest 2016). This is because
647 such loci can maintain relatively high mutation-selection-drift balance (Roff 1998), which in
648 turn is because genetic variants typically have no phenotypic effect if occurring in a liability
649 background which is far from the threshold, and are consequently sheltered from selection.
650 Yet, by the same logic, any liability-scale SSDRs will not necessarily be phenotypically
651 expressed (e.g. Figure 5), meaning that otherwise neutral dominance modifiers will not be
652 subject to (indirect) selection. It is consequently unclear to what degree, or under what
653 circumstances, direct liability-scale dominance modifiers in threshold(-like) traits could
654 evolve.

655 Overall, therefore, there is considerable scope for evolutionary dynamics of both
656 phenotypic and liability-scale SSDRs in threshold(-like) traits to be formally considered
657 through new models that jointly track (co-)evolution of multiple routes to generating and
658 resolving sexual conflict, including sexual dimorphisms and complex reproductive systems.

659

660 **Opportunities for empirical advances**

661 There is also considerable scope for future empirical studies to explicitly examine the basis
662 and modulation of phenotypic SSDRs in threshold(-like) traits. First and most obviously, we
663 should more explicitly distinguish whether observed phenotypic SSDRs (or lack of SSDRs)
664 result from direct SSDRs acting on underlying liability scales, or from the properties of defined
665 non-linear genotype-phenotype or genotype-fitness maps (given purely additive underlying
666 genetic effects), or both. This distinction requires estimating appropriate liability-scale fixed

667 effects and variance components and back-transforming onto observed phenotypic scales,
668 which has not yet been a primary focus of empirical studies of SSDRs in threshold traits
669 (Supporting Information S5, but see Debes et al. 2021). Such analyses can be enacted using
670 established machineries of generalized linear mixed models (GLMMs), which intrinsically
671 distinguish liability and observed scales, and where algorithms for back-transforming fixed
672 effects and random effect variances (and variances conditional on fixed effects) are available
673 (de Villemereuil et al. 2016). Specifically, GLMMs with binomial error distributions and probit
674 link functions correspond to the threshold trait model.

675 Second, we should more explicitly quantify the degree to which phenotypic SSDRs are
676 modulated by ecological and environmental conditions, thereby treating SSDRs as dynamic
677 rather than fixed entities. This could be achieved, for example, by manipulating
678 environmental conditions that affect the degree of sexually antagonistic selection, or the
679 degree or form of competition for reproductive success. Any experiment designed to reveal
680 SSDRs requires major efforts, even without any ambition to replicate across different
681 conditions (e.g. Grieshop and Arnqvist 2018). Yet, experiments designed to quantify variation
682 in SSDRs could potentially be streamlined, for example by focussing on fewer targeted crosses
683 experiencing different environments.

684 Third, we should more extensively quantify the frequency, dynamics and net
685 magnitude of SSDRs arising in threshold(-like) traits in wild populations. This objective will
686 require attention to how locus-specific or genome-wide heterozygosity arises, and to the
687 overall phenotypic consequences of such heterozygosity. It has been widely emphasised that
688 substantial heterozygosity is required for evolution of dominance modifiers (Otto and
689 Bourguet 1999; Spencer and Priest 2016; Connallon and Chenoweth 2019). Yet, even when
690 SSDRs arise as intrinsic properties of threshold(-like) traits (or other non-linear systems with

691 purely additive underlying genetic effects, e.g. Gilchrist and Nijhout 2001; Fry 2010; Vasseur
692 et al. 2019) where initial heterozygosity is not required for system evolution, SSDRs will not
693 be maximally expressed and hence will have reduced biological impact if there is little
694 heterozygosity across contributing loci. The two recent studies that demonstrated SSDRs in
695 free-living salmonids focused on large-effect sexually-antagonistic loci (Barson et al. 2015;
696 Pearse et al. 2019), greatly facilitating direct identification and comparison of heterozygotes
697 and homozygotes. But, such architectures may generally be more exceptional than typical.
698 SSDRs involving highly polygenic variation, where individual loci have very small liability
699 effects that may not be directly phenotypically expressed, should now be explicitly examined
700 in wild or wild-derived populations in at least semi-natural environmental conditions. This
701 could potentially be achieved by quantifying sex-specific fitness of known offspring of
702 immigrant-native crosses relative to parental populations in structured meta-population
703 systems, or of individuals with different degrees of genome-wide heterozygosity resulting
704 from local inbreeding versus outbreeding. Emergence of SSDRs can then be evaluated in the
705 context of architectures that shape the relative fitness of polygenic heterozygotes and
706 homozygotes, notably the degree of directional dominance (which underpins both inbreeding
707 depression and heterosis, Falconer and Mackay 1996; Lynch and Walsh 1998). Such data on
708 genome-wide heterozygosity and fitness components will be increasingly available through
709 multi-generation individual-based and/or genomic studies of wild populations, and should be
710 central to ascertaining the potential and actual impacts of dynamic SSDRs in maintaining
711 genetic variation and resolving sexual conflict in nature.
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JMR conceived the ideas and wrote the manuscript.

Data

There are no primary data associated with this conceptual manuscript. R code underlying the illustrative figures is provided as Supporting Information.

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Figure 1. Basic illustration of (partial) sex-specific dominance reversal (SSDR), generating (partial) phenotypic optimisation in both sexes. Given two possible alleles (a and A) at a focal large-effect locus, the aa homozygote has a lower phenotypic value than the AA homozygote in both sexes (shown in black and grey). The phenotypic value of the Aa heterozygote is closer to that of the AA homozygote in the black sex and to that of the aa homozygote in the grey sex, constituting SSDR. If high and low phenotypic values lead to higher fitness in the black and grey sexes respectively (asterisks, implying sexually antagonistic selection) then there will be net heterozygote advantage across the population, generating balancing selection that can help maintain genetic variation. The dashed line highlights the expected phenotypic value of the Aa heterozygote given purely additive allelic effects. The illustrated scenario shows symmetrical SSDR with no phenotypic sexual dimorphism in either homozygote. However more generally, the two sexes could show different degrees of partial or complete dominance with some degree of sexual dimorphism in the homozygotes. Sex-specific dominance, but not SSDR, would arise if phenotypic values for the Aa heterozygotes are above (or below) the additive expectation in both sexes, but to different degrees. SSDR is typically defined on the phenotypic scale (as depicted). By analogy, genome-wide rather than single-locus SSDRs could arise if heterozygous offspring of crosses between (relatively) homozygous parental lines show mean phenotypes that resemble different parental lines in the two sexes.

925 **Figure 2.** Basic concept of a threshold trait. Individuals have liabilities (x-axis) comprising
926 genetic and environmental effects which translate into expression of phenotype 2 versus
927 phenotype 1 when above versus below the threshold (T, black vertical line), generating an
928 intrinsically non-linear genotype-phenotype map. Dark and light grey curves show
929 hypothetical distributions of liabilities for two populations or groups (which could be sexes)
930 with the same number of individuals in each group (i.e. same area under each curve). The
931 mean (vertical dashed lines) and standard deviation (horizontal dashed lines) of the liability
932 distributions both differ between the two groups (the dark grey group has a lower mean and
933 greater standard deviation and hence greater variance). Nevertheless, the proportion of
934 individuals that expresses phenotype 2 (i.e. the relative area under each curve that exceeds
935 the threshold), and hence the mean phenotype, is the same for both groups (0.21 in the
936 depicted example). Hence, sexual dimorphism in liability will not necessarily translate into
937 sexual dimorphism in observed phenotype. Mathematical treatments are in Supporting
938 Information S1.
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Figure 3. Illustration of emergence of (partial) sex-specific dominance reversal (SSDR) in a threshold trait with sexual dimorphism in mean baseline liability and a large-effect locus with purely additive allelic effects on liability. Blue and grey curves show the population-wide distributions of liabilities for the two alternative homozygotes at the large-effect locus (aa and AA, assuming an additional polygenic architecture) in (A) females and (B) males. Red curves show the population-wide distributions of liabilities for the heterozygotes (Aa), assuming additive effects of the alternative alleles (i.e. co-dominance) on the liability scale that are the same in both sexes. The black vertical line denotes the threshold, above which the alternative phenotype is expressed. Accordingly, inset panels show the proportions of individuals of each homozygote (blue and grey) and the heterozygote (red) that express the alternative phenotype. Dotted lines link the proportions for the two homozygotes, visualising that the proportions for the heterozygotes lie below versus above the additive expectations in females versus males, constituting SSDR (e.g. Figure 1). On the main figures, vertical dashed lines denote mean liabilities. Black horizontal lines denote the distances from each sex-specific mean for the lower homozygote (i.e. blue vertical line) to the threshold. The blue horizontal line highlights the degree of sexual dimorphism in mean liability (i.e. distance between the blue vertical lines for males versus females). Red horizontal lines highlight the additive effect of the alternative allele at the large-effect locus (here, the same in both sexes). Illustrated liability distributions are Gaussian, but this is not essential to generate SSDRs (Supporting Information S3). Parameter values for the illustrated example are in Supporting Information S2.

Figure 4. Illustrations of emergence of (A,B) complete phenotypic sex-specific dominance reversal (SSDR) or (C,D) an absence of SSDR, given a threshold trait with sexual dimorphism in mean baseline liability and a large-effect locus with purely additive allelic effects on liability. Specifications are as for Figure 3, where blue and grey denote the alternative homozygotes (aa and AA) and red denotes the heterozygote (Aa). (A,B) Same scenario as Figure 3 except with smaller variances in liability. Liability distributions for the heterozygotes therefore fall almost entirely on opposite sides of the threshold in (A) females versus (B) males, resulting in almost complete SSDR (inset panels). (C,D) Same scenario as Figure 3 except with higher mean baseline liabilities in both (C) females and (D) males. Liability distributions for the heterozygotes therefore fall predominantly on the same side of the threshold in both sexes, resulting in no SSDR (inset panels: red points lie above the dotted lines in both sexes). Parameter values are in Supporting Information S2. Plotted y-axis scales differ between panels A and B versus C and D.

Figure 5. Illustrations of (A,B) strong phenotypic sex-specific dominance reversal (SSDR) or (C,D) an absence of phenotypic SSDR, given a threshold trait with sexual dimorphism in mean liability and liability-scale SSDR in allelic effects at a large-effect locus. Specifications are as for Figure 3, where blue and grey denote the alternative homozygotes (aa and AA) and red denotes the heterozygote (Aa). (A,B) Same scenario as Figure 3 except that the alternative allele at the large-effect locus shows partial liability-scale SSDR rather than sex-independent additivity (baseline allele is dominant in females, alternative allele is dominant in males). Strong phenotypic SSDR emerges (inset panels). (C,D) Same scenario as A,B except that the alternative allele at the large-effect locus shows reversed partial liability-scale SSDR (baseline allele is dominant in males, alternative allele is dominant in females). The inset panels show that the proportions of heterozygotes that exceed the threshold match the additive expectations (i.e. lie on the dotted lines in both females and males). Consequently, there is no phenotypic SSDR, and in fact no phenotypic dominance, despite liability-scale SSDR. On all panels, red horizontal lines highlight the sex-specific effects of one copy of the alternative allele at the large-effect locus relative to the baseline homozygote, encompassing allelic effect size and dominance coefficient. Parameter values are in Supporting Information S2.

Figure 6. Illustration of emergence of (partial) sex-specific dominance reversal (SSDR) in a threshold trait with sexual dimorphism in the mean and variance in baseline liability, following hypothetical experimental evolution and subsequent backcrossing. Blue curves show the distributions of baseline liabilities in the stock population in (A) females and (B) males. Grey curves show the distributions of liabilities following experimental evolution. Red curves show the distributions of liabilities in hybrids resulting from backcrosses between evolved and stock populations given purely additive genetic effects on means. Here, variance in liability might be slightly higher in males, depending on what mechanisms create and maintain sexual dimorphism in variance in the stock population. Black vertical lines denote the threshold, above which the focal trait (e.g. survival through bacterial exposure) is expressed. Accordingly, inset panels show the proportions of individuals of the stock (blue), evolved (grey) and hybrid (red) populations that express the phenotype (i.e. survive). There is little sexual dimorphism in either the stock or evolved populations, since similar proportions of the liability distributions exceed the threshold in both sexes. Dotted lines link the proportions for the stock and evolved populations, visualising that the proportions for the hybrids lie above versus below the basic additive expectation in females versus males, representing partial SSDR. On the main figures, vertical dashed lines denote mean liabilities. Blue horizontal dashed lines highlight the standard deviations in liability in the stock population. There is therefore sexual dimorphism in both mean and variance in liability in the stock population, but not necessarily in the evolved population. Illustrated distributions are Gaussian, but this is not essential to generate SSDR. Parameter values are in Supporting Information S2.

Figure 7. Summary of simulations that generate sex-specific dominance reversals (SSDRs) in competitive fitness in a full diallel line-cross given underlying additive genetic effects. (A) Form of the assumed non-linear relationship between an individual's additive genetic value and its probability of paternity or maternity in competition with a reference individual. The depicted relationship is relatively extreme 'winner takes all', designed to illustrate key concepts. Simulations with less extreme relationships are in Supporting Information S4. The vertical dashed line indicates the mean genetic value of simulated lines. (B) Emerging negative cross-sex correlation between covariances between competitive fitness measured in F1 offspring of crosses between each focal line and each other line (i.e. cross success) versus F1 of the other line (i.e. line success). In the depicted simulation, the emerging correlation coefficient was strongly negative (-0.60). The solid line denotes the linear regression. (C,D) Illustrations of the relationships between cross success and line success for three representative focal lines (white, grey and black symbols) showing opposite covariances in (C) males versus (D) females. For example, the black-symbol line shows a small line success versus cross success covariance in males but a large positive covariance in females, and these effects are reversed in the grey-symbol line. These covariances form the points depicted in panel B across 50 simulated lines. Details of simulations and illustrative parameterisations are in Supporting Information S4.

Supporting Information

S1. Derivations of SSDRs given a threshold trait with a large-effect locus

S2. Parameter values

S3. Illustration of emergence of SSDRs given uniform distributions of liabilities

S4. Emergence of genome-wide SSDRs in a full diallel line-cross

S5. Empirical estimation of SSDRs

Supporting Information

Intrinsic emergence and modulation of sex-specific dominance reversals in threshold traits

Jane M. Reid

Supporting Information S1. Derivations of SSDRs given a threshold trait with a large-effect locus

Conditions for emergence of sex-specific dominance reversals (SSDRs) given a quantitative genetic (i.e. polygenic) threshold trait with an architecture that includes a large-effect locus can be examined by generating expressions for the proportions of homozygote and heterozygote individuals in any focal population or sex whose liabilities fall below versus above the threshold given any distribution of liabilities.

In quantitative genetics, distributions of liabilities underling threshold traits are typically assumed to be Gaussian (or transformable to Gaussian, Falconer and Mackay 1996, Ch. 18; Lynch and Walsh 1998, Ch. 25). The proportion (P_G) of any group of individuals whose liabilities (X) lie below any defined threshold (T) given mean liability μ_G and standard deviation in liability σ_G can then be calculated given well known properties of the cumulative normal distribution, giving:

$$P_G(X<T) = \tfrac{1}{2}[1+erf((T-\mu_G)/\sigma_G\sqrt{2})] \quad \textbf{(S1.1)}$$

where *erf* denotes the error function.

While the *erf* for the normal distribution cannot be evaluated in closed form in terms of elementary functions (and is typically evaluated approximately or numerically), equation S1.1 shows that the outcome depends on the deviation of the group mean liability μ_G from the threshold T (i.e. T-μ_G) and on the group standard deviation in liability σ_G (and hence the variance in liability, Gianola 1982). Since the mean and variance in liability both affect P_G, they are non-identifiable based solely on point phenotypic observations. Consequently, the deviation of the mean liability from the threshold for any group is typically expressed as a proportion of the group's standard deviation in liability (Falconer and Mackay 1996). However, to facilitate conceptual development rather than estimation, equation S1.1 retains the full parameterisation.

The conditions for emergence of phenotypic SSDRs can then be derived given a standard expression for quantifying dominance (E.g. following Czorlich et al. 2018, Geeta Arun et al. 2021):

$$D_1 = (P_{Het1} - P_{aa1})/(P_{AA1} - P_{aa1}) \quad \textbf{(S1.2)}$$

where D_1 is the degree of dominance of allele A versus a in sex 1 and P_{Het1}, P_{aa1} and P_{AA1} are the mean phenotypes for heterozygotes and the two homozygotes in sex 1. Here, D_1 is the deviation of the heterozygote from the defined baseline homozygote (here, aa), standardised by the difference between the two homozygotes. Values of $D_1<0.5$ and $D_1>0.5$ respectively denote dominance of the baseline and alternative alleles (a and A respectively). Values of 0 and 1 denote complete dominance, and 0.5 denotes co-dominance (i.e. additive allelic effects).

Substituting equation S1.1 into all four elements of equation S1.2 and simplifying gives the phenotypic dominance at a large-effect locus underlying a threshold trait in sex 1:

$$D_1 = [erf((T-\mu_{Het1})/\sigma_1\sqrt{2}) - erf((T-\mu_{aa1})/\sigma_1\sqrt{2})] / [erf((T-\mu_{AA1})/\sigma_1\sqrt{2}) - erf((T-\mu_{aa1})/\sigma_1\sqrt{2})] \quad \textbf{(S1.3)}$$

This substitution applies because the mean phenotype for a dichotomous threshold trait equals the proportion of individuals that express one phenotype versus the other (i.e. $P_G(X<T)$).

Equation S1.3 can then be re-parameterised in terms of the liability-scale homozygote effect size (β_1) and dominance coefficient (h_1) of the alternative allele at the large-effect locus acting in sex 1 such that:

$$D_1 = [erf((T-\mu_{aa1}+h_1.\beta_1)/\sigma_1\sqrt{2}) - erf((T-\mu_{aa1})/\sigma_1\sqrt{2})] / [erf((T-\mu_{aa1}+\beta_1)/\sigma_1\sqrt{2}) - erf((T-\mu_{aa1})/\sigma_1\sqrt{2})] \quad \textbf{(S1.4)}$$

This is because $\mu_{AA1}=\mu_{aa1}+\beta_1$ and $\mu_{Het1}=\mu_{aa1}+h_1.\beta_1$.

Consequently, the phenotypic dominance of allele A versus a in sex 1 (D_1) depends on four key parameters: the deviation of the mean liability for the baseline homozygote from the threshold ($T-\mu_{aa1}$), the homozygote effect size (β_1) and dominance coefficient (h_1) of the alternative allele, and the sex-specific standard deviation (and hence variance) in liability (σ_1). This expression assumes that the standard deviation in liability (σ_1) is the same irrespective of the genotype at the large effect locus (i.e. AA, aa or Aa), but this can be relaxed (see below).

Similarly, the dominance of allele A versus a in sex 2 (D_2) is:

$$D_2 = [erf((T-\mu_{aa2}+h_2.\beta_2)/\sigma_2\sqrt{2}) - erf((T-\mu_{aa2})/\sigma_2\sqrt{2})] / [erf((T-\mu_{aa2}+\beta_2)/\sigma_2\sqrt{2}) - erf((T-\mu_{aa2})/\sigma_2\sqrt{2})]$$

(S1.5)

Equations S1.4 and S1.5 allow sexual dimorphism in all four key parameters (i.e. μ_{aa}, σ, β and h). The threshold T is assumed constant and identical in both sexes, but this is arbitrary since the values of μ_{aa1} and μ_{aa2} can be re-calibrated as deviations from any desired threshold. Indeed, T is typically taken as 0, but is retained in equations S1.1-S1.5 for completeness. Conceptualising genetic and environmental effects on liabilities rather than thresholds facilitates formulations in terms of basic quantitative genetic theory without requiring any restrictive assumptions (e.g. no gene-by-environment or sex-by-environment interactions), and facilitates estimation of fixed effects and (co)variances using established machineries of Generalized Linear Mixed Models (e.g. Lynch and Walsh 1998; de Villemereuil et al. 2016; Reid and Acker 2022).

In general, the definition of phenotypic SSDR is that $D_1<0.5$ and $D_2>0.5$ (or conversely $D_2<0.5$ and $D_1>0.5$), where D_1 and D_2 are the phenotypic dominance values in sexes 1 and 2. Hence the two resulting inequalities need to be simultaneously satisfied. For sex 1:

$$[erf((T-\mu_{aa1}+h_1.\beta_1)/\sigma_1\sqrt{2}) - erf((T-\mu_{aa1})/\sigma_1\sqrt{2})] / [erf((T-\mu_{aa1}+\beta_1)/\sigma_1\sqrt{2}) - erf((T-\mu_{aa1})/\sigma_1\sqrt{2})] < 0.5$$

Which reduces to:

$$erf((T-\mu_{aa1}+h_1.\beta_1)/\sigma_1\sqrt{2}) < 0.5[erf((T-\mu_{aa1}+\beta_1)/\sigma_1\sqrt{2}) + erf((T-\mu_{aa1})/\sigma_1\sqrt{2})] \quad \textbf{(S1.6)}$$

By analogy for sex 2:

$$erf((T-\mu_{aa2}+h_2.\beta_2)/\sigma_2\sqrt{2}) > 0.5[erf((T-\mu_{aa2}+\beta_2)/\sigma_2\sqrt{2}) + erf((T-\mu_{aa2})/\sigma_2\sqrt{2})] \quad \textbf{(S1.7)}$$

These inequalities cannot be straightforwardly generically reduced due to the complex properties of the error function. However some further simplifications can be helpful. For example, if the alternative alleles at the large-effect locus are co-dominant in both sexes (hence $h_1=h_2=0.5$) with equal allelic effects in both sexes (hence $\beta_1=\beta_2$), then for sex 1:

$$erf((T-\mu_{aa1}+0.5\beta_1)/\sigma_1\sqrt{2}) < 0.5[erf((T-\mu_{aa1}+\beta_1)/\sigma_1\sqrt{2}) + erf((T-\mu_{aa1})/\sigma_1\sqrt{2})] \quad \textbf{(S1.8)}$$

For sex 2:

$$erf((T-\mu_{aa2}+0.5\beta_1)/\sigma_2\sqrt{2}) > 0.5[erf((T-\mu_{aa2}+\beta_1)/\sigma_2\sqrt{2}) + erf((T-\mu_{aa2})/\sigma_2\sqrt{2})] \quad \textbf{(S1.9)}$$

Then, trivially, if there is no sexual dimorphism in the mean or variance in liability ($\mu_{aa1} = \mu_{aa2}$ and $\sigma_1=\sigma_2$) then inequalities S1.8 and S1.9 are incompatible and there cannot be SSDR. Otherwise, the degree of SSDR depends on the deviations of the sex-specific mean liabilities from the threshold relative to the effect size of the alternative allele at the large effect locus, scaled by the sex-specific standard deviations.

Expressions S1.3-S1.9 assume that sex-specific variances in liabilities do not depend on genotype at the large-effect locus. However this could be relaxed to give for sex 1:

$$erf((T-\mu_{aa1}+h_1.\beta_1)/\sigma_{Het1}\sqrt{2}) < 0.5[erf((T-\mu_{aa1}+\beta_1)/\sigma_{AA1}\sqrt{2}) + erf((T-\mu_{aa1})/\sigma_{aa1}\sqrt{2})] \quad \textbf{(S1.10)}$$

where σ_{Het1}, σ_{AA1} and σ_{aa1} are the standard deviations in liability in the heterozygote and the two homozygotes respectively.

By analogy for sex 2:

$$erf((T-\mu_{aa2}+h_2.\beta_2)/\sigma_{Het2}\sqrt{2}) > 0.5[erf((T-\mu_{aa2}+\beta_2)/\sigma_{AA2}\sqrt{2}) + erf((T-\mu_{aa2})/\sigma_{aa2}\sqrt{2})] \quad \textbf{(S1.11)}$$

Instead of considering a large-effect locus, this same formulation could be interpreted as considering the outcomes of crosses between ancestral and derived (evolved) lines (e.g. as in Geeta Arun et al. 2021). Here, the values for the two homozygotes in expressions S1.3-S1.11 can be taken as the values for the two parental lines, and the values for the heterozygotes can be taken as the values for the backcross hybrids. The value of β then denotes the degree of divergence of mean value between the ancestral and derived lines, and h denotes the degree of genome-wide dominance. In this circumstance, it becomes more plausible that the liability scale variances could differ substantially between sexes and/or lines and resulting hybrid crosses.

All these expressions and outcomes could become even more complex if the distributions of liabilities are skewed, where the form of skewness could differ between the sexes. Indeed, broadly analogous expressions could be generated given any other (i.e. non-Gaussian) distributions of liabilities (see Supporting Information S3).

Since expressions S1.8-S1.11 contain ratios (of means to variances) there is a large parameter space where SSDRs could arise. Even though there are no closed form solutions for the error function, outcomes for any parameter space of interest can be readily evaluated using known values for the cumulative normal distribution. R code is provided.

Environmentally-induced variation in SSDRs, for example among years or cohorts, could be examined by including additional terms in the expression for P_G, for example:

$$P_G(X<T) = \tfrac{1}{2}[1+erf((T-\mu_G+\gamma_{Gi})/\sigma_G\sqrt{2})] \quad \textbf{(S1.12)}$$

where γ_{Gi} is an additive effect on mean liability of group G associated with year i.

Supporting Information S2. Parameter values

Parameter values used to generate Figures 3-6 are shown in Tables S2.1 and S2.2. Values are arbitrary and simply chosen to illustrate key conceptual points.

Table S2.1. Parameters values for illustrative examples of conditions affecting emergence of SSDRs in threshold traits with a large-effect locus, as shown in main figures. The threshold value is taken as zero in all cases. SD is the standard deviation (i.e. square root of the variance). Dominance values of 0.5 imply co-dominance (i.e. additive effects) on the liability scale.

Parameter	Fig 3	Fig 4A,B	Fig 4C,D	Fig 5A,B	Fig 5C,D
Mean baseline liability, females	-15	-15	-7	-15	-15
Mean baseline liability, males	-5	-5	3	-5	-5
SD in liability, females	6.5	2.5	6.5	6.5	6.5
SD in liability, males	6.5	2.5	6.5	6.5	6.5
Additive effect size of single copy of the alternative allele at the large-effect locus, both sexes	10	10	10	10	10
Dominance of alternative allele, females	0.5	0.5	0.5	0.68	0.32
Dominance of alternative allele, males	0.5	0.5	0.5	0.32	0.68

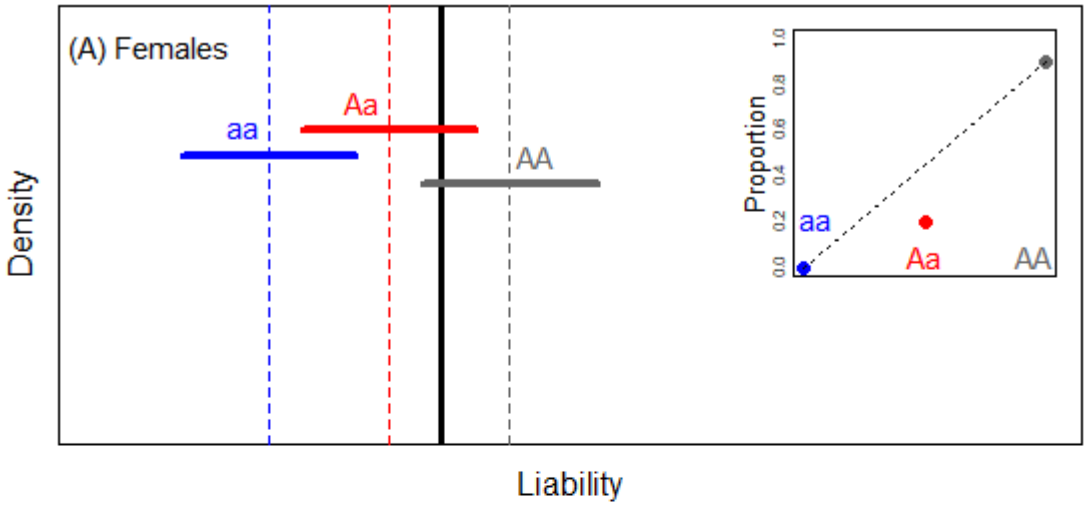
Table S2.2. Parameters values for illustrative example of conditions causing emergence of SSDRs in threshold traits in hybrids of crosses between baseline (stock) and evolved lines (shown in main Figure 6). The threshold value is taken as zero. SD is the standard deviation (i.e. square root of the variance).

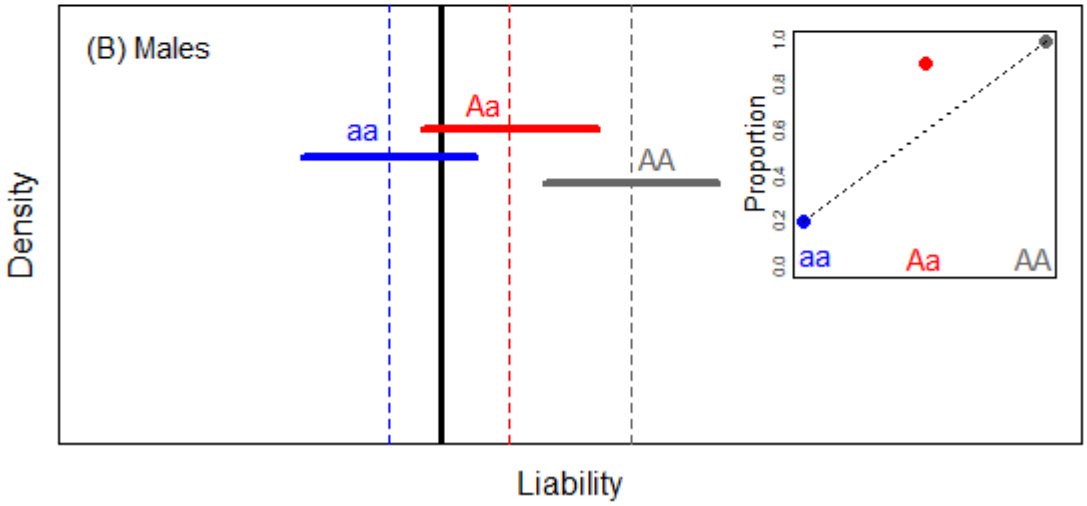
Parameter	Fig 6
Mean baseline liability, females	-2.5
Mean baseline liability, males	-11
SD in baseline liability, females	3
SD in baseline liability, males	9
Mean liability of evolved line, both sexes	5
SD in liability of evolved line, both sexes	5.5
Mean liability of hybrids, females	1.25
Mean liability of hybrids, males	-3
SD in liability of hybrids, females	5
SD in liability of hybrids, males	6

Supporting Information S3. Illustration of emergence of SSDRs given uniform distributions of liabilities

Emergence of SSDRs in threshold traits does not necessarily require underlying distributions of liabilities to be Gaussian, or indeed require any form of curved (concave or convex) density distribution. For example, Figure S3.1 illustrates that SSDRs can arise given uniform distributions. Figure S3.1 envisages the same kind of scenario as main figure 3, with sexual dimorphism in mean baseline liability but not in the variance, and a large-effect locus with co-dominance of alternative alleles (and hence additive effects on liability that are the same in both sexes). This example is not intended to imply that uniform distributions of liability are likely to occur, but simply serves to illustrate the generality of the principle by which threshold traits can generate phenotype SSDRs given additive effects on underlying liabilities. Mathematical conditions for SSDRs given uniform distributions of liabilities could readily be derived (analogous to those presented for Gaussian distributions in Supporting Information S1).

Figure S3.1. Illustration of emergence of (partial) sex-specific dominance reversal (SSDR) in a threshold trait with sexual dimorphism in mean liability and a large-effect locus with purely additive allelic effects given uniform distributions of liabilities. Blue and grey lines show the ranges of the uniform distributions of liabilities for the two alternative homozygotes (i.e. aa and AA) at the large-effect locus (assuming an additional polygenic architecture) in (A) females and (B) males. Red lines show the ranges of the uniform distributions of liabilities for the heterozygotes (i.e. Aa), assuming additive effects of the alternative alleles (i.e. co-dominance) on the liability scale that are the same in both sexes. The y-axis dimension is effectively meaningless; the elevations of the red, blue and grey lines are jittered for visual clarity. The black vertical line denotes the threshold, above which the alternative phenotype is expressed. Accordingly, inset panels show the proportions of individuals of each homozygote (blue and grey) and the heterozygote (red) that express the alternative phenotype. Dotted lines link the proportions for the two homozygotes, visualising that the proportions for the heterozygotes lie below versus above the additive expectations in females versus males, representing SSDR. On the main figures, vertical dashed lines denote mean liabilities for the aa, Aa and AA genotypes.


(A) Females
aa
Aa
AA
Density
Liability
Proportion
0.0
0.2
0.4
0.6
0.8
1.0
aa
Aa
AA


(B) Males
aa
Aa
AA
Density
Liability
Proportion
0.0
0.2
0.4
0.6
0.8
1.0
aa
Aa
AA

Supporting Information S4. Emergence of genome-wide SSDRs in a full diallel line-cross

Simple simulations illustrate how phenotypic SSDRs could emerge in a full diallel line-cross experiment given purely additive genetic effects on individuals' values for reproduction and some form of competition that causes non-linear (i.e. non-additive) outcomes.

Consider N isogenic lines, each of which is assigned additive genetic values for hypothetical traits that determine capability for reproductive success (i.e. fitness) in females and males. These sex-specific values can be negatively correlated across lines, envisaging sexually antagonistic selection (i.e. a negative cross-sex genetic correlation). Values are draw from a multivariate normal distribution, with means μ_F and μ_M for females and males and variance-covariance matrix where σ^2_F and σ^2_M are the sex-specific variances and σ_{FM} is the cross-sex covariance (giving a cross-sex correlation r_{FM}). All N lines are then subject to a full diallel cross, where sex-specific genetic values for F1 offspring are taken as the arithmetic mean of the sex-specific values of their parental lines. This effectively assumes purely additive sex-specific line effects with no SSDR on the scale of genetic values (and no sampling variance, but these assumptions could be relaxed).

The probability of successful parentage (i.e. maternity or paternity) for each F1 in competition with a reference individual is taken as:

$$P(\text{Success}) = (e^{Xi})^{\alpha}/((e^{Xi})^{\alpha} + (e^{Xr})^{\alpha}) \quad \text{(S4.1)}$$

where X_i is the additive genetic value of the focal individual, X_r is the additive genetic value of the competing reference individual and α is a parameter that controls the outcome of competition. This function has previously been used in models of competitive reproductive outcomes (e.g. Bocedi and Reid 2015). Values of $\alpha>1$ skew the outcome towards 'winner takes all', such that the individual with the higher additive genetic value has a disproportionately higher probability of parentage. Values of $\alpha<1$ generate more equal probabilities of parentage than otherwise expected, with the extreme that $\alpha=0$ yields probabilities of 0.5 for both the focal and competing reference individuals irrespective of their additive genetic values. For the scenario shown in main Figure 7, P(Success) was computed taking $\alpha=1.75$ in both sexes, and X_r as a constant of 1.5 less than the sex-specific mean. This decrement represents a reproductive disadvantage of the reference individuals, which could reflect adaptation of focal lines and/or inbreeding depression in reference individuals relative to the F1s (which is plausible since F1 offspring of isogenic line crosses will be highly heterozygous). Together, these conditions yield an asymmetric function for P(Success), with a fairly strong degree of 'winner takes all' (main Figure 7A).

Realised reproductive success for each F1 offspring is then generated as a binomial outcome given its P(Success) and a fixed maximum possible reproductive success. For each line and sex, the covariance between the realised reproductive success of each crossed F1 and that for the other line involved in the cross was calculated. The cross-sex correlation in covariances was then calculated across lines (as done by Grieshop and Arnqvist 2018).

To illustrate key concepts, main Figure 7 envisages a strong 'winner takes all' scenario in both sexes. Figure S4.1 illustrates a simulation with a lower value of α, yielding less strong 'winner

takes all' in both sexes. Figure S4.2 illustrates a simulation with sex-specific values of α, yielding less strong 'winner takes all' in females than males. All parameter values are summarised in Table S4.1, and were chosen to illustrate conceptual points, not to attempt to quantitatively replicate results in Grieshop and Arnqvist (2018) or any other particular biological system. Numerous different mathematical forms of competition, and translation into observed reproductive success, could be formulated given an aim to capture key aspects of any particular real system. The simulated number of isogenic lines was set to 50 to reduce sampling variance in the cross-line correlation (large full diallel crosses are much easier to do in a computer than in reality!), envisaging one observed offspring per cross. Full R code is provided as additional Supporting Information.

Figure S4.1. Summary of simulations that generate evidence of sex-specific dominance reversals (SSDRs) in competitive fitness in line-cross experiments given purely additive underlying genetic effects. (A) Form of the assumed non-linear relationship between an individual's additive genetic value and its probability of paternity or maternity in competition with a reference individual. Here, the relationship is a less extreme 'winner takes all' scenario than in main Figure 7. The vertical dashed line indicates the mean genetic value of simulated lines. (B) Emerging negative cross-sex correlation between line covariances between competitive fitness measured in F1 offspring of crosses between each focal line and each other line (i.e. cross success) versus F1 of the other line (i.e. line success). In the depicted simulation, the emerging correlation coefficient was strongly negative (-0.55). The solid line denotes the linear regression. (C and D) Illustrations of the relationships between cross

success and other line success for three representative focal lines (white, grey and black symbols) showing opposite covariances in (C) males versus (D) females.

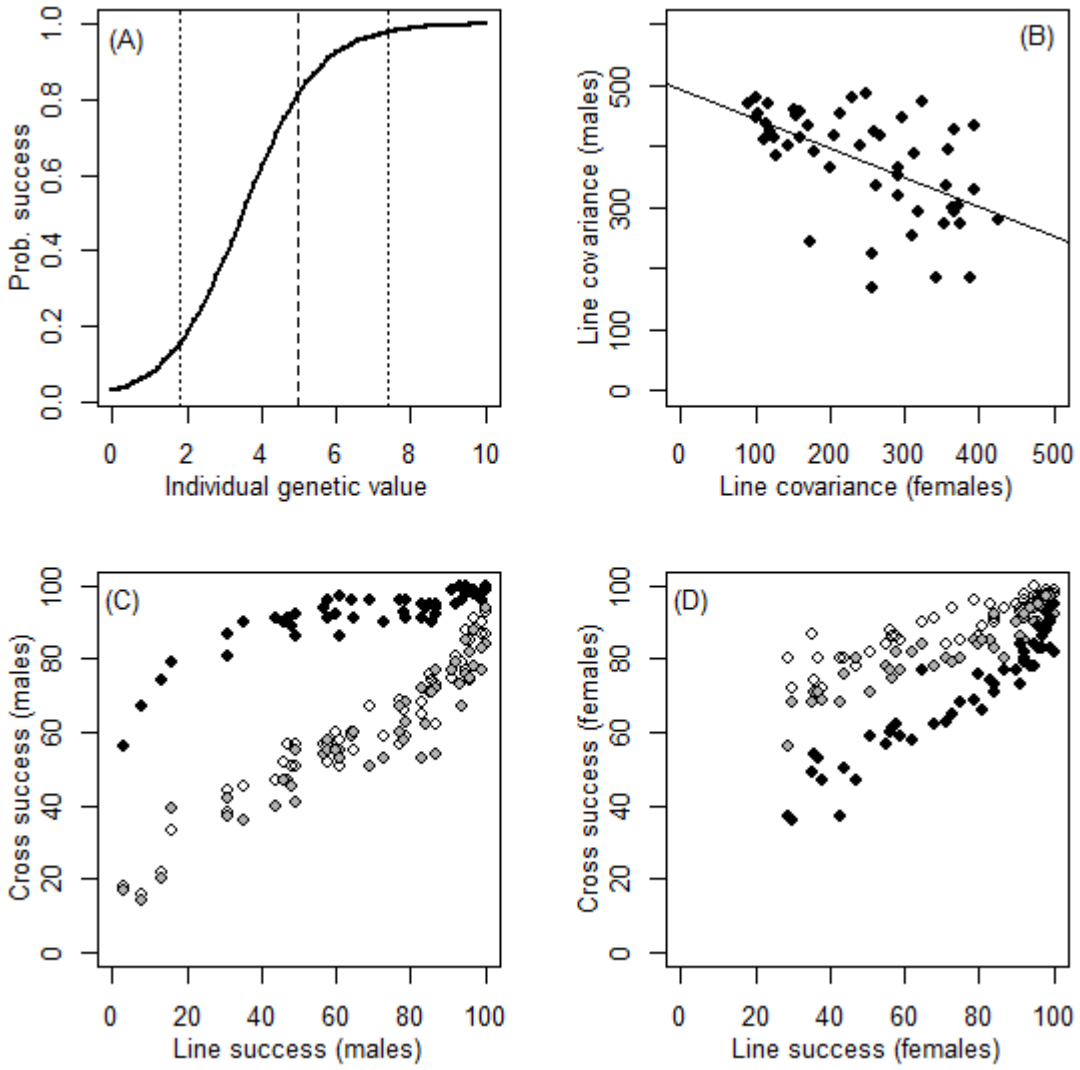


Figure S4.2. Summary of simulations that generate evidence of sex-specific dominance reversals (SSDRs) in competitive fitness in line-cross experiments given purely additive underlying genetic effects. (A) Form of the assumed non-linear relationships between an individual's additive genetic value and its probability of paternity or maternity in competition with a reference individual. Here, the relationships differ between males (black, steeper relationship) and females (blue, less steep relationship). The vertical dashed line indicates the mean genetic value of simulated lines. The vertical dotted lines indicate the 5% and 95% quantiles of the ranges of values for males (black) and females (blue). These values differ slightly between the sexes due to sampling variance. (B) Emerging negative cross-sex correlation between line covariances between competitive fitness measured in F1 offspring of crosses between each focal line and each other line (i.e. cross success) versus F1 of the other line (i.e. line success). In the depicted simulation, the emerging correlation coefficient was strongly negative (-0.59). The solid line denotes the linear regression. (C and D) Illustrations of the relationships between cross success and other line success for three representative focal lines (white, grey and black symbols) showing opposite covariances in (C) males versus (D) females.

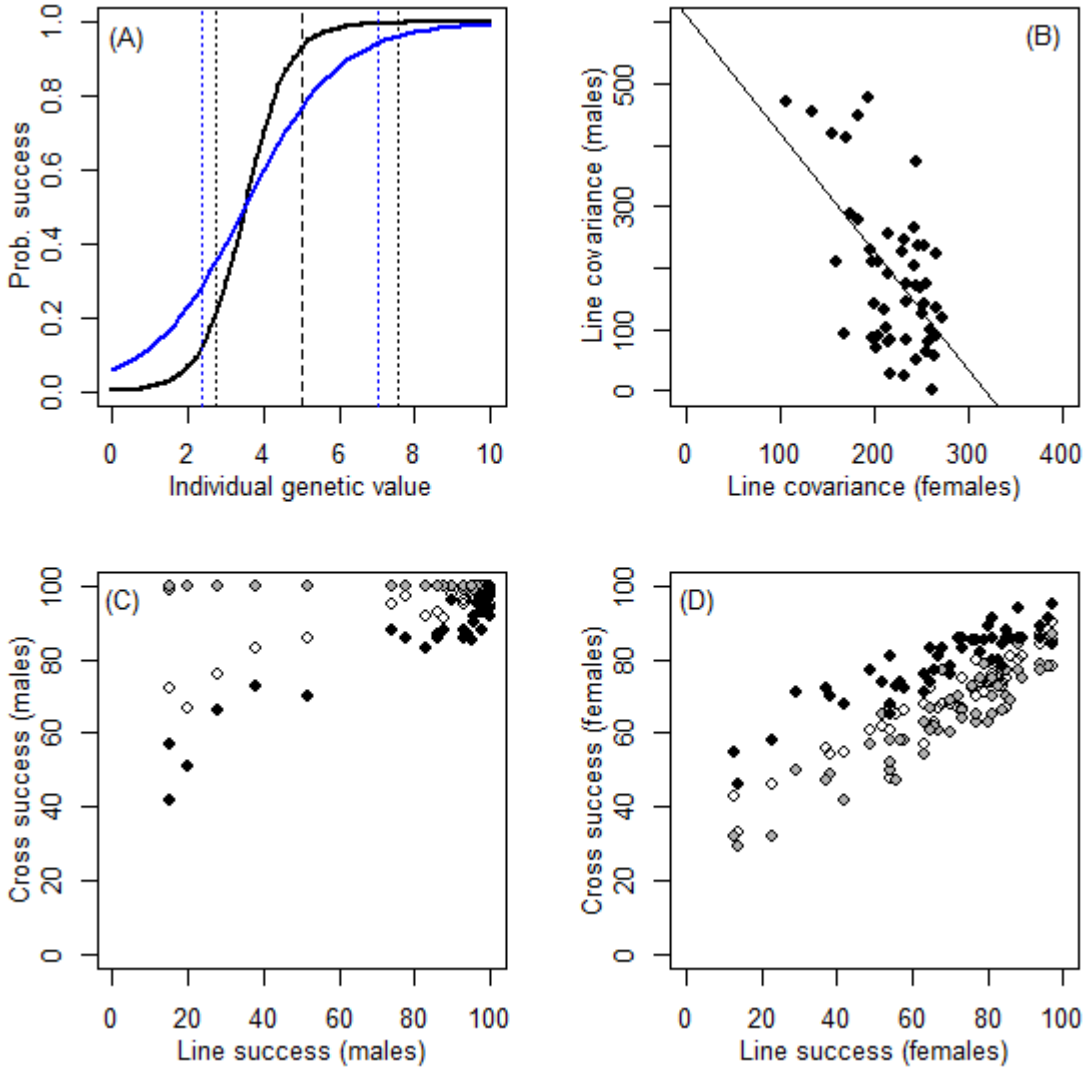

(A)
Prob. success
0.0
0.2
0.4
0.6
0.8
1.0
0
2
4
6
8
10
Individual genetic value
(B)
Line covariance (males)
0
100
300
500
0
100
200
300
400
Line covariance (females)
(C)
Cross success (males)
0
20
40
60
80
100
0
20
40
60
80
100
Line success (males)
(D)
Cross success (females)
0
20
40
60
80
100
0
20
40
60
80
100
Line success (females)

Table S4.1. Summary of parameter values used in simulations of full diallel crosses shown in main and supporting figures. Parameter values apply to both females and males unless denoted F or M.

Parameter	**Fig 7**	**Fig S4.1**	**Fig S4.2**
Number of isogenic lines (N)	50	50	50
Mean genetic value (μ)	5	5	5
Variance in genetic value (σ^2)	2	2	2
Cross-sex genetic covariance (σ_{FM})	-1	-1	-1
Resulting cross-sex genetic correlation (r_{FM})	-0.5	-0.5	-0.5
Maximum reproductive success	100	100	100
Parentage function parameter (α)	1.75	1	1.75(M), 0.8(F)
Relative value of reference population	-1.5	-1.5	-1.5

Supporting Information S5. Empirical estimation of SSDRs

The four recent empirical studies used diverse statistical approaches to test for SSDRs on phenotypic and/or underlying scales, and thereby achieve their immediate objectives. However, none formally or comprehensively examined models for threshold(-like) traits representing the scenarios depicted in main Figures 3-7 (i.e. explicitly encompassing means and variances in baseline liabilities, or forms of reproductive competition). Consequently, it is not possible to fully or directly infer which scenarios apply, or to quantitatively compare aspects of the different studies.

For example, Barson et al. (2015) depict phenotypic SSDRs in salmon age at maturity (their Figure 3a) and test for SSDRs on an underlying latent scale (a threshold logistic model using a logit link, e.g. their Extended Data Figure 5, Extended Data Table 2), considering genotype-specific but sex-independent thresholds.

Pearse et al. (2019) depict phenotypic SSDRs in the probability of detecting a tagged individual near the focal stream mouth at a particular size (interpreted to represent anadromy, their Figure 3 and Extended Data Figure 7). The data were analysed using Generalized Additive Models but the scale is unclear, and a model with sexual dimorphism and additive allelic effects was apparently not considered (their Supplementary Table 5).

Geeta Arun et al. (2021) depicted phenotypic SSDRs in proportional survivorship (their Figures 1 and S2), and present multiple data analyses comprising direct analysis of proportional

survivorship and also logistic regression analyses of survival at the end of a 96-hour observation period, further backed up by cox proportional hazards models (their Table 1).

Grieshop and Arnqvist (2018) calculated the required line covariances, and the cross-sex correlation in covariances, based on residual values after standardising for environmental and epistatic variances in the full diallel cross.

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