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Genotype-by-Environment Interactions and Sexual Selection: Female Choice in a Complex World

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1.1   Introduction

"When the males and females of any animal have the same general habits of life, but differ in structure, colour, or ornament, such differences have been mainly caused by sexual selection" (Darwin, 1859, p. 89). Female choice of mates and male–male reproductive competition were the two mechanisms causing sexual selection proposed by Darwin. Darwin proposed male–male reproductive competition as an explanation for the evolution of male-limited structures, like antlers, horns, fangs, and claws, which function in reproductive combat among males. But, he proposed female mate choice as the explanation for the evolution of exaggerated male traits, which have no apparent function in reproductive competition like plumage, color, and ornamentation. Darwinian sexual selection accounted for two patterns in nature: (1) males and females of the same species differ from one another; and, (2) males of closely related species tend to be much more different from one another in structure and behavior than the females.

In an insightful elaboration of Darwin's theory, Fisher (1930) gave formal expression to the "run-away" process of sexual selection, wherein the existence of a female mating preference by itself favors the evolutionary exaggeration of the favored male trait. When females differ from one another in mate preference and males vary from one another in the preferred trait, then males with the most extreme trait values have more mates as a result of satisfying the mating preferences of more females. Sons of these males inherit the father's more extreme trait value and their daughters inherit their mothers' preferences, making them

more selective (Lande, 1981). It is this positive feedback between the female mating preference and the male preferred trait that results in run-away sexual selection, where the male trait mean is dragged off its natural selection optimum through its mating advantage.

Bateman (1948) found empirically that the variance in male relative fitness was greater than that of females owing to the variance among males in mate numbers. Wade (1979; 1995) derived the formal relationship between the variance in male relative fitness and that of females, generalizing Bateman's inference from observations. This finding is important because selecting for a gene in one sex but against it in the other averages to a fairly small change in a gene's frequency (Shuster & Wade, 2003). And, such weak selection is a poor candidate for the selective force behind the large differences in morphology and behavior between males of closely related species. However, when the strength of selection on males is several times that acting on females, sex-limited divergence among closely related species is to be expected.

The modern view of female choice, which emphasizes "good genes" and "sexual conflict," differs somewhat from that of Fisher and Bateman. In a complex world, one with genotype-by-environment interactions ($G \times E$) and gene-by-gene interactions ($G \times G$ or epistasis), it is very difficult for a female to choose her mates in order to obtain "good genes." With $G \times E$ and $G \times G$, a gene's effect on fitness is context-dependent; a gene can be good for fitness in one context but a bad for it in another. Furthermore, recent genomic studies of the determinants of feather quality, an often discussed target of female mate choice in birds, find that the quality of a male's feathers depends more on the genes in his neighbors' genomes than it does on the genes in his own (Biscarini *et al.*, 2010). That is, the social environment of other males contains genes that affect feather quality. Such genetic indirect effects are often represented as $G \times E_G$ to emphasize the notion that "the environment contains genes." And, $G \times E_G$ in evolutionary theory behaves somewhat like a hybrid of the concepts $G \times E$ and $G \times G$. In the context of female mate choice, it is important to recognize not only that $G \times E_G$ plays a role in competitive interactions, including competition for mates, but also why it responds poorly or not at all to individual selection. In this chapter, I will discuss the difficulty in obtaining good genes by female choice in a complex world, where male traits are affect by $G \times E$, $G \times G$ and $G \times E_G$. First, however, I want to resurrect the history behind "good genes" theory in order that the arguments in its favor are clear.

1.2   Classical female choice

What do females gain by choosing mates? In their influential paper on female mate choice, Hamilton and Zuk (1982) answered in this way:

> *Whether mate choice could be based mainly on genetic quality of the potential mate has been a puzzle to evolutionary biologists … females of many species act as if they are choosing males for their genes; thus "good genes" versions of sexual selection have been frequently, albeit tentatively, suggested.*

They went further, specifying how a female should select a mate:

> *The methods used should have much in common with those of a physician checking eligibility for life insurance. Following this metaphor, the choosing animal should unclothe the subject, weigh, listen, observe vital capacity, and take blood, urine, and fecal samples. General good health and freedom from parasites are often strikingly indicated in plumage and fur, particularly when these are bright rather than dull or cryptic.*

Since that time, "good genes" has become one of the predominant answers to the question of why do females chose mates. Under this view, certain male traits are a signal, indicating whether or not a male possesses a compliment of genes good for offspring survival. A potential problem with the good genes theory is that such genes will fix in a population rather rapidly, because they enjoy a two-fold fitness advantage. First, they have the advantage that attends increasing survival and, second, they have a fertility advantage stemming from female mating preferences. MacKay (2010) argues that such genes are rapidly fixed, just as genes with a comparable two-fold disadvantage are rapidly removed from populations, leaving only those genes with antagonistic effects on viability and fertility segregating in a population. Once fixed, there is no genetic variance among males and, hence, no force maintaining female choice. There is little or no point in females choosing when there is nothing thereby to be gained.

Hamilton and Zuk (1982) addressed this secondary problem by presenting evidence of an association across taxa between the incidence of blood parasites and features of male courtship displays. They argued that the evidence was consistent with the hypothesis that hosts and their parasites exhibited "co-adaptational cycles," wherein the most fit host genotype changed overtime owing to selective pressures exerted by adapting parasites. (Similar arguments play a role in theories for the evolution and maintenance of sexual reproduction: e.g., Lively & Dybdahl, 2000.) This adaptive cycling maintains genetic variation for parasite resistance in the host population, for the fittest genotype in one generation diminishes in fitness in future generations as it becomes common and, thus, the target for parasite adaptation. In this circumstance, genetic variation for host resistance to parasites always exists in a population. As long as this variation tends to be associated with male plumage, fur or elements of the courtship display, females can scrutinize males for "*characters whose full expression is dependent on health and vigor,*" choosing those males whose parasite resistance genes will improve offspring fitness. This is different from Fisher's run-away process where the preferred male traits are arbitrary and under stabilizing selection for an intermediate mean value; it is the female's preference for them that imbues high values of them with positive directional selection for increased health and vigor. Under the good genes theory, the preferred male traits themselves are "truthful signals" of male condition and the underlying genes. (In defense of Fisher's run-away, it has been argued that, even if a male trait initially signaled underlying good genes, the evolution of the exaggerated female mating preference will so distort the male trait's fitness that its mean will run-away well beyond the optimum trait value

for natural selection: Lande, 1981; Shuster & Wade, 2003. As a result, a male trait initially indicating genes good for survival will come to indicate genes poor for survival, but good for attracting mates.)

Using red jungle fowl, Zuk *et al.* (1990, p. 235) experimentally tested the good gene's hypothesis that "*Male ornaments are thus facultative among individuals within a species, providing reliable indicators of a potential mate's health, and therefore his resistant genotype.*" They tested the hypothesis by quantifying feather quality on control and parasitized male and, subsequently, testing their attractiveness to females. They found that parasites diminished male feather quality and, concomitantly, male attractiveness to females. Zuk *et al.* (1990, p. 240–241) concluded that,

> *If ornaments are indeed truthful signals of male condition, and in particular of heritable genetic resistance to disease, then they should be reliable indicators of their bearer's having suffered (or thrown off) the effects of infection. Our results suggest that male ornaments signal male ability to cope with parasites, and that female choice functions to select males who can cope with parasites. Male ornaments thus do not appear to be arbitrary indicators of attractiveness.*

1.3   The instability of "good genes" when male quality is a complex trait

Complex traits are those whose genetic variation is affected by interaction with the environment (G × E), interaction with other genes (G × G), or interaction with other genotypes (G × E_G). Each of type of interaction can influence the effect of a gene on fitness and so that the effect of an allele can change from positive to negative or vice versa. These types of interactions have largely been ignored in sexual selection theory, and especially in good genes theory. One of the primary reasons that interactions have not been considered lies with the influential argument put forward in the classic monograph, *Adaptation and Natural Selection* by Williams (1966, p. 56):

> *Obviously it is unrealistic to believe that a gene actually exists in its own world with no complications other than abstract selection coefficients and mutation rates. The unity of the genotype and the functional subordination of the individual genes to each other and to their surroundings would seem, at first sight, to invalidate the one-locus model of natural selection. Actually these considerations do not bear on the basic postulates of the theory.*

> *No matter how functionally dependent a gene may be, and no matter how complicated its interactions with other genes and environmental factors, it must always be true that a given gene substitution will have an arithmetic mean effect on fitness in any population. One allele can always be regarded as having a certain selection coefficient relative to*

another at the same locus at any given point in time. Such coefficients are numbers that can be treated algebraically, and conclusions inferred from one locus can be iterated over all loci. Adaptation can thus be attributed to the effect of selection acting independently at each locus.

In short, Williams is asserting that the interactions affecting the genetic basis of complex traits have no consequences for evolutionary genetic theory. From this perspective, it is clear that a gene can be good, bad or neutral for fitness and that, despite the complexity of interaction, each gene can be evaluated on its own merit without regard to other genes or environmental factors.

Williams' view is only approximately correct, however, and then only for very large, randomly mating populations (Figure 1.1; see also Goodnight, 1988). The significance of gene interactions in regard to single gene effects in small populations is rarely mentioned in behavioral evolutionary discussion of sexual selection. An insightful, diagrammatic exposition by Goodnight can be found at https://blog.uvm.edu/cgoodnig/2013/07/31/drift-and-epistasis-the-odd-effects-of-small-population-sizes/. Williams' view is not at all correct when there are interactions in genetically subdivided metapopulations, where the advocated global "averaging" is a poor reflection of the local context. One could hope that Williams' view would apply within demes so that allelic effects would be locally

Metapopulation   Panmictic Population
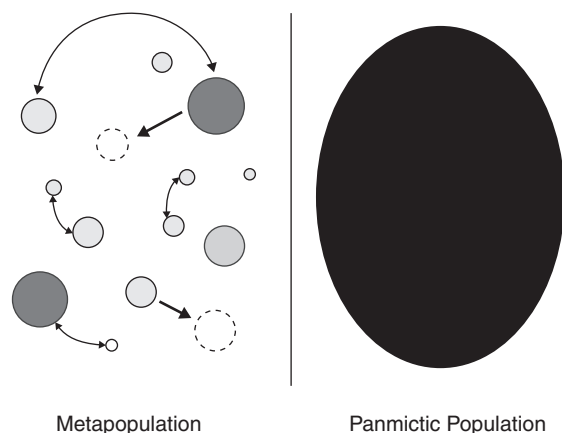
Fig. 1.1 A schematic illustration contrasting a genetically subdivided metapopulation (*left*) with a large, randomly mating and mixing, panmictic population (*right*). The small circles (*left*) represent component demes of the metapopulation, which differ in size and local environment (*shading*). The circles with the dotted circumferences suggest local extinctions. The dotted arrows between demes are migration or gene flow, while the heavier arrows show colonization events. It is the variation in environmental (G × E), genetic (G × G), and social (indirect genetic effects) contexts among demes in a metapopulation that causes the effect of a gene on fitness to vary from deme to deme, causing significant local heterogeneity in its evolutionary trajectory. In a large, panmictic population (*right*), the simple averaging over context as advocated by Williams (1966; see text) reduces variation in a gene's effect on fitness and thus limits its evolutionary trajectory.

invariant and unchanging over evolutionary time. However, this depends upon the relevant epistatic context becoming fixed locally. At present, we have little direct evidence that that is the case but a growing body of evidence indicating that it is not the case (Huang *et al.*, 2012; Swarup *et al.*, 2012). Differently put, if genomic studies reveal "extensive epistasis for olfactory behaviour, sleep and waking activity" in model organisms (Swarup *et al.*, 2012), it is reasonable to expect comparable levels of epistasis in other behaviors in other organisms.

The error in William's heuristic is that interactions, by definition, change gene effects. Change in the magnitude of gene effects changes the calculus of the fitness costs to a female of choosing as well as the fitness benefits accruing to her offspring. Change in the sign of a gene's effect is worse for it can convert a "good gene" in one context into a "bad gene" in another. With $G \times E$, $G \times G$, or $G \times E_G$ interactions, what a female sees in one generation at the time of mate choice may not be indicative of what her offspring get, because context changes from one generation to the next. Thus, adaptive female choice in a world made complex by interactions requires a female not only to recognize good genes in potential mates but also to recognize and transmit context to her offspring.

In the following sections, I will explain how each kind of context introduces variation or instability into the effect of a gene on an individual's genotypic value using simple population genetic theory.

1.3.1   Additive effects of genes on genotypic value

This is the foundational model, which is insensitive to interactions and conforms in every respect to the Williams view. When the phenotypic effect of a gene is independent of the alleles present at all other loci, independent of the environments experienced by the individuals bearing those genes, and independent of the neighbors with which a bearer interacts, it is considered a gene with a wholly additive effect. In a wholly additive world of the sort described by Williams (1966), the total phenotypic value of the individual can be calculated as the *sum* of the independent contributions of its component genes. And, the heritable differences among individuals can be attributed to the additive genetic variance. However, as Falconer and Mackay (1996, p. 128) have emphasized, "*the existence of additive variance is not an indication that any of the genes act additively.*"

For evolution in a purely additive, two-allele, single gene model, fitnesses are assigned to genotypes (AA, Aa, and aa) by first establishing a scale of variation. The scale is the difference in phenotype or fitness between the two homozygotes (AA − aa); the heterozygote lies at the mid-point between them. Often, a constant, such as 1, is added to the fitness of each genotype to obtain, (1 − s) aa, (1) Aa, and (1 + s) AA. (A completely equivalent scaling is (1) aa, (1 + s) Aa, and (1 + 2s) AA.) The "effect" of an A allele on fitness is **s**, the selection coefficient, and is equal to half the difference between the alternative homozygotes. If the frequency of the A allele is **p**, this gives the familiar expression for gene frequency change, $\Delta p_A = spq/W$, where W is the genotypic mean fitness, which is a simple function of the gene frequency (1 + 2**sp**). Interactions violate the assumptions of

this model and change the evolutionary dynamic equation, Δp_A, by changing the effects of alleles.

1.3.2 Genotype-by-environment interaction

For a set of genotypes, $G \times E$ is a violation of the additivity assumption discussed in the section above. $G \times E$ is defined as change in the magnitude or order of a gene's phenotypic effect with change in the environment. Changes in magnitude of effect result in change in the rate of evolution in different environments. Changes in the order of effects result in a change in the direction of evolution, that is, changes sign of Δp_B, in different environments.

In Figure 1.2/Plate 1, I have depicted an idealized additive genetic norm of reaction to environmental variation in temperature (upper graph) and a norm of reaction characteristic of $G \times E$ (lower graph). This is an example of so-called
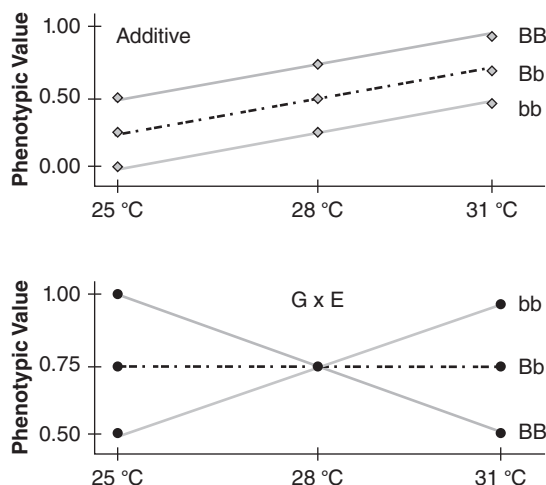
Fig. 1.2 A schematic illustration of the norms of reaction of three genotypes for a gene with an additive effect across a series of thermal environments (upper graph) and for a gene with $G \times E$ (lower graph). With $G \times E$, the effect of the B gene changes with temperature while in the additive case it does not. This variation in gene effect with temperature can be averaged over in a large panmictic population to obtain a unitary selection coefficient (see Figure 1.1, right panel). However, in a metapopulation with temperature changing from deme to deme and larger phenotypic values favored, the selection coefficient of the B gene will be positive in demes with colder micro-climates and negative in demes with hotter micro-climates. This variation in sign of the selection coefficient causes variation from one deme to another in the direction of gene frequency change, so that the B allele increases in frequency in some demes but decreases in frequency in others. That is, with $G \times E$, the B allele is a "good gene" in some localities but a "bad gene" in others, complicating the problem of female mate choice for "good genes." For color details, please see Plate 1.

"crossing-type" G × E, which is believed to play a role in the maintenance of polymorphism and in the evolution of adaptive plasticity (see Hughes *et al.*, 2002 for a recent review). In the upper graph, no matter what the temperature, there is a "best genotype" that produces the largest phenotypic value. However, it is also clear from Figure 1.2/Plate 1 (lower graph) that with G × E there is no "best" genotype; the genotype with the highest value at 25°C is the homozygote, BB, while the genotype with the highest value at 31°C is the opposite homozygote, bb. It is also clear in the lower graph that within the two environments (25° and 31°), alleles at the B-locus act additively. What is the effect of a gene when genotypic values change in rank with a change in the environment?

Let the frequency of each of the three environments equal f_{25}, f_{28}, and f_{31}, respectively, where the sum equals 1. Also assume that a large phenotypic value is favored in all environments. The overall effect of an allele on phenotypic value is equal to its average effect across the three environments. (Because all three genotypes intersect at the same point at 28°C, neither allele has an effect in this environment.) With the values give in the Figure 1.2/Plate 1 (lower graph), the effect of a B allele equals $+0.25(f_{25} - f_{31})$ and the effect of the b allele equals $-0.25(f_{25} - f_{31})$. Whether the B allele is a gene of major or minor effect depends upon the relative frequencies of the 25°C and 31°C environments, that is, on the predominant environmental context. When the frequencies of the two environments are very different, B is a gene of major effect. In contrast, when the two environments occur equally often, B has no effect at all and is neutral with respect to our fitness assumption. Whenever f_{25} exceeds f_{31}, B is a "good gene," but whenever f_{31} exceeds f_{25}, it is a "bad gene." Spatial and temporal variation in the frequencies of the thermal environment like that modeled earlier can introduce instability into the definition of a gene's effect. There are many, more complex patterns of environmental variation that may characterize situations in natural populations. Furthermore, organisms at different life stages might well respond differently to such variation. The problem for a mate-choosing female under the good genes hypothesis is to get it right for her offspring despite these complexities.

From the perspective of female mate choice, we also need to consider the likely possibility that the environmental frequencies are functions of time, changing from generation to generation. If larger phenotypic value means higher fitness, then a female choosing a mate in the 25°C environment for his "good" B gene is dooming her brood if instead they develop in a 31°C environment where B is a "bad gene." If a female could choose both good genes and the appropriate offspring context, part of the problem posed by G × E would be resolved. However, the fitness cost of choosing is likely to be greater if females need both to assess males and to assess the pattern of environmental change. Female mate choice as an adaptation depends upon the ratio of fitness costs of choice to the female relative to the fitness gains of her progeny; a changing environment changes this calculus. If the 25°C environment is more common than the 31°C environment at the time a female choses a mate, but the two environments become more equitable in frequency during the life of her offspring, the female's perceived fitness gain may well diminish though her fitness costs, already incurred, remain the same.

   The Hamilton–Zuk solution for maintaining variance in male good genes was based on a temporal version of this G × E model. If we replaced the x-axis in our G × E Figure 1.2/Plate 1 (lower graph) with parasite genotypes, we would see that some host genotypes at the B-locus are more resistant (i.e., better adapted) to certain parasite genotypes than they are to others. Reversing the y and x axes illustrates that some parasite genotypes are better adapted to exploit some host genotypes than they are to others. That is, *both* the host and the pathogen have G × E, where the E is associated with genotypes in the other species. The genes in one individual that affect the phenotype of another are referred to as genes with *indirect genetic effects*. The Hamilton–Zuk model therefore is a model of interspecific indirect genetic effects. An important feature of such indirect genetic effects is that, because the environment contains genes, the environment can evolve and, in some metapopulations, this permits local co-evolution of genotype and environment. In a large panmictic population, there cannot be co-evolution between genotype and environment because, by virtue of averaging, the necessary variation in environmental context is lacking.

   Adaptive change in the frequency of parasite genotypes under the Hamilton–Zuk hypothesis has effects just like those discussed for changing the frequencies of temperature environments. A host gene, say B, is a gene of major positive effect when rare, because it has few adapted parasites. The effects of the host gene diminish as it becomes more common and, concomitantly, the population of hosts bearing B alleles is a larger target for the adapting parasite. Eventually, the B allele becomes a bad gene because the parasite environment has adapted to it. The effect of a B allele for our hypothetical model equals $+0.25(P_{non-A} - P_A)$, where P_A is the frequency of parasitic genotypes adapted to BB hosts and P_{non-A} is the frequency of parasitic genotypes not adapted to them. It is clear that the Hamilton–Zuk model maintains heritable variation at the B locus through a cyclically changing (adapting) parasitic environment. Specifically, when B is rare, P_A is small and P_{non-A} is large, and B is a "good gene," by virtue of its parasite resistance. Conversely, when B is common, P_A is large and P_{non-A} is small, and B is a "bad gene," by virtue of its parasite vulnerability. However, it is less clear that the careful balance of fitness costs and benefits to female choice can be maintained in the face of such a mechanism, because the gain to offspring fitness from a "good gene" diminishes throughout its evolutionary trajectory from rare to common. Unfortunately, rare male mating advantage, where the rare are always favored by mating females, has a controversial history owing to equivocal evidence outside of laboratory studies of mutant fruit flies.

   I find it difficult to understand how models based on this type of underlying genetics can drive male trait exaggeration as a symbol of male health. Even if the expression of exaggerated male characters is limited by parasite infection, selection in males on the genes for the exaggeration of the male trait must be an indirect effect of the frequency-dependent selection on the male immune system genes used to resist the parasite. That is, a locus for exaggeration of the male trait must be linked to or associated with the locus affording parasite resistance. The condition where the main effect of one locus depends upon the heterozygote at another locus is called dominance-by-additive epistasis

(Wade, 2002). Here the larger main effects at one locus occur when the frequency of heterozygotes at the other locus is higher.

1.3.3 Gene-by-gene interaction

For a set of genotypes, $G \times G$ is another type of violation of the additivity assumption. $G \times G$ is defined as change in the magnitude or order of a gene's phenotypic effect with change in the genetic background at another locus in the genome. Just like $G \times E$, changes in magnitude of effect result in change in the rate of evolution in different environments. Changes in the order of effects result in a change in the direction of evolution, that is, changes in sign of Δp_A, in different genetic backgrounds. The similarities between $G \times E$ and $G \times G$ in evolutionary genetic theory have been emphasized by referring to the genotypic interactions with the former as interactions with the "external" environment and with the latter as interactions with the "internal" environment (e.g., Gimelfarb, 1994).

There are many kinds of $G \times G$ interactions (Wade, 2001; 2002) and the "crossing type" interaction identical to our $G \times E$ figure is called additive-by-additive epistasis. If the three temperatures on the x-axis are replaced with three genotypes at the A locus, AA, Aa, and aa, then we have a graph of additive-by-additive $G \times G$ between alternative alleles of the B and A loci. On the AA genetic background, the B allele is a "good gene," but on the aa background it is a "bad allele." When the two genotypes occur equally often, B has no effect at all and is neutral with respect to fitness. For this type of interaction, the formal effect of a B allele (Wade, 2001; 2002) equals $+0.25(G_{AA} - G_{aa})$. When a female selects a mate, B is a good gene when her genotype and that of her mate are both AA. If she is aa__ and he is AABB, her offspring gain nothing from her choice of a high value AABB male, since alleles at the B locus are neutral on the Aa background and all offspring would be Aa heterozygotes. Whereas, an AABB male provides "good genes" to the offspring of AA females, an aabb male provides "good genes" to the offspring of aa females. Thus, AA and aa females should favor alternative male B-locus homozygotes when mating.

The "good genes" model of female mate choice depends critically upon Williams' hypothesis of gene independence because otherwise the effect of a gene on a male's phenotype is not necessarily the same, even in sign, of its effect on his offspring. With epistasis, the genic effects necessary for the model to work are unstable and change with genetic background. Hamilton and Zuk (1982) and Zuk *et al*. (1990) argued that, when females choose mates for "good genes," they are basing their choice on male traits that accurately reflect a male's genetic basis for disease resistance. Molecular genomic studies in humans have revealed that the genetic basis for disease resistance is commonly epistasis. For example, Moore (2003, p. 73) reviews the evidence and concludes that "*… epistasis is a ubiquitous component of the genetic architecture of common human diseases and that complex interactions are more important than the independent main effects of any one susceptibility gene.*" Much earlier, Wright (1968, p. 425) had argued similarly with respect to fitness that "*selective value as a character usually imposes interaction effects of the most extreme sort.*" The problem that

epistasis for disease resistance poses for choosy females is that their offspring inherit genes and not gene combinations.

Recently, sexual conflict has been put forward as a likely basis for female choice of mates (Gavrilets *et al.*, 2001; Arnquist & Rowe, 2005; Andersson & Simmons, 2006). Sexual conflict occurs when a gene is good for male fitness but deleterious to female fitness (Rice, 1992); such genes are also referred to as sexually antagonistic genes (Figure 1.3). This version of the "good genes" theory is referred to as the "sexy son hypothesis" because the harm the genes may do to daughters is outweighed by the good they do for sons (Weatherhead & Robertson, 1979). Although a distinction is often drawn between intra-locus and inter-locus sexual conflict, whenever the effect of a gene on fitness changes sign with genetic background, it is epistasis as can be seen in Figure 1.3. The problem for choosy females remains that their sons and their grand-offspring inherit genes from their mates but not gene combinations.

1.3.4 Indirect genetic effects *sensu* quantitative genetics

The term "indirect effects" has different and somewhat confusing meanings in the mate choice literature and in the quantitative genetics literature. In the mate choice literature, the terms direct and indirect refer to the receiver of the fitness benefits of mate choice. If a female enjoys an increased number of her offspring, for example, by avoiding sexually transmitted parasites or by acquiring reproductive resources from a male, these are considered "direct effects" of her mate choice. If, as a result of a female's mate choice, the quality or viability of her
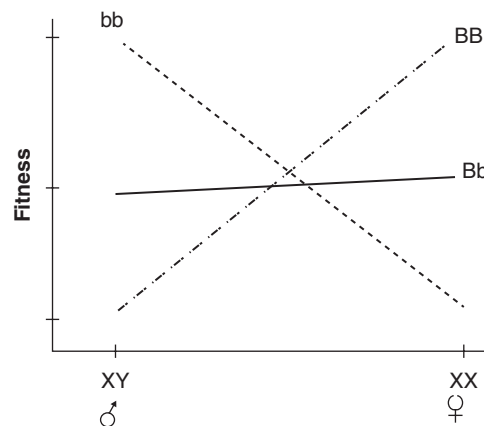
Fig. 1.3 Sexually antagonistic genes, like the one depicted here, are examples of additive-by-additive epistasis or "crossing type" G × G. Such genes play a role in versions of the "sexy son hypothesis," wherein females choose mates to gain "good genes" for their sons, despite the fact that they are "bad genes" for their daughters. See text for discussion.

offspring or her grand-offspring is enhanced, these are considered the "indirect effects" of female mate choice.

In quantitative genetics, direct and indirect effects refer to the individual whose phenotype is affected by a gene *vis a vis* the location of the gene. A gene in an individual that affects its own phenotype or its own fitness is a gene with a direct effect. Indirect genetic effects are those effects on an individual's phenotype that arise in the genotypes of other individuals, which can be either conspecifics or hetero-specifics (as in the parasite examples above). The earlier quotation from Williams (1966) refers to the selection coefficient, the direct effect of a gene on fitness. The "good genes" hypothesis of female mate choice assumes that females can recognize genes affecting viability in males and use this as the criterion of mate choice to obtain viability-enhancing genes for the fitness benefit of their offspring. Thus, the "good" in the classic "good genes" hypothesis refers to a gene's "direct effect" on fitness *sensu* quantitative genetics but it is an "indirect effect" in the mate choice literature, because the benefit of mate choice accrues to the offspring and not to the choosing female. In this section, I use the term "indirect effect" with its quantitative genetic meaning.

An additive indirect effect of a genotype in one individual on its neighbour's phenotype is measured in a manner similar to an additive direct effect. The primary difference is that the phenotype is measured in the neighbours and not in the individuals themselves. So, for genotypes AA and aa, one would measure the mean phenotypic values of their neighbours, say P_{AA} and P_{aa}, respectively, and the indirect effect of the A allele would equal $(P_{AA} - P_{aa})/2$. Consider cannibalism as a type of genetic individual behaviour with effects on the viability phenotype of others. To measure the indirect effect of alternative alleles at a "cannibalism" locus, one would have to set up arenas that offered potential victims to different genotypes of cannibals. The indirect effect of a cannibalism gene would be estimated from the mean inviability of its victims. Genes that influence social behaviours, whether positive (like altruism) or negative (like cannibalism), are indirect effect genes. The direct and indirect effects of genes do not need to differ in sign. The only general survey to date (Biscarini *et al.*, 2010) found only 2–3% of genes with *both* direct and indirect effects. In one-gene models of kin selection, an allele for altruism is assumed to have a negative direct effect on the fitness of its bearer but a positive indirect effect on the fitness of its neighbours. In social competition, it has been argued that it may be common for a gene to have a direct effect that differs in sign from its indirect effect (Wolf, 2003). In general, indirect genetic effects make the phenotype of an individual "the property of the genotypes of multiple individuals" (Wolf, 2003, p. 4655).

When the quality of male plumage is affected by interactions with neighbors, female mate choice for "good genes" becomes more difficult. In laying hens, feather pecking by *other* birds is the primary determinant of an individual's feather quality (Craig & Muir, 1996, a and b). Similarly, weight gain in hogs is primarily determined by *others* in the same pen (Wade *et al.*, 2010). With indirect genetic effects, the "good genes" affecting plumage quality may well reside in the genomes of neighbors rather than in the genome of the focal male. In this circumstance, a female choosing a mate for his feather quality gains nothing

for her offspring. If indirect effects are the predominant determinant of male plumage quality as they are in laying hens and if they differ in sign from genes with direct genetic effects on feather quality (as they also do in laying hens), a female choosing a male for his high plumage quality might obtain genes with "bad direct effects" on plumage for her offspring. Wolf (2003), on theoretical grounds, argues that, for single genes with both kinds of effects, it may be common for a gene to have a direct effect that differs in sign from its indirect effect.

In red jungle fowl, Zuk and Johnson (2000) report evidence that the social environment affects male immune status and the expression of male secondary sex characters, especially the comb. That is, independent of parasite status, male feather quality is affected by interactions with neighboring males. This species, *Gallus gallus*, is believed to be the ancestor of the modern laying hen, where indirect genetic effects on viability have been documented (Ellen *et al.*, 2008). Recently, whole genome association studies have been carried out to screen domestic breeds for genes with direct and indirect effects on feather condition (Biscarini *et al.*, 2010). Biscarini *et al.*, (2010) used 1022 single-nucleotide polymorphisms (SNPs) and reared hens in four-hen cages, in order to estimate the numbers of genes with direct effects on feather condition as well as the numbers of genes with indirect effects on feather condition. They interpreted genes with direct effects as genes conferring resistance or susceptibility to pecking by cage-mates. Reciprocally, they considered genes with indirect effects as genes conferring a propensity to or a reluctance to peck at the feathers of cage mates. Dual interacting traits like these are common to most social competitive interactions between conspecifics, including those mediating sexual conflict. And, they bear a striking similarity to the dual interacting traits of hosts and symbionts.

Biscarini *et al.*, (2010) discovered 11 genes with direct effects and 81 genes with indirect effects. (Only one or two genes had both direct and indirect effects.) The indirect effects (in standard deviation units) were often of greater magnitude than the direct effects, explaining a larger portion of the variance in feather condition. The genes identified included several in the serotonergic system, which affects social dominance, aggression, appetite, memory, learning, growth and aging. This system, which mediates social stress, has strong interactions with the immune system and disease susceptibility (Sapolsky, 2004). The evolutionary response of genes with indirect effects depends on both relatedness and the degree of multilevel selection and not one or the other factor. Moreover, the evolutionary response is symmetric in relatedness and the degree of multilevel selection, indicating that both factors have exactly the same quantitative effect (Bijma & Wade, 2008).

Because genes with indirect genetic effects evolve differently from genes with direct effects (Moore *et al.*, 1997; Wolf *et al.*, 2002), the "good genes" theory of mate choice based on the direct effects of genes is inadequate for understanding the evolution of social interactions during mating (McGlothlin *et al.*, 2010). The Biscarini *et al.*, (2010) study establishes that, as far as feather condition is concerned, genes with indirect effects are predominant, in numbers, effect size and variance explained in *G. gallus*. As a consequence, a female who chooses a

mate based on variations in feather condition among males is more likely to be selecting on the genetic quality of his interacting neighbors than on genes in the male's own genome. For that reason, she is not likely to obtain "good genes" for her offspring.

1.4   Discussion

$G \times E$ and $G \times G$ cause variation in the magnitude and sign of gene effects associated with variations in environment or in genetic back ground, respectively. Such variation in context matters little in a large, randomly mating and mixing populations (Figure 1.1, right panel), where a gene's average effect across all environments and backgrounds determines its evolutionary trajectory. Here, a gene can be identified reliably and consistently as a "good gene" or a "bad gene," in the manner assumed by the "good genes" hypothesis of female mate choice. However, in metapopulations, local variations in context with $G \times E$ and $G \times G$ result can cause a single gene to have alternative evolutionary fates in different demes. In these circumstances, a gene's relationship to fitness cannot be as reliably and consistently assigned, complicating models of female mate choice based on "good genes."

Choosing mates for their "good genes" is complicated in a different way whenever social context plays a significant role in determining mate phenotype. That is, the situation when there are genes with indirect effects, $G \times E_G$, is different from that of $G \times E$ and $G \times G$. Here, the difficulty for female mate choice based on "good genes" lies in the causal structure of a gene's effect on male phenotype. When a male phenotype is influenced by effects of genes in other males, that is, by genes in the social context, much of the variation in male phenotype will be the result of variation among males in their experience of the social environment and not variation among them in the genes they carry. Mate choice based on phenotypic variation caused by social context does not result in the transmission of "good genes" to one's offspring, unless females can influence or recognize the relevant social context.

It is not impossible for females to influence the social context of mate choice; in fact, it may be quite common. Females can influence male social context by inciting male-male competition and then mating with the winner. That is, there can be interactions between the direct and the indirect effects of genes and these might be made visible by female behaviors that precede mate choice. Another way to affect male social context would be for females to mate multiply and allow post-copulatory, pre-zygotic competition among male sperm to determine brood paternity.

The general message from evolutionary genetic theory for sexual selection by female mate choice is that identifying "good genes" is greatly complicated by $G \times E$, $G \times G$, and $G \times E_G$. In a world with a complex genetic architecture, it is unlikely that any one male phenotype will be a reliable, honest indicator of the underlying quality of his genes when quality with respect to fitness is so context dependent.

Acknowledgments

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