INVITED REVIEW

Genetic quality and sexual selection: an integrated framework for good genes and compatible genes

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Abstract

Why are females so choosy when it comes to mating? This question has puzzled and marveled evolutionary and behavioral ecologists for decades. In mating systems in which males provide direct benefits to the female or her offspring, such as food or shelter, the answer seems straightforward — females should prefer to mate with males that are able to provide more resources. The answer is less clear in other mating systems in which males provide no resources (other than sperm) to females. Theoretical models that account for the evolution of mate choice in such nonresource-based mating systems require that females obtain a genetic benefit through increased offspring fitness from their choice. Empirical studies of nonresource-based mating systems that are characterized by strong female choice for males with elaborate sexual traits (like the large tail of peacocks) suggest that additive genetic benefits can explain only a small percentage of the variation in fitness. Other research on genetic benefits has examined nonadditive effects as another source of genetic variation in fitness and a potential benefit to female mate choice. In this paper, we review the sexual selection literature on genetic quality to address five objectives. First, we attempt to provide an integrated framework for discussing genetic quality. We propose that the term ‘good gene’ be used exclusively to refer to additive genetic variation in fitness, ‘compatible gene’ be used to refer to nonadditive genetic variation in fitness, and ‘genetic quality’ be defined as the sum of the two effects. Second, we review empirical approaches used to calculate the effect size of genetic quality and discuss these approaches in the context of measuring benefits from good genes, compatible genes and both types of genes. Third, we discuss biological mechanisms for acquiring and promoting offspring genetic quality and categorize these into three stages during breeding: (i) precopulatory (mate choice); (ii) postcopulatory, prefertilization (sperm utilization); and (iii) postcopulatory, postfertilization (differential investment). Fourth, we present a verbal model of the effect of good genes sexual selection and compatible genes sexual selection on population genetic variation in fitness, and discuss the potential trade-offs that might exist between mate choice for good genes and mate choice for compatible genes. Fifth, we discuss some future directions for research on genetic quality and sexual selection.

Keywords: direct benefit, Fisherian, genetic benefits, genetic compatibility, indirect benefit, mate choice, multiple mating

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Introduction

Evolutionary and behavioral ecologists have long been interested in, and puzzled by mate choice. In many species, females are highly selective when it comes to mating (Darwin 1871; Bateson 1983; Andersson 1994; Kokko et al. 2003). In some of these species, females are congruent in their mate preference for a particular male, while in other species, females are incongruent in their preference, with each preferring a different male. The least controversial models of female mate choice emerged from resource-based mating systems. In such systems, males provide resources
directly to females or offspring such as food, shelter, parental care and protection from predators. These resources obviously could have a profound impact on female fitness. Therefore, it was straightforward to posit that natural selection could lead to the evolution of the preference through direct selection. Furthermore, researchers realized that natural selection could lead to the evolution of male indicator traits that facilitated mate choice by advertising the quality or quantity of a male’s resources (reviewed in Möller & Jennions 2001).

However, there are many other mating systems (and perhaps most mating systems) in which females receive no resources from males (called nonresource-based mating systems), yet females still express a preference among males. For example, in some taxa, males display at fixed courtship, territories known as leks and these males provide only genes (i.e. sperm) to their mates. Females visiting leks typically show congruence in their mating preference for males with the most elaborate trait (Höglund & Alatalo 1995). This congruence appears paradoxical given that a female only receives genes from the male she selects (termed the ‘paradox of the lek’; reviewed in Kirkpatrick & Ryan 1991; Tomkins et al. 2004). Attempts to resolve the paradox have postulated that females receive an indirect benefit in the form of increased genetic quality of their offspring. Specifically, models have shown that the preferred male must provide genes that increase the survivorship or mating success of the offspring as compared to the genes provided by less desirable males (reviewed in Kokko et al. 2003; Mead & Arnold 2004). Empirical research on lek mating systems, as well as other nonresource-based mating systems have confirmed the association between mate preference and increased offspring viability, although the fitness effects appear small at only a few percent (Möller & Alatalo 1999; Jennions et al. 2001; also see Kirkpatrick & Barton 1997). However, few studies have examined the association between mate preference and the subsequent mating success of offspring, which might be a particularly important component of fitness in systems where females choose mates on the basis of elaborate secondary sexual ornaments (Hunt et al. 2004).

What about mating systems in which females each prefer a different male and yet receive no resources from any of them? Researchers have postulated that these females also must be selecting males that increase the genetic quality of their offspring. However, unlike good gene mating systems, in these mating systems genetic quality reflects interactions between paternal and maternal genomes. Based on these gene–gene interactions, the genetic compatibility hypothesis was proposed (Trivers 1972; Zeh & Zeh 1996; Zeh & Zeh 1997). This hypothesis suggests that favorable interactions between genes within an individual can lead to increased survivorship through, for example, heterozygote advantage (overdominance).

The purpose of this review is to provide a synthesis of the literature on genetic quality from the perspective of sexual selection. We build on previous reviews, which have focused on either additive genetic effects (e.g. Möller & Alatalo 1999; Hunt et al. 2004) or nonadditive genetic effects (e.g. Zeh & Zeh 1996, 1997; Tregenza & Wedell 2000), and provide a framework to integrate both types of genetic quality. We begin by (re)defining genetic quality in terms of both ‘good genes’ and ‘compatible genes’, providing examples of each from biological systems, and distinguishing between genetic quality and genetic benefits.

**Defining genetic quality based on good genes and compatible genes**

We define genetic quality based on the contribution a gene variant (allele) or genotype (alleles) makes to an individual’s fitness; an individual is of higher genetic quality when it possesses an allele or genotype that increases its fitness relative to that of an individual with a different allele or genotype. Fitness, in turn, can be defined by the individual’s lifetime reproductive success (LRS), which is composed of both survivorship and breeding success: $LRS = \sum l_x \times m_x$, where $l_x$ is the survivorship to age $x$, $m_x$ is the breeding success (number of offspring produced) at age $x$, and the summation is over an individual’s lifetime (Stearns 1992). Thus, genetic quality can be defined without explicitly differentiating between benefits of increased survivorship or increased breeding success. Conversely, it is not just one of these components but both $l_x$ and $m_x$ are important for determining genetic quality (Kokko et al. 2002; Hunt et al. 2004). Because genetic quality is defined based on an individual’s fitness, it must have two components—additive genetic effects, which we refer to as ‘good genes’, and nonadditive genetic effects, which we refer to as ‘compatible genes’ (Box 1–3).

Consider the following examples. Studies of the major histocompatibility complex (MHC) have provided some of the best examples of compatible genes (reviewed by Potts & Wakeland 1990; Apanius et al. 1997; Edwards & Hedrick 1998; Tregenza & Wedell 2000; Bernatchez & Landry 2003). MHC is found in all vertebrates and is a cluster of linked genes broadly classified into either class I or class II (in humans, MHC is referred to as the HLA, human leukocyte antigen). The protein products of these genes are involved in immune response regulation. In many populations, the MHC is highly polymorphic and most individuals are heterozygous at the coding loci possibly because heterozygous individuals are able to present a wider range of foreign peptides to T-cells (Klein & Figueroa 1986). In such populations, any nonidentical homologues at either the coding loci possibly because heterozygous individuals are able to present a wider range of foreign peptides to T-cells (Klein & Figueroa 1986). In such populations, any nonidentical homologues at either the class I or II genes can be considered compatible.

For example, Arkush et al. (2002) used in vitro fertilization techniques with chinook salmon (Oncorhynchus tshawytscha)
Box 1 Defining genetic quality

Genetic quality has two components, good genes and compatible genes:

A good gene is defined as an allele that increases fitness independent of the architecture of the remaining genome, which, in diploid organisms, includes the homologue to the particular ‘good allele’. Across the genome, good genes will show additive genetic variation. Thus, when variation in fitness exists as a result of good genes, the population will respond to directional selection.

A compatible gene is defined as an allele that increases fitness when in a specific genotype; i.e. when paired with a specific homologue (overdominance) or allele at another gene locus (epistasis). Across the genome, compatible genes will show nonadditive genetic variation. Thus, when variation in fitness exists because of compatible genes, the population will not respond to directional selection, but the mechanisms of acquiring compatible genes (e.g. preference alleles) will respond to directional selection.

NB. We use the term ‘gene’ broadly in the sense of a region of DNA that can be inherited independent of another region of DNA. Thus, a gene may include several different coding regions when these regions are in close proximity on a chromosome such that recombination is infrequent.

to produce individuals that varied in their diversity at the MHC. Specifically, they were able to generate full-siblings that were either homozygous or heterozygous at the MHC class II set of genes. The researchers then exposed the families to infectious hematopoietic necrosis virus (IHVN). IHVN causes epizootics among salmonid fish and is considered to be one of the most important viral pathogens to bacterial infection by \( A.\) salmonicida. The \( e \) allele would clearly confer a fitness advantage and thereby represent a good gene. A similar result also has been demonstrated in whitefish, \( C. \) sp. (Wedekind \textit{et al}. 2004).

Measuring genetic quality and genetic benefits

To measure genetic quality and genetic benefits (see box 2), variation in both genes and fitness must be assessed. An individual’s fitness includes both survivorship and breeding success (LRS) and, ideally, the LRS of the individual’s sons and daughters (Hunt \textit{et al}. 2004). Researchers have employed a variety of approaches to assess genetic benefits. These approaches can be grouped into three categories: (1) measuring genetic benefits from good genes; (2) measuring genetic benefits from compatible genes; and (3) measuring genetic benefits from both good genes and compatible genes.

Measuring genetic benefits from good genes

Many studies of good genes have used a correlational approach, whereby a phenotypic attribute of a set of parents, usually of males, is related to a surrogate of fitness in their offspring. The square of the correlation coefficient represents the proportion of variation in fitness attributable to good genes. These studies make two important assumptions. First, they assume that the measured phenotypic trait captures genetic variation among individuals. This assumption should be well supported when condition-dependent indicator traits (e.g. sexual ornaments) are measured because such traits should capture additive genetic variation (Rowe & Houle 1996; Tomkins \textit{et al}. 2004; also see Cotton \textit{et al}. 2004). Second, they assume that nongenetic effects are uniform or random (with respect to the trait)
Box 2 Distinguishing between genetic quality and genetic benefits

We have defined genetic quality based on both good gene effects and compatible gene effects on fitness (Box 1). Previous work instead has defined genetic quality more narrowly as the ‘breeding value for total fitness’, where the breeding value is the ‘sum of the additive effects of the genes of an individual on a given trait’ (Hunt et al. 2004). We emphasize our broader definition, which includes both additive and nonadditive genetic effects, because both effects clearly can contribute to an individual’s fitness and thus both components will be subject to natural and sexual selection.

Based on our definition of genetic quality, females do not necessarily obtain a genetic benefit — increased genetic quality of their offspring — by mating with a male that is himself of high genetic quality (Table 1). Only the good gene portion of the genome is heritable and provides a genetic benefit. For example, all else being equal, the offspring of a male with good genes will, on average, have higher fitness than the offspring of a male without the good genes. Thus, all females will benefit from mating with the male with the good gene through increased offspring fitness. Conversely, the offspring of a male with compatible genes will not have higher (or lower) fitness than the offspring of a male without compatible genes, all else being equal, and each female will benefit from mating with a different male that may or may not be of high genetic quality himself.

Consider the following example of a nonresource-based mating system and a simple single-locus model with two alleles denoted A and B. If the A allele is a good gene, for example the A allele provides resistance to a common pathogen, then the AA male has the highest genetic quality, and all females will maximize the genetic quality of their offspring by mating with the AA male because this ensures that their offspring obtain at least one copy of the good gene (Fig. 1a). Conversely, if the A and B alleles instead are compatible genes, for example when there is overdominance, then the AB male has the highest genetic quality, but each female will maximize the genetic quality of her offspring by mating with a different male (Fig. 1b). The AA female should mate with the BB male to ensure that all of her offspring are heterozygous. The BB female should mate with the AA male for the equivalent reason. The AB female could mate with any male because in any case half of her offspring will be heterozygous and half will be homozygous. Only when eggs can differentiate among sperm based on haplotype (reviewed by Zeh & Zeh 1997; Birkhead & Pizzari 2002), will the AB female maximize the fitness of her offspring by mating exclusively with the AB male because in this case all of her offspring potentially can be heterozygous — i.e. an A egg can select a B sperm, the B egg can select an A sperm.

In resource based mating systems, genetic benefits from compatible genes will trade-off with nongenetic (direct) benefits when direct benefits are positively correlated with male genetic quality. Consider the example in which the A and B alleles are compatible genes. From the AA female’s perspective, mating with the BB male will produce offspring with the highest genetic quality, but the BB male is himself of low genetic quality (because he is homozygous) and may have less of direct benefits, such as food or shelter, to provide the female or her offspring (Table 1). Such a trade-off does not occur with good genes because the male that will produce offspring of high genetic quality from the perspective of any female is himself also of high genetic quality (e.g. the AA male in the good genes example above).

Box 2, Table 1 In resource based mating systems, genetic and nongenetic benefits can tradeoff

<table>
<thead>
<tr>
<th>Male genetic quality</th>
<th>Direct benefit to female or offspring (nongenetic)*</th>
<th>Indirect benefit to offspring (genetic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good genes (AA)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Compatible genes (AB)</td>
<td>+</td>
<td>–</td>
</tr>
</tbody>
</table>

*Assumes that males of high genetic quality provide more direct benefits to females.

Fig. 1 Genetic quality can be classified as either good genes (additive effects on fitness) or compatible genes (non-additive effects on fitness). (a) When the A allele is a good gene, all females will maximize the fitness of their offspring by mating with the AA male, all else being equal. (b) When the A and B alleles instead represent compatible genes, each female will maximize the fitness of their offspring by mating with a different male, all else being equal. In the absence of haplotype-specific sperm selection by the egg (see text), the AB female could mate with any male because regardless of male genotype, half of her offspring will be heterozygous (dashed line).
Across families. This assumption should be well supported in nonresource-based mating systems (Barber & Arnott 2000; Jennions & Petrie 2000; but see Reyer et al. 1999), but may not be well supported in resource-based mating systems (Burley 1988; Sheldon 2000b; Kotiaho et al. 2003).

For example, in one of the first studies of mate choice for good genes, Reynolds & Gross (1992) mated female guppies to males that varied in body length at maturation. Guppies are live-bearing, promiscuous tropical fish with a nonresource-based mating system. Reynolds and Gross show that male body length is a trait preferred by females in their population. The authors then estimated the fecundity of daughters when they sexually matured based on offspring weight of their first two broods, and correlated fecundity to their father’s body length. The correlation coefficient was \( r = 0.65 \), and therefore good gene effects explained 42% (= 0.65\(^2\)) of the variation in daughter fecundity, which is one component of fitness (there was no apparent effect of male body length on daughter survivorship). There is no evidence that female guppies can adjust investment in offspring postfertilization, so this paper demonstrated a strong effect of good genes quality, at least in the laboratory environment in which it was conducted.

In a study on peacocks (\( Pavo cristatus \)), Petrie (1994) assigned groups of four females to each of eight males in a random breeding design. Peacocks are a lekking species where males provide no resources to their mates or offspring. Males have elaborate tail feathers (called a train) that they display to females during mate choice. The average area of the ‘eyes’ — brilliant green and blue spots on the tail feathers — is a good measure of the elaboration of the train and of a male’s attractiveness to females (Petrie & Halliday 1994). Petrie therefore calculated the average eye area for the eight males and correlated this with the growth rate and survival of each male’s offspring. She found that offspring sired by males with greater eye area had higher survivorship when released into a seminatural environment (correlation between father eye area and offspring survivorship: \( r = 0.79 \), \( r^2 = 0.62 \)). Petrie concluded that females gain good genes for their offspring by mating with males that have large eyes on their train. However, in other birds, it has been suggested that females put more resources into eggs (by laying larger eggs or by adding more testosterone) that are sired by attractive males (Gil et al. 1999; Cunningham & Russell 2000). If peahens are also capable of such differential investment then the effect size resulting from good genes from Petrie’s study may be inflated (but see Petrie et al. 2001).

Møller & Alatalo (1999) preformed a meta-analysis on 22 studies that examined the correlation between a phenotypic trait of sires and the survivorship of their offspring. They estimated the overall effect of good genes to be \( r = 0.22 (r^2 = 0.048) \), which is consistent with estimates of heritability of fitness as a result of additive genetic variation (Gustafsson 1986; Charlesworth 1987; Burt 1995; Morjan & Rieseberg 2004; but see Houle 1992). A second meta-analysis performed on 47 studies (40 species total) was consistent with the original study (Jennions et al. 2001). However, many of the studies included in the meta-analyses may have been confounded by environmental effects across families because the mating systems analyzed were resource-based, therefore the survivorship estimates may have included direct effects such as parental care. If males with a larger or otherwise better trait provided more food or other direct benefits to their offspring than males with a smaller trait (e.g. Keyser & Hill 2000), then the estimated
effect size would be an overestimate of good gene effects. Conversely, if males with a larger trait provided less food to their offspring than males with a smaller trait (e.g. Duckworth et al. 2003), then the estimated effect size would be an underestimate of good gene effects. Additionally, if the good genes underlying the expression of the male trait also increase the breeding success ($m_x$), then the estimated good gene effect size would further be underestimated. Thus, the mean fitness effect of good genes is unclear (Hunt et al. 2004; Tomkins et al. 2004).

To avoid confounding effects of direct benefits and differential maternal investment, other studies have utilized split-clutch in vitro fertilization (e.g. Welch et al. 1998; Barber et al. 2001; Sheldon et al. 2003; Neff 2004). For example, Welch et al. (1998) split clutches of eggs from female gray tree frogs (Hyla versicolor) and fertilized one half with sperm from a male that called for a long duration and the other half with sperm from a male that called for a short duration. Long calling males are preferred over short calling males by most females. The authors then compared the performance (e.g. growth rate, survivorship) of the maternal half-siblings and found that those sired by long calling males generally outperformed those sired by short calling males. For instance, in 1 year of their high food treatment, they found that survivorship during the larval period was 10% higher (0.702 vs. 0.637) for offspring sired by long calling males than offspring sired by short calling males.

In bluegill sunfish (Lepomis macrochirus), Neff (2004) split clutches from females and fertilized one half with sperm from a male adopting the parental life history, and the other half with sperm from a male adopting the cuckolder life history. Females may prefer to mate in the presence of cuckolders as they appear to release three times as many eggs when mating simultaneously with a cuckolder male and parental male than when mating only with a parental male (Fu et al. 2001). Neff found that offspring sired by cuckolder males were 5% larger at the end of the endogenous feeding period than the half-sibling counterparts sired by parental males. Based on size-dependent predation by fed parental males. Based on size-dependent predation by

Measuring genetic benefits from compatible genes

A male with good genes should produce offspring with higher fitness regardless of the maternal genetic contribution, while a male with compatible genes will produce offspring with higher fitness only when matched with a specific maternal haplotype. Based on this premise, Johnsen et al. (2000) examined genetic quality in bluethroat (Luscinia svecica) offspring and provided the first evidence for compatible gene mate choice in an extra-pair mating system. Bluethroats are a socially monogamous passerine bird with biparental care. Females frequently copulate with extra-pair males (i.e. males that are not their social mate). The extra-pair males provide no direct benefits and, as in other birds, there is no evidence that male parents differentiate between their own offspring and extra-pair young (see Kempenaers & Sheldon 1996). To examine offspring genetic quality, Johnsen and colleagues measured cell-mediated immunity for each chick in their study by a subcutaneous injection of phytohemagglutinin (PHA) in one of the wings. PHA causes a local swelling response that reflects T-cell reactivity, and the response is heritable and correlated with survival and longevity in other passerines (e.g. Saino et al. 1997; Birkhead et al. 1999). The authors compared the immune response of a male’s offspring from his social mate (within-pair young, WPY) and his offspring with a second extra-pair female (extra-pair young, EPY). Johnsen and colleagues (2000) postulated that if females seek extra-pair matings for good genes, then there should be no difference in the immune response of the WPY and EPY for a given male (i.e. paternal half-siblings). Conversely, if females seek extra-pair matings for compatible genes then the immune response of EPY should be better than that of the WPY for a given male. Across 14 paternal half-sibling comparisons, the authors found that for 12 comparisons, the EPY had better immune competence than that of the WPY. Furthermore, offspring type (EPY or WPY) captured 13% of the variation in immune response, while paternal identification captured only 4%. These data are best explained by mate choice for compatible genes through extra-pair matings (also see Blomqvist et al. 2002; Foerster et al. 2003; Freeman-Gallant et al. 2003).

A second approach to quantify the potential genetic benefits from compatible genes is to analyze the effect of specific genes known to contribute to nonadditive genetic variation. For example, Penn et al. (2002) exposed mixed populations of MHC homzygous and heterozygous mice (Mus domesticus) to various strains of avirulent and virulent Salmonella enterica serovar, Salmonella typhimurium and Listeria monocytogenes. Over a 30-week trial, they found that heterozygous individuals had an approximately 2% survivorship advantage to the avirulent strains than homozygous individuals, but no advantage to the virulent strains. In a second mixed population that was not experimentally exposed to specific pathogens (but was exposed to uncontrolled, ‘natural’ pathogens), they found that heterozygous individuals had approximately 19% higher survivorship than homozygous individuals over the 30-week trial.

Measuring genetic benefits from both good genes and compatible genes

In many mating systems, females mate with more than one male during a single reproductive event (Andersson 1994;
### Table 1: Multiple mating and genetic quality

<table>
<thead>
<tr>
<th>Species</th>
<th>Measure of fitness</th>
<th>Degree of multiple mating*</th>
<th>Effect size (%)†</th>
<th>Controlled direct benefits‡</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Australian field cricket</strong></td>
<td>hatching success</td>
<td>low 0.48, high 0.55</td>
<td>15</td>
<td>yes</td>
<td>Simmons 2001</td>
</tr>
<tr>
<td>(Teleogryllus oceanicus)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Bulb mite</strong></td>
<td>offspring number produced by daughters (standardized)</td>
<td>low 0.93, high 1.2</td>
<td>29</td>
<td>yes</td>
<td>Konior et al. 2001; also see Kozielska et al. 2004</td>
</tr>
<tr>
<td>(Rhizoglyphus robini)</td>
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</tr>
<tr>
<td><strong>Bumble-bee</strong></td>
<td>offspring number (males [top] or queens [bottom])§¶</td>
<td>low 19, high 37</td>
<td>95</td>
<td>yes</td>
<td>Baer &amp; Schmid-Hempel (1999)</td>
</tr>
<tr>
<td>(Bombus terrestris)</td>
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<tr>
<td><strong>Cuis</strong> (Galea musteloides)</td>
<td>offspring survivorship</td>
<td>low 0.54, high 0.92</td>
<td>70</td>
<td>no</td>
<td>Keil &amp; Sachser (1998)</td>
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<tr>
<td><strong>Decorated cricket</strong></td>
<td>offspring survivorship (ad libitum treatment)¶</td>
<td>low 0.65, high 0.69</td>
<td>ns</td>
<td>no</td>
<td>Sakaluk et al. (2002)</td>
</tr>
<tr>
<td>(Gryllodes sigillatus)</td>
<td></td>
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<tr>
<td><strong>Field cricket</strong></td>
<td>hatching success</td>
<td>low 0.41, high 0.53</td>
<td>29</td>
<td>yes</td>
<td>Tregenza &amp; Wedell (1998)</td>
</tr>
<tr>
<td>(Gryllus bimaculatus)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Grain beetle</strong></td>
<td>hatching success</td>
<td>low 0.82, high 0.84</td>
<td>ns</td>
<td>yes</td>
<td>Worden &amp; Parker (2001)</td>
</tr>
<tr>
<td>(Tenebrio molitor)</td>
<td></td>
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<tr>
<td><strong>Ground cricket</strong></td>
<td>hatching success</td>
<td>low 0.19, high 0.55</td>
<td>189</td>
<td>yes</td>
<td>Fedorka &amp; Mousseau (2002)</td>
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<tr>
<td>(Allonemobius socius)</td>
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<tr>
<td><strong>Guppy</strong> (Poecilia reticulata)</td>
<td>offspring number§</td>
<td>low 5.1, high 8.8</td>
<td>73</td>
<td>no</td>
<td>Evans &amp; Magurran (2000)</td>
</tr>
<tr>
<td><strong>Pseudo scorpion</strong></td>
<td>offspring number§</td>
<td>low 38, high 49</td>
<td>29</td>
<td>no</td>
<td>Zeh (1997)</td>
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<tr>
<td>(Cordylocheres scorpoides)</td>
<td></td>
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<tr>
<td><strong>Red flour beetle</strong></td>
<td>offspring number§</td>
<td>low 1.4, high 2.0</td>
<td>43</td>
<td>no</td>
<td>Pai &amp; Yan (2002)</td>
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<tr>
<td>(Tribolium castaneum)</td>
<td>sired by sons (average of 3 trials)</td>
<td></td>
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<tr>
<td><strong>Sierra dome spider</strong></td>
<td>hatching success</td>
<td>low 0.65, high 0.78</td>
<td>ns</td>
<td>no</td>
<td>Watson (1998)</td>
</tr>
<tr>
<td>(Neriene litigiosa)</td>
<td></td>
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*For all studies 'low' refers to females mated to a single male except for the bees, in which case the singly mated females were mated to four males which were brothers. When more than two multiple mating groups were examined, 'high' represents the group with the largest number of mates; †Calculated from high value/low value – 1; ‡Controlled for potential direct benefits passed to female via ejaculates; for example, by controlling the number of matings or the number of spermatophores; §Offspring number is a measure of offspring survivorship (see text); ¶Values were approximated from results reported in a figure in the cited reference.

Birkhead & Møller (1998). In the absence of direct benefits from males, such as food or shelter, it has been hypothesized that female multiple mating evolved as a mechanism to increase overall genetic quality of the offspring (reviewed by Jennions & Petrie 2000). Presumably, a female could obtain sperm from multiple males and fertilize her egg with the sperm that would produce an offspring of the highest possibly genetic quality. Thus, to calculate the fitness effects of overall genetic quality (both good genes and compatible genes), researchers have taken advantage of mating systems in which females multiply mate and employed experiments that randomly allocate females to either a single mating group, in which females are given one male with which to mate, or a multiple mating group, in which females are given multiple males with which to mate (Table 1). Females in the multiple mating group should produce offspring of higher fitness than females in the single mating group, and the magnitude of the genetic benefits can be calculated from the difference in the fitness of offspring from the two groups. These studies typically cannot distinguish between good gene and compatible gene effects on fitness. They assume that there are mechanisms that enable the selective utilization of sperm based on genotype (e.g. Eberhard 1996; also see biological
mechanisms in succeeding section), and sperm is not limited in the single mating group. Furthermore, several of these studies did not control for the number of matings between the single and multiple mating groups and therefore assumed that there are no direct benefits passed to the female via, for example, nutrients in the ejaculate.

As an example, Zeh (1997) studied pseudoscorpions (Cordylochernes scorpioides) and mated one group of females to a single male and a second group of females to two or three males. Females were then left largely undisturbed until the offspring hatched from the female’s brood sac, at which time the offsprings were counted. The number of offspring each female produced was adjusted for her size (using cephalothorax length as a covariate in the analysis) in an attempt to remove maternal environmental effects such as variation in fecundity because of body size. Thus, Zeh’s measure of offspring number represents the viability (early survivorship) of the offspring through to emergence from the brood sac. She found that females from the multiple mating group produced 29% more offspring than females from the single mating group. However, Zeh did not control for the number of matings between her two groups and thus the number of spermatophores accepted by females in each group. Nevertheless, a follow-up study by her group, which controlled for the number of spermatophores, found nearly identical results (Newcomer et al. 1999). In an attempt to tease apart good gene and compatible gene effects, Zeh (1997) also mated a set of males each to a different pair of females and compared offspring viability. She found no correlation between the number of offsprings hatched by the pairs of females and therefore suggested that the increased viability of offspring from females in the multiple mating group was attributable to compatible gene effects. However, in this latter experiment, any paternal good gene effect might be masked by differences in genetic and environmental effects between the two females.

In a similar study on field crickets (Gryllus bimaculatus), Tregenza & Wedell (1998) created three experimental groups. In the first group, females each were mated to a single male four times, in the second group, females were mated to two different males twice each, and in the third group, females were mated to four different males once each. Their design therefore controlled for mating number and potential direct benefits that males may pass to females along with their ejaculate. Tregenza and Wedell (1998) found no significant difference in the number of eggs laid by females in the three treatments (consistent with an assumption of no difference in maternal environmental effects across the three treatments), but they did find a significant difference in the number of eggs that hatched. On average, 41% of the eggs hatched from females mated to a single male, 47% hatched from females mated to two males, and 53% hatched from females mated to four males. Thus, offspring from females that mated with four males had 29% higher (= 53/41) hatching success than offspring from females that mated with only one male.

In total, across 14 experimental studies on 12 different species, researchers have found anywhere from no significant difference in offspring fitness between single mated and multiple mated females to 189% increase in fitness for offspring from multiple mated females (Table 1).

Other studies have taken advantage of natural variation in the degree of multiple mating among females to investigate genetic quality (e.g. Madsen et al. 1992; Olsson et al. 1994, 1996; Kempenaers et al. 1999). For example, Madsen et al. (1992) examined multiple mating and offspring genetic quality in adders (Vipera berus), a small venomous snake. Using detailed behavioral observations during the breeding season, they were able to determine the number of males the females mated with. Females were then collected and maintained in the laboratory until they gave birth. The authors found that females that mated with more males had a smaller proportion of their brood still born (r = −0.40, n = 34, P < 0.02). They propose that by multiply mating, females increase intrauterine sperm competition, which would increase the genetic quality of the offspring if sperm competitiveness was correlated with the quality of its genes (also see Olsson & Madsen 2001). Correlative studies arguably are not as strong as experimental manipulation studies because the correlative studies cannot easily rule out confounding effects, such as maternal environmental effects, that might be associated with the degree of multiple mating.

A third type of study has attempted to measure offspring genetic quality in nonresource-based mating systems by mating some males or females to a preferred mate and other males or females to a nonpreferred mate. These studies attribute differences in the fitness of offspring from preferred and nonpreferred matings to offspring genetic quality. For example, in house mice (Mus musculus), Drickamer et al. (2000) found that offspring from preferred matings had higher survivorship than offspring from nonpreferred matings. Specifically, offspring from preferred matings had a 76% survivorship more days after being introduced into seminatural enclosures while offspring from nonpreferred matings only had a 44% survivorship (also see Drickamer et al. 2003; Gowaty et al. 2003). The authors, however, could not rule out direct benefits (differential investment) because females may pass more resources to their embryos via the placenta when mated to a preferred mate. In deep-snouted pipefish (Syngnathus typhle), Sandvik et al. (2000) found that offspring of preferred matings had higher survivorship than the offspring of nonpreferred matings, both when females were allowed to select a mate (proportion surviving predation: c. 68% vs. 48%) and when males were allowed to select a mate (c. 58% vs. 39%). In guppies (Poecilia reticulata), however, Nicoletto (1995) found no evidence for a difference in offspring fitness from the two types of matings.
A more comprehensive approach for measuring genetic benefits from both good genes and compatible genes is the use a breeding design that examines all crosses between two sets of individuals (sometimes referred to as the ‘North Carolina Design II’; see Lynch & Walsh 1998; p. 598). A set of $N_s$ sires are mated in all combinations with a set of $N_d$ dams and $N_s \times N_d$ families are generated. Some measure of fitness, such as hatching success or survivorship, is obtained for each family, and a two-way ANOVA can be used to partition the variation in fitness among additive genetic effects (good genes), nonadditive genetic effects (compatible genes), environmental maternal effects and other (unmeasured) environmental effects.

The North Carolina Design II was utilized by Wedekind et al. (2001) to examine genetic quality of alpine whitefish (*Coregonus* sp.). The authors performed all 100 crosses of 10 males and 10 females (i.e. a statistically balanced design). Whitefish are external fertilizers and therefore eggs can be easily stripped from females and fertilized with milt from a male. Each family was then split into four to provide a replicated design. The eggs were reared in the same environment and mortality for each family replicate was documented during two phases of development: (1) early mortality—the proportion of eggs that were dead at day 30; and (2) late mortality—the proportion of eggs that died during the period from day 30 to hatching. Mortality within each family was not correlated during the two phases; thus, early and late mortality provided two different measures of offspring quality (Wedekind et al. 2001).

The authors entered sire and dam identification as random factors because the 10 sires and 10 dams were representative of a larger population. If the sires and dams had represented the entire population or the individuals that were of specific interest, then their identifications instead would be entered as fixed factors. Overall, dam, sire and dam × sire effects explained 67% ($= [1.35 \times 10^{-2} + 1.48 \times 10^{-4} + 7.75 \times 10^{-4}] / 1.65 \times 10^{-2}$) of the phenotypic variation in mortality (Table 2). Although all three effects were statistically significant, most of the explained variation was attributed to dam effects, which include both maternal genetic effects and environmental effects such as egg nutrients. Because males in this species provide only genes to the offspring, the sire effect provides an estimate of additive genetic effects (good genes). Specifically, assuming that epistatic genetic variance is of negligible importance, the additive genetic effects can be calculated from four times the Sire component of variance (Lynch & Walsh 1998; p. 509); the negative variance component was treated as zero, for discussion on negative variance components see Graham & Edwards (2001; p. 507); the negative variance component was treated as zero, for discussion on negative variance components see Graham & Edwards (2001; p. 509).

| Table 2 | Summary of the two-way ANOVA results in whitefish from Wedekind et al. (2001). The results include source of variation, sum of squares (SS), degrees of freedom (DF), mean square (MS), $F$ statistic, $P$-value, and variance ($\sigma^2$) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Source of variation | SS | DF | MS | $F$ | $P$ | $\sigma^2$ |
| Early egg mortality | | | | | | |
| Dam | 4.91 | 9 | 0.5456 | 104.39 | < 0.0001 | 1.35 × 10^{-2} |
| Sire | 0.10 | 9 | 0.0111 | 2.14 | 0.035 | 1.48 × 10^{-4} |
| Dam × Sire | 0.42 | 81 | 0.0052 | 2.52 | < 0.0001 | 7.75 × 10^{-4} |
| Error | 0.62 | 300 | 0.0021 | | | 2.07 × 10^{-3} |
| Total | | | 1.65 | 10^{-2} | | |
| Late egg mortality | | | | | | |
| Dam | 1.21 | 9 | 0.1344 | 4.69 | < 0.0001 | 2.64 × 10^{-3} |
| Sire | 0.85 | 9 | 0.0944 | 3.28 | 0.002 | 1.64 × 10^{-3} |
| Dam × Sire | 2.32 | 81 | 0.0286 | 0.85 | 0.81 | 3.39 × 10^{-2} |
| Error | 10.17 | 300 | 0.0339 | | | 3.82 × 10^{-2} |

*Variance estimates were calculated from formulas presented in Lynch & Walsh (1998; p. 600) and Table 1 of Graham & Edwards (2001; p. 507); the negative variance component was treated as zero, for discussion on negative variance components see Graham & Edwards (2001; p. 509).
account for 3.5%, 19% and 81% of the variance in early mortality in the Alpine whitefish population studied by Wedekind et al. (2001). When there is epistatic genetic variance, the estimate of good gene effects and maternal environmental effects will be overestimated. This may explain why the percentages in the whitefish example add up to more than 100%.

During the second phase of development, dam, sire and dam × sire effects explained only 11.2% of the phenotypic variance in mortality (Table 2). Additive genetic effects (good genes) accounted for 17% of the phenotypic variance in late mortality, maternal environmental effects accounted for less than 3%, and the interaction effect was not significant, indicating no nonadditive genetic effects. Interestingly, only the late phase of mortality was correlated with the size of the sires' breeding tubercles, a sexually selected character (Wedekind et al. 2001), and good gene effects were about 11-fold higher for late mortality than early mortality.

Two difficulties with using an ANOVA in the North Carolina Design II are the possibility of negative variance components and its sensitivity to an unbalanced design (e.g., when there is variance in the number of offspring analyzed from each family). Modifications to the model design and sum of squares have been proposed to account for such effects (Searle et al. 1992), although the sampling properties of the modified sum of squares are not yet well understood. Alternatively, maximum likelihood (ML) and restricted maximum likelihood (REML) estimators that are analogous to the ANOVA have been developed, and these estimators do not yield negative variance components and are not particularly sensitive to unbalanced designs (see Lynch & Walsh 1998; p. 779).

### Biological mechanisms for acquiring genetic benefits

We propose that there are three fundamental stages during breeding which are important for differentiating among mechanisms of increasing offspring genetic quality: (1) precopulatory [mate choice]; (2) postcopulatory, prefertilization [sperm utilization]; and (3) postcopulatory, postfertilization [differential investment] (Fig. 1).
Mate choice (precopulatory)

Choosy females can increase the genetic quality of their offspring by mating only with males that will contribute good genes or compatible genes to their offspring. Good genes can be conveyed by condition-dependent traits (Rowe & Houle 1996). For example, we have discussed that female guppies prefer to mate with longer males and peahens prefer to mate with males with larger eye-spots because these males pass on to the offspring good genes that increase their fitness (Reynolds & Gross 1992; Petrie 1994). Mate choice also can be used to select males with compatible genes. For example, Wedekind et al. (1995) examined mate preference in humans for HLA dissimilarity. In humans, heterozygosity of HLA loci can increase survivorship (e.g. Thursz et al. 1997). The authors asked females to rank the pleasantness of the odor of t-shirts that were worn for two days by various males. Specifically, each female was asked to rank six t-shirts, three of which were worn by males that were dissimilar to the female (dissimilar males) at the HLA loci (based on the HLA-A, -B and -DR regions) and the other three were worn by males that were similar to the female at the HLA loci (similar males). Females not taking oral contraceptives ranked the pleasantness of dissimilar males higher than that of similar males, and also indicated that the dissimilar males reminded them of their mate or ex-mate more so than did the similar males. Thus, these data suggest that human females use odor during mate choice to increase diversity at the MHC of their offspring (or perhaps increase genome-wide diversity; see Wedekind & Füri 1997). Interestingly, females taking oral contraceptives ranked the pleasantness of dissimilar males higher than that of similar males, possibly because the contraceptives hormonally mimic pregnancy.

Mate choice for genetic quality also may involve multiple mating (e.g. Yasui 1997). Females of several species have been shown to ‘trade-up’ to a second mate with good genes relative to their first mate (e.g. Gabor & Halliday 1997; Bateman et al. 2001). For example, in great reed warblers (Acrocephalus arundinaceus), Hasselquist et al. (1996) found that male song repertoire size was positively correlated with the survival of their offspring and that females selected extra-pair mates (which provide no direct benefits) that had greater repertoire size than their social mate. In fish, Pitcher et al. (2003) presented two male guppies, which differed in the amount of orange area they had on their bodies, sequentially to females. In the population studied by the authors, females prefer to mate with males that have greater orange area, presumably because these males have good genes (e.g. Evans et al. 2004). Based on detailed behavioral data, they showed that females were more receptive to mating with the second male when he had more orange area than the first male that she mated with. The authors also showed that the difference in orange area between the second and first male was correlated with the difference in their paternities; the more orange area the second male had relative to the first male, the more paternity he garnered.

Females also may trade-up for compatible genes, for example, as discussed in bluethroats (Johnsen et al. 2000). In addition, Freeman-Gallant et al. (2003) found that female yearling Savannah sparrows (Passerculus sandwichensis) avoided pairing with MHC-similar males and females paired to MHC-similar males were more likely to seek extra-pair matings than females paired to MHC-dissimilar males. Presumably, MHC-similarity of parents is negatively correlated with their offspring’s fitness (also see Blomqvist et al. 2002; Foerster et al. 2003).

Sperm utilization (postcopulatory, prefertilization)

Females may increase the genetic quality of their offspring by differentiating among sperm and utilizing only sperm with good or compatible genes. There are two basic mechanisms by which this can be accomplished, sperm competition and cryptic female choice (Eberhard 1996; Birkhead & Möller 1998). First, by facilitating sperm competition, females can increase the genetic quality of their offspring when the sperm from the male that will generate the fittest offspring with her is most successful at fertilizing her eggs. There is some support emerging from the literature that the competitiveness of a male’s sperm (ejaculate) is an indicator of good genes. For example, in a laboratory experiment with yellow dung flies (Scathophaga stercoraria), Hosken et al. (2003) randomly paired males and mated each male with a different female. They then compared the development time of the offspring of each paired male as a measure of fitness. Development time is an indicator of offspring survivorship because of the ephemeral nature of dung in the wild. Next, the authors allowed the pairs of males to compete with each other and copulate with a third female. Across the pairs, they found that males that sired fitter offspring also had more competitive sperm (i.e. sperm that was more likely to fertilize the eggs when in competition with another male’s sperm).

In another study, Evans et al. (2003) used artificial insemination to investigate male genetic quality and sperm competitiveness in guppies. They introduced equal numbers of sperm into females from two males that differed in the amount of orange area on their bodies (orange area may be an indicator of offspring viability; Evans et al. 2004). Using genetic markers, they were able to show that the difference in orange area between the two males was correlated with the difference in their paternities; males with more orange area sired more offspring than males with less orange area.

When sperm competitiveness is heritable and most females multiply mate, the genes that underlie sperm competitiveness are themselves good genes (Curtsinger 1991;
Keller & Reeve 1995; Yasui 1997; but see Pizzari & Birkhead 2002). There are two lines of evidence that provide support for the heritability of sperm competitiveness: (i) direct measures of heritability of sperm competitiveness or sperm traits correlated with sperm competitiveness such as length or speed (Woolley & Beatty 1967; Radwan 1998; Ward 1998, 2000; Morrow & Gage 2001); and (ii) indirect measures which compare the competitiveness of sperm from sons of polyandrous vs. monandrous females (Holland & Rice 1999; Bernasconi & Keller 2001; Pitnick et al. 2001; Pai & Yan 2002). Thus, in addition to potential viability benefits, females that facilitate sperm competition also may ensure that their offspring obtain the sperm competitiveness genes.

Second, females may exercise ‘cryptic choice’ where they directly manipulate sperm usage and bias fertilization to the male that will produce offspring of higher genetic quality. Several mechanisms by which females manipulate sperm have been reported in the literature (reviewed by Eberhard 1996). Pizzari & Birkhead (2000) studied sperm ejection in a free-living population of feral fowl (Gallus gallus domesticus). In feral fowl, male social rank is presumed to be an indicator of good genes. The authors found that males of low social rank were more likely to have their sperm ejected by females — through cloacal contractions immediately after insemination — than males of high social rank. Next, the authors removed some males from their population to experimentally manipulate the social status of the males that remained. Once a new social hierarchy was established, the authors again quantified the probability of sperm ejection for each male, and found results analogous to those of the first experiment; males that increased in social status after the manipulation experienced a decrease in the probability that their sperm was ejected. This latter result suggests that females reassess the relative genetic quality of males and select the sperm from the best available male.

The reproductive tract, ovarian fluids or even the eggs themselves may also play an important role in facilitating the use of sperm with good genes or compatible genes (reviewed by Birkhead et al. 1993; Eberhard 1996; Zeh & Zeh 1997; Birkhead 1998; Vacquier 1998; Birkhead & Pizzari 2002; also see Rifflé et al. 2004). For example, Tregenza & Wedell (2002) used families of field crickets to assign one of four sisters to each of the following treatments: (1) one mating to each of two of the female’s brothers (sibling-sibling, SS) (2) one mating to each of two males that were brothers but unrelated to the female (nonsibling-nonsibling, NN) (3) one mating to the female’s brother and then one mating to an unrelated male (SN), and (4) one mating to an unrelated male then one mating to the female’s brother (NS). Eggs were collected shortly after laying and reared until hatching when the hatching success was calculated. There was no significant difference in the number of eggs each of the four sisters laid, so hatching success provided a measure of offspring survivorship. The authors found that mean hatching success was about 34% for the SS treatment, 53% for the NN treatment, 58% for the SN treatment and 51% for the NS treatment. A randomized block analysis (with sisters representing the blocks) revealed that the hatching success in the SS treatment was significantly lower than that in the other three treatments, which were not significantly different from each other. Furthermore, the hatching success in the SN and NS treatments were greater than the mean of the hatching success for the SS and NN treatments combined (which represents the null hypothesis under the assumption that sperm fertilization was random). The authors ruled out several alternative hypotheses such as differential allocation to the eggs, differential sperm allocation by males, and differences in pre-copulatory behavior of females. Therefore, these results imply that compatible sperm — i.e. sperm from an unrelated male — are differentially selected for fertilization. Indeed, a follow-up study confirmed that unrelated males were in fact more successful at garnering paternity than were siblings of the females in the SN and NS trials (Bretman et al. 2004).

In another study, Calsbeek & Sinervo (2004) presented data that suggest physiological mechanisms exist in side-blotched lizards (Uta stansburiana) to differentiate between sperm carrying an X chromosome and sperm carrying a Y chromosome. Apparently, sons of large males have higher fitness than daughters of large males because of negative genetic effects of growth genes on the female reproductive functions. The opposite is true for the offspring of small males — daughters have higher fitness than sons. Thus, it might be adaptive if there was a physiological mechanism by which Y sperms were preferentially used from large males and X sperms were preferentially used from small males to fertilize the offspring (assuming that daughters from small males have higher fitness than daughters from large males). The authors test this hypothesis by examining the paternity and sex of progeny from polyandrous females collected from the wild. They found statistical support that within multiply mated clutches, the larger male sired a greater proportion of sons and the smaller male sired a greater proportion of daughters. Interestingly, across 2 years of data, it appears that small and large males sire similar numbers of offspring. The authors ruled out some male mechanisms of sperm selection based on a laboratory breeding experiment which showed that large and small males both appear to produce similar numbers of X and Y sperm. The possibility that the female reproductive physiology can differentiate between X and Y sperm is fascinating and suggests that mechanisms may exist to differentiate between other aspects of the genes carried by a sperm such as their genetic compatibility with the egg (also see Birkhead & Pizzari 2002).
Differential investment (postcopulatory, postfertilization)

After fertilization, parents may be able to promote the overall genetic quality of their brood through differential investment among the offspring. Specifically, females that invest proportionately more resources into offspring of high genetic quality than offspring of low genetic quality may ensure that their surviving young are of the highest possible genetic quality. This is the so-called ‘differential allocation hypothesis’ first proposed by Burley (1988) in the context of good genes (reviewed by Sheldon 2000). For example, Kotiaho et al. (2003) reported results from an experiment on the horned dung beetle (Onthophagus taurus) and showed that females differentially allocate parental resources (dung) to their offspring based on the offspring’s genetic quality. Male horned dung beetles exhibit dimorphic horn morphology in which some males have virtually no horns (minor males) while other males have large, well-developed horns (major males). Major males may have good genes because they typically are competitively superior and have higher fitness than minor males (Hunt & Simmons 1997, 2000), although heritability of life history appears to be low (Emlen 1994; but see Hunt & Simmons 2002; Kotiaho et al. 2003). The authors housed 106 males from the field, including both minor and major males, each with four laboratory-reared virgin females. After all of the females mated with their assigned male, they were placed in breeding chambers (without their mate to exclude paternal care effects). After 7 d, each female’s brood mass, which consists mostly of dung that the developing young use for nutrients, was weighed as a measure of maternal investment. They found that females mated to males with large horns had brood masses that were about 10% heavier than females mated to males with small horns. Because the authors showed that females invest more in offspring sired by males with good genes (males with larger horns), any observed effect on fitness is not only attributable to paternal good genes effects, but also maternal environmental effects. Indeed, the authors showed that the additive genetic variation attributable to paternal good genes would have been overestimated by 10%–20% had they not accounted for the maternal environmental effects. Another extreme example of differential investment occurs when females abort offspring with low genetic quality. This type of mechanism likely is to be more common in viviparous species — i.e. those where females nourish developing embryos via a placenta or other means (Zeh 1997). For example, in humans, spontaneous abortion has been linked to genetic defects in the embryo such as X-linked recessive disorders (Lanasa et al. 2001; also see Campana et al. 1986). In laboratory mice, Yamazaki et al. (1983) demonstrated that females are more likely to prevent embryo implantation (called the Bruce effect) when a new suitor is MHC-dissimilar to their previous mate. In humans, Ober et al. (1998) showed that couples that share antigens for one or more HLA loci have a greater chance of spontaneous abortion. In pseudoscorpions, Newcomer et al. (1999) found that females that mated with two different males gave birth to 32% more offspring than did females that mated with the same male twice. The difference in offspring production was because of an elevated rate of spontaneous abortion by females that mated with only a single male. Spontaneous abortion could be adaptive if these females were able to re-mate sooner and produce offspring of higher genetic quality than singly mated females that did not terminate pregnancy.

Selective second meiotic division after the sperm has entered the egg may represent another mechanism of differential investment. In a laboratory population of mice, Wedekind et al. (1996) have argued that eggs that are fertilized prior to the second meiotic division may selectively discard genetic material via the polar body to ensure the offspring contain compatible genes. They used in vitro fertilization to cross two inbred mouse strains congenic for their MHC. Specifically, they were able to cross eggs from MHC heterozygous females (containing the $b$ and $k$ alleles at the H-2 locus) with males homozygous for either the $b$ or $k$ allele. If eggs selectively discard genetic material, then they predicted that there should be a significant deviation from a 1:1 ratio of homozygous to heterozygous offspring. Although they found no deviation, they found a negative relationship between that proportion and the date the experiment was conducted. They suggest that the negative relationship is consistent with their proposed mechanism because they found no relationship between mortality rate and experimental date — i.e. no evidence of MHC genotype dependent mortality postfertilization. However, they did not actually know the genotype of the fertilized eggs that died, and it is unclear what advantage females gain by adjusting the proportion of MHC-heterozygous offspring based on mating date.

Mate choice and population genetic variation in fitness

We propose that there are two types of mating systems with respect to genetic quality that define a continuum. First, there are mating systems in which fitness variation from genetic quality predominately is the result of additive genetic variation and female mate choice (or male mate choice in sex-role reversed species or species in which mating costs limit polygyny) primarily is for good genes. Second, there are mating systems in which fitness variation from genetic quality predominately is resulting from nonadditive genetic variation and female mate choice primarily is for compatible genes. In a population that is dominated by good gene effects, females should have congruent mate preference for the male with the good genes. Such mate preference will lead to a large skew in male reproductive
success and strong directional selection on the good genes. Assuming the environment is stable (i.e. the directional selection is consistent through evolutionary time), additive genetic variation in fitness should decrease. This process of directional selection typifies polyandrous, nonresource based mating systems, such as leks (Höglund & Alatalo 1995), where at least some additive genetic variation may be maintained in the population through mutation (assuming that many genes underlie good gene quality; Pomiankowski & Möller 1995; Rowe & Houle 1996).

Conversely, compatible genes are dependent on the interaction of female and male genotypes and thus different pairings are required to increase offspring fitness. In a population dominated by compatible gene effects, females will be incongruent in their mate preference and no directional selection will occur (albeit there likely will be directional selection on the genes underlying the mechanism used to obtain compatible genes, but not on the compatible genes themselves). In compatible gene mating systems, female choice should maintain nonadditive genetic variation in fitness, while enabling mutation to increase additive genetic variation.

Recently, Colegrave et al. (2002) used a modeling approach to address the potential trade-off between mate choice for good genes and mate choice for compatible genes. Although they did not specifically model population genetic variation, their model included parameters representing the benefits from good genes (\( Q \)) and benefits from compatible genes (\( I \)). Basically, the model showed that females will mate for good genes when \( Q/I > \beta \), but will mate for compatible genes when \( Q/I < \beta \) (where \( \beta \) depends on the relative cost for females to acquire good genes vs. compatible genes). If we assume that mate choice for good genes reduces \( Q \) relative to \( I \) and mate choice for compatible genes has the opposite effect, then it is plausible that a mating system will oscillate across the equilibrium condition \( Q/I = \beta \); i.e. between a good genes mating system and a compatible genes mating system (Fig. 2a).

We envision two scenarios that might emerge from the mate choice trade-off between good genes and compatible genes (Fig. 2b). First, additive and nonadditive genetic variation may settle at an intermediate level with only small fluctuations in variation through evolutionary time. This may occur when females evolve mate choice for both good genes and compatible genes. Such simultaneous choice might be mediated through an evolutionarily stable strategy (ESS; Maynard Smith 1982) where all females simultaneously optimize their choice for good genes and compatible genes. Roberts & Gosling (2003) provide supporting evidence for such an ESS from a laboratory population of mice. They show that females consider indicators of both good genes (scent-marking rate) and compatible genes (cues regarding MHC dissimilarity mediated by urinary odor) when selecting mates; although compatible genes influenced female

\[
I = \frac{Q}{Q + \beta}
\]

Fig. 2 Consequences of variation in good genes and compatible genes on the evolution of female mate choice. (a) When fitness effects of compatible genes are greater than those of good genes, females should evolve mate choice predominately for compatible genes (upper left portion of graph). Conversely, when fitness effects of good genes are greater than those of compatible genes, females should evolve mate choice predominantly for good genes (lower right portion of graph). The line represents an equilibrium between good genes and compatible genes fitness effects. Figure adopted from Colegrave et al. (2002). (b) Schematic of potential cycling of female mate choice strategies for good genes and compatible genes. When additive genetic variation is high and nonadditive variation is low, natural selection leads to a female evolutionarily stable strategy of mate choice for good genes (ESS 1), which erodes additive genetic variation. When additive genetic variation is low and nonadditive variation is high, natural selection leads to a female evolutionarily stable strategy of mate choice for compatible genes (ESS 2), which leads to an increase in additive genetic variation. When both additive and nonadditive genetic variation are intermediate, natural selection may lead to a female evolutionarily stable strategy of mate choice that optimally trades off fitness benefits from good genes and compatible genes (ESS 3) or to two alternative strategies in an evolutionarily stable state (ESS) in which some females exclusively choose mates for good genes and other females exclusively choose mates for compatible genes. For both the ESS1 and ESS 3, their should be only small fluctuations in additive and nonadditive genetic variation.

choice only when there was relatively little variation in good genes quality among potential mates. Alternatively, simultaneous choice might be mediated through an evolutionarily stable state (ESS) where some females choose
only for good genes and other females choose only for compatible genes. The ESS would be stable when there is negative frequency dependent selection on the two female types.

Second, additive and nonadditive genetic variation may continually cycle between low and high levels (Fig. 2b). When the population is in a state of high additive genetic variation, but low nonadditive genetic variation, natural selection should favor the evolution of an ESS, in which all females choose good genes. High mating skew should deplete additive genetic variation, yet increase nonadditive genetic variation through, for example, an increase in genetic load. Subsequently, when the population is in a state of low additive genetic variation but high nonadditive genetic variation, natural selection should favor the evolution of an ESS in which all females choose for compatible genes. Low mating skew should deplete nonadditive genetic variation (e.g. reduce genetic load), yet increase additive genetic variation through mutational buildup and thereby return the population to good genes mating system.

Conclusion and future directions

There now is substantial evidence that mate choice for genetic benefits is an important component of many breeding systems. Indeed, many sophisticated biological mechanisms that have been described increase offspring genetic quality. The magnitude of the fitness effect of genetic quality, however, remains to be established. An initial meta-analysis suggests that good gene effects are variable among mating systems (effect size range for Pearson’s correlation $r = −0.30–0.79$) and on average explained only about 1.5% of the variation in survivorship (Moller & Alatalo 1999; also see Jennions et al. 2001). This initial estimate may be conservative because the studies did not examine variation in breeding success ($mx$), which might be a particularly important component of fitness in the underlying studies which focused on indicator traits — i.e. traits expressed in males that females use in mate choice decision-making (Kokko et al. 2002; Hunt et al. 2004). Our analysis of 14 studies that experimentally manipulated the degree of multiple mating by females and examined effects of overall genetic quality averaged 44% higher fitness, but ranged from no effect to 189% higher fitness; the latter result representing hatching success in a ground cricket (Fedorka & Mousseau 2002). If good gene effects are actually in the order of a few percent, then much of this 44% increase in fitness would be the result of compatible gene effects. The three studies that we discussed which were able to directly estimate the effects resulting from compatible genes found that these effects explained between 2% and 19% of the variation in fitness (Johnsen et al. 2000; Wedekind et al. 2001; Penn et al. 2002). The data from those three studies suggest that compatible gene effects are more important than good gene effects.

In nonresource-based mating systems, fitness effects as a result of compatible genes will likely show up only in the survivorship component ($lx$) of fitness because compatible genes are not themselves heritable and therefore not likely to increase a male’s mating success (the same is not true for resource-based mating systems; see Box 2). Furthermore, mate choice for compatible genes does not impose directional selection on the underlying genes and therefore such choice can maintain genetic diversity in fitness within a population. We have suggested that compatible gene mate choice and good gene mate choice may cycle in populations (over evolutionary timescales) along with the variance in the two types of genetic quality (see Fig. 2). However, only a few models have examined the interaction of good gene and compatible gene mate choice (e.g. Colegrave et al. 2002).

One difficulty with many of the studies of genetic benefits is confounding environmental effects. For example, several of the studies that compared singly mated females to multiply mated females were unable to control for potential differences in direct benefits such as the number of spermatophores which females receive. Direct benefits could increase the fitness of the offspring independent of its genetic quality and could result in an overestimation of genetic benefits. Conversely, when mating has direct costs to the female, such as sexually transmitted diseases, it is plausible that these costs could lead to reduced offspring fitness and an underestimate of genetic benefits. Females may also invest disproportionately in offspring based on their genetic quality by providing more resources to offspring of high genetic quality. For example, Kotiaho et al. (2003) showed in the horned dung beetle that the additive genetic variation attributable to paternal good genes would have been overestimated by 10%–20% had they not accounted for the maternal environmental effects.

Mating systems with external fertilization and no parental care may provide the ideal systems to assess the potential genetic benefits from good genes and compatible genes. Breeding experiments based on the North Carolina Design II approach can effectively partition fitness variation among good genes, compatible genes, and maternal environmental effects. For mating systems with internal fertilization, researchers must carefully control for maternal environmental effects (differential investment). Artificial fertilization techniques may provide one method of accomplishing this goal (e.g. Evans et al. 2003), but this approach will be effective only when there are postcopulatory mechanisms (sperm utilization) of acquiring genetic quality. Regardless of the experimental approach, it is imperative that measures of fitness incorporate multiple components including both survivorship and reproductive success (Hunt et al. 2004). For example, Dawson (1965)
the natively, in an environment where
cies of bacterium (allele A in environment 1, Fig. 3). Alter-
environment where there is intense exposure to this spe-
vironmental interaction effects (for exceptions see Welch
natural pathogen or predator.
a realistic environmental challenge such as exposure to a
or artificial environments should be designed to present
the organism’s natural environment as may be true
used to assess genetic quality does not accurately reflect
effect will be particularly important when the environment
likely will vary in quality across environments to some
extent, few studies calculate fitness of individuals in
multiple environments and therefore ignore genetic ×
environmental interaction effects (for exceptions see Welch
alleles found no significant genetic effects (Pai & Yan 2002).
A second difficulty with many of the studies of genetic
benefits is they ignore genetic × environmental interaction
effects on fitness (Fig. 3). The interaction effect occurs
when the quality of a gene or genotype varies across en-
environmental contexts. For example, the MHC e allele iden-
tified by Lohm et al. (2002) confers resistance to infection
by Aeromonas salmonicida and may be a good gene in any
environment where there is intense exposure to this spec-
cies of bacterium (allele A in environment 1, Fig. 3). Alter-
natively, in an environment where A. salmonicida is absent,
the e allele may have little fitness benefit (allele A in en-
vironment 2, Fig. 3). Although most genes or genotypes
likely will vary in quality across environments to some
extent, few studies calculate fitness of individuals in
multiple environments and therefore ignore genetic ×
environmental interaction effects (for exceptions see Welch
et al. 1998; Sakaluk et al. 2002; Welch 2003). An interaction
effect will be particularly important when the environment
used to assess genetic quality does not accurately reflect
the organism’s natural environment as may be true
for many laboratory environments. Ideally, experiments
should be conducted in an organism’s natural environment,
or artificial environments should be designed to present
a realistic environmental challenge such as exposure to a
natural pathogen or predator.

What about the kinds of genes that underlie genetic
quality? To date, the best examples of nonadditive genetic
effects have come from studies on the MHC (Bernatchez &
Landry 2003). However, there likely are other important
loci involved in compatible gene effects, which deserve
attention (reviewed by Zeh & Zeh 1996, 1997). For example,
the gene complex underlying the P450 enzyme system may
provide evidence of compatible gene effects (Gonzalez &
Nebert 1990; Grahn et al. 1998). P450 enzymes are involved
in the metabolism of organochlorine pollutants into water-
soluble products that can be excreted from the body.
Variants of the P450 enzymes differ in their efficiency
of metabolizing various organochlorine pollutants. Thus,
individuals that are heterozygous for P450 genes may be
better able to excrete a broader range of the pollutants than
individuals that are homozygous for P450 genes.

Loci underlying foraging polymorphisms also might
provide excellent candidates for compatible gene effects
through the action of coadapted gene complexes. Foraging
polymorphisms have been described in many populations
and typically involve two morphs that are morphologically
and behavioral specialized to feeding in one type of habitat
or another (Robinson & Wilson 1994; Smith & Skúlason
1996). For example, in pumpkinseed sunfish (Lepomis gibbosus)
some individuals develop into a pelagic morph, which in-
habits open waters, while other individuals develop into a
benthic morph, which inhabits shoreline waters (Robinson et al.
1993). Each morph appears to be ‘adapted’ to swimming and
feeding in their respective environments (Robinson et al.
1996). If the variation between morphs has a genetic com-
ponent, the complexes might display compatible gene effects.

Nearly all of the examples of good gene effects have
come from studies of condition-dependent traits (Møller &
Alatalo 1999). Perhaps surprisingly there are few examples
of individual genes that contribute to good gene effects.
Lohm et al. (2002) provided an example from Atlantic
salmon where the e allele at the MHC conferred upwards
of a 49% fitness advantage. It is possible that most good
genomes each only have a tiny effect on fitness and thus studying
a specific good gene would be difficult and largely
uninformative.

The importance of genetic quality to conservation
biology recently has been recognized (Grahn et al. 1998;
Wedekind 2002; Rowe & Hutchings 2003). However, few
programs have been developed that capitalize on natural
biological mechanisms, such as sexual selection, to ensure
the maintenance and propagation of genetic quality. For
example, many enhancement programs use fertilization
techniques designed to maximize genetic diversity as
measured by indices such as heterozygosity (reviewed by
Grahn et al. 1998; Keller & Waller 2002; Wedekind 2002).
These programs may be effective when populations are
inbred (low effective population size) and have high
 genetic load (e.g. Saccheri et al. 1998; Madsen et al. 1999).
They might also be effective when the goal is to maintain or maximize the ‘evolvability’ of the population (i.e. preserve future genetic quality). For example, if the environment that a species occupies is likely to change unpredictably then the goal of the program might be to maintain as much genetic diversity as possible in hopes of retaining genes that can persist in the new environment. However, if the goal is to enhance or rehabilitate current populations then simply maximizing genetic diversity fails to recognize the importance of good genes (which can depend on specific environmental context) and compatible genes outside of those associated with inbreeding depression. It is conceivable that in some situations — for example hatchery programs designed to enhance wild fish populations — approaches that incorporate natural breeding mechanisms will produce offspring of higher genetic quality than would approaches that simply maximize genome-wide diversity. Surprisingly, there has been limited attempt to incorporate sexual selection into enhancement breeding protocols and insufficient evaluation of its potential impact for species conservation (but see Roberts & Gosling 2004; Rowe & Hutchings 2003; Wedekind et al. 2004).

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References


The authors are interested in mating system evolution.