Evolution of haploid selection in predominantly diploid organisms

Sarah P. Otto^{a,1}, Michael F. Scott^b, and Simone Immeler^c

^aDepartment of Zoology & Biodiversity Research Centre, University of British Columbia, Vancouver, BC, Canada V6T 1Z4; ^bDepartment of Botany & Biodiversity Research Centre, University of British Columbia, Vancouver, BC, Canada V6T 1Z4; and ^cDepartment of Ecology and Genetics, Evolutionary Biology, Uppsala University, 752 36 Uppsala, Sweden

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Diploid organisms manipulate the extent to which their haploid gametes experience selection. Animals typically produce sperm with a diploid complement of most proteins and RNA, limiting selection on the haploid genotype. Plants, however, exhibit extensive expression in pollen, with actively transcribed haploid genomes. Here we analyze models that track the evolution of genes that modify the strength of haploid selection to predict when evolution intensifies and when it dampens the “selective arena” within which male gametes compete for fertilization. Considering deleterious mutations, evolution leads diploid mothers to strengthen selection among haploid sperm/pollen, because this reduces the mutation load inherited by their diploid offspring. If, however, selection acts in opposite directions in haploids and diploids (“ploidy antagonistic selection”), mothers evolve to reduce haploid selection to avoid selectively amplifying alleles harmful to their offspring. Consequently, with maternal control, selection in the haploid phase either is maximized or reaches an intermediate state, depending on the deleterious mutation rate relative to the extent of ploidy antagonistic selection. By contrast, evolution generally leads diploid fathers to mask mutations in their gametes to the maximum extent possible, whenever masking (e.g., through transcript sharing) increases the average fitness of a father’s gametes. We discuss the implications of this maternal–paternal conflict over the extent of haploid selection and describe empirical studies needed to refine our understanding of haploid selection among seemingly diploid organisms.

pollen competition | antagonistic selection | haploid selection | sperm competition | evolutionary theory

Although the sexual cycle necessitates the existence of both a haploid (postmeiotic) and a diploid (postsyngamy) phase, it does not necessitate selection in both phases. In predominantly diploid organisms, parents can modify the extent of selection experienced at the haploid phase via a number of mechanisms. The goal of this study is to investigate, using mathematical models, how evolution is predicted to shape the “selective arena” within which haploids compete for fertilization, given that diploid mothers and fathers may modify this arena.

That diploid organisms have evolved to modify the extent of haploid selection is evidenced by the variety of mechanisms that effectively dampen or intensify selection among gametes and gametophytes. In mammalian egg development, cell divisions arrest early in life, and eggs remain dormant until ovulation; because meiosis II is triggered only when the egg is fertilized by a sperm, the haploid phase of selection is largely avoided by mammalian egg cells. Sperm in many animals also appear to circumvent selection in the haploid phase, but by an entirely different route. Diploid spermatogonia actively divide, producing spermatocytes that undergo meiosis throughout the lifespan of reproductively mature males. During spermatogenesis, however, protein and RNA products are shared among cells across cytoplasmic bridges (“syncytium”) into the late postmeiotic stages, so that cells carry a nearly diploid complement of genes (1, 2). Furthermore, although haploid sperm actively swim to reach an egg, their genomes are compactly packaged, restricting haploid expression to a few genes

(2). Among plants, angiosperms have evolved relatively little scope for selection among female gametophytes, as few haploid eggs are produced within an ovule. By contrast, gymnosperms have many more haploid eggs per ovule, increasing the opportunity for selection among female gametophytes (3).

Among male gametophytes, haploid pollen are thought to experience extensive selection, as pollen tubes compete for access to ovules (4–6). In turn, the strength of this selection can be modulated by the maternal plant by altering style length (7–9), delaying stigma receptivity (10, 11) and/or delaying pollen tube growth in the pistil (12). Paternal plants could also potentially alter the extent to which pollen are supplied with diploid transcripts, thereby modifying the extent of selection on the haploid genome. Although allele-specific expression data from single pollen grains are lacking, some pollen components are known to be effectively diploid (provisioned by the pollen parent). Particularly noteworthy are flavanoids involved in pollen tube growth (13) and a related enzyme, UDP-flavonoid-glucosyl-transferase (14), as well as RNA polymerases required for transcription (15). Furthermore, the difference between sporophytic and gametophytic self-incompatibility systems stems from pollen being phenotypically diploid vs. haploid, respectively (16) (see also ref. 17 for evidence of diploid sporophytic effects on pollen–style incompatibilities between species of tomato).

That selection acts during the haploid phase of predominantly diploid organisms has been confirmed experimentally in a number of studies (18). One of the earliest experiments found that placing pollen farther from the ovaries on the stigma of the

Significance

Predominantly diploid organisms shape the extent to which their haploid gametes and gametophytes experience selection. Although animals are thought to experience only mild selection in the haploid stage, plants often experience strong haploid selection. When should parents limit exposure of gametes to haploid selection and when should they strengthen this selection? We develop mathematical models that consider the “selective arena” within which male gametes or gametophytes (sperm or pollen) compete for fertilization, examining how the intensity of this selective arena evolves when controlled by the mother or the father. These models predict substantial variation in the outcome, depending on whether mothers or fathers exert more control over the selective arena, with mothers often favoring stronger haploid selection than fathers.

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¹To whom correspondence should be addressed. Email: otto@zoology.ubc.ca.

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$\hat{q}_{AS}$, respectively (we use $\hat{q}$ to refer to either one, depending on the form of selection being considered). The model recursions are given in Eq. S2.

We then consider the fate of a new allele m that modifies the extent of haploid selection. Allele m spreads if its long-term relative fitness is greater than that of the resident allele, M , that is, if the leading eigenvalue, λ , of the local stability matrix is greater than one. We calculate λ assuming weak selection and loose linkage (r large relative to selection), keeping only leading-order terms [see *Mathematica* package deposited at Dryad (doi:10.5061/dryad.4gn47)].

In all of the models of maternal control considered, the leading eigenvalue is

$$\lambda \approx 1 + \delta q \hat{q}(1 - \hat{q}) \delta W. \quad [1]$$

The term $\delta q \hat{q}(1 - \hat{q})$ represents the impact that mothers have on the allele frequency of pollen used to fertilize ovules, comparing Mm mothers to resident MM mothers, where δq is the effective strength of gametic selection against a alleles, which is multiplied by the probability that the a allele is found in the pollen pool ($\hat{q}$) and replaced by the A allele ($1 - \hat{q}$). The term δW is the impact of this gametic selection on offspring fitness, calculated as the average fitness effect of replacing an a allele with an A in daughters and in sons, including the impact on the pollen success of sons. With weak selection, subsequent effects on future generations, as well as terms involving the recombination rate, enter only as lower-order terms. We next evaluate Eq. 1 under different forms of selection.

Case 1: Mutation–Selection Balance. Unconditionally deleterious alleles are expected to favor expansion of selection in the haploid phase, as mothers with stronger selective sieves will fertilize ovules with fitter pollen (6, 18). Indeed, assuming very weak mutation rates, we find that all of the terms in Eq. 1 are positive when Mm mothers select more strongly among their pollen ($c_{Mm} > c_{MM}$). The effect of the modifier on selection against a in the pollen pool is $\delta q = (c_{Mm} - c_{MM})t$, the equilibrium equals

$$\hat{q}_{MS} \approx \frac{\mu}{(1/2)(h^{\circ} s^{\circ} + h^{\delta} s^{\delta} + c_{MM} t)}, \quad [2]$$

and the effect of replacing an a pollen with an A pollen on the mean offspring fitness is

$$\delta W = \frac{1}{2} h^{\circ} s^{\circ} + \frac{1}{2} h^{\delta} s^{\delta} + \frac{1}{4} c_{MM} t. \quad [3]$$

The last term in Eq. 3 represents the effect on sons' pollen success and is multiplied by 1/4 because only half the time is the offspring a son and only half of the time would he transmit the allele inherited from his father's pollen. Plugging these terms into Eq. 1, using $\hat{q}_{MS}(1 - \hat{q}_{MS}) \approx \hat{q}_{MS}$, yields equation 10 in ref. 36.

Case 2: Antagonistic Selection. A polymorphic equilibrium can also be maintained by opposing selection pressures in different life phases (ploidally antagonistic selection) or in different sexes (sexually antagonistic selection) (39). In a population fixed for the M allele, the a allele equilibrates at a frequency

$$\hat{q}_{AS} \approx \frac{-\eta^{\circ} \sigma^{\circ} - \eta^{\delta} \sigma^{\delta} - c_{MM} \tau}{-\sigma^{\circ} (2\eta^{\circ} - 1) - \sigma^{\delta} (2\eta^{\delta} - 1)}, \quad [4]$$

as long as

$$-(1 - \eta^{\circ}) \sigma^{\circ} - (1 - \eta^{\delta}) \sigma^{\delta} < c_{MM} \tau < -\eta^{\circ} \sigma^{\circ} - \eta^{\delta} \sigma^{\delta}. \quad [5]$$

At an equilibrium with antagonistic selection, modifiers that cause mothers to reduce expression in the haploid phase

($c_{Mm} < c_{MM}$) are always favored. Again, $\delta q = (c_{Mm} - c_{MM})\tau$, but now the impact of stronger gametic selection on the offspring is negative and can be simplified to $\delta W = -c_{MM}\tau/4$ (Eq. S16). Intuitively, mothers are expected to reduce the strength of haploid selection if the main effect of haploid selection is to promote alleles that harm their diploid offspring.

Net Selection on Modifier. We now consider how the above forces would scale up from one selected locus to the entire genome. Assuming that all selected loci act independently on the modifier (i.e., loci are loosely linked and nonepistatic), we can approximate the net strength of selection acting on a modifier as the sum of indirect selective forces arising from each locus ($S_{\text{net}} = \lambda_{\text{net}} - 1 = \sum (\lambda_i - 1)$ where the sum is over all loci, including L_{MS} loci subject to purifying selection and L_{AS} loci subject to antagonistic selection). For simplicity, we assume constant selection coefficients and mutation rates across loci subject to a particular form of selection, but more precise results could be obtained by summing over the distributions of effects, if known.

The net selection on a modifier is then

$$S_{\text{net}} = (c_{Mm} - c_{MM}) \left\{ t \Psi \mu L_{MS} - \frac{c_{MM} \tau^2 \hat{q}_{AS} (1 - \hat{q}_{AS})}{4} L_{AS} \right\} \quad [6]$$

with

$$\Psi = \frac{h^{\circ} s^{\circ} + h^{\delta} s^{\delta} + \frac{1}{2} c_{MM} t}{h^{\circ} s^{\circ} + h^{\delta} s^{\delta} + c_{MM} t}.$$

Note that genes selected only in the pollen phase favor strengthening haploid selection (contributing solely to the L_{MS} term with $s^{\circ} = s^{\delta} = 0$), because of the increased pollen fitness experienced by sons.

For sufficiently high deleterious mutation rates across the genome, the term in braces in Eq. 6 is positive for $c_{MM} \approx 1$, so selection will maintain organisms at this maximum level of haploid selection. Defining $\Upsilon = \mu L_{MS}/L_{AS}$ as the genome-wide deleterious mutation rate per antagonistic locus, maximal haploid selection is maintained whenever $\Upsilon > \Upsilon^*$, where

$$\Upsilon^* = \left(\frac{\tau^2 \hat{q}_{AS} (1 - \hat{q}_{AS})}{4 t \Psi} \right)_{c_{MM}=1}. \quad [7]$$

Conversely, for sufficiently low deleterious mutation rates, one might expect antagonistic selection to drive c_{ij} to zero, representing the complete suppression of haploid selection. This does not occur, however, when selection is ploidally antagonistic. As haploid selection weakens, the allele favored in diploids rises in frequency and eventually fixes. Specifically, c_{ij} evolves toward a minimum $c_{\min}$, where $c_{\min} \tau$ reaches the bottom of the interval in Eq. 5, after which polymorphism is lost. At this point, antagonistic selection is resolved in favor of the diploid-beneficial allele and no longer exerts selection on the modifier ($\lambda = 1$ when $\hat{q}_{AS} = 1$). That said, as the extent of haploid selection (c_{MM}) declines, different sets of loci might exhibit variation, with polymorphism switching to loci experiencing stronger haploid selection. Alternatively, with sexually antagonistic selection, polymorphism can be maintained even with the complete loss of haploid selection (as long as the interval in Eq. 5 spans zero). Under these circumstances, evolution can lead to the complete cessation of haploid selection.

The evolutionarily stable strategy (ESS) for the level of haploid selection, c^* occurs when $S_{\text{net}} = 0$. Because $\hat{q}_{AS}$ is a function of c_{MM} , Eq. 6 is a quartic function of c_{MM} whose solutions represent potential evolutionarily stable strategies. These solutions are plotted in Fig. 1 for various values of the deleterious mutation rate per antagonistic locus (Υ) and the strength of antagonistic

selection in haploids (τ). According to Eq. 6, if we multiply all of the selection coefficients ($s^{\delta}, s^{\sigma}, t, \sigma^{\delta}, \sigma^{\sigma}, \tau$) by a constant factor, the ESS value c^* would remain the same as long as Υ was also multiplied by the same factor. Thus, for a given Υ , mutation–selection balance becomes the more dominant force with weaker selection, favoring the evolution of more extensive gametic selection, whereas antagonistic selection dominates with stronger selection.

Sex Linkage. So far, we have considered only autosomal loci. Sex chromosomes are thought to accumulate sexually antagonistic loci (40) and have been found empirically to exhibit disproportionately high levels of sexually antagonistic genetic variation (41, 42). In *SI Text* we extend the above treatment to sex linkage. The evolution of the haploid selective arena is then driven, in the first place, to equalize the birth sex ratio, *BSR*. For example, if Y-bearing gametes have low fitness, a modifier that increases the strength of haploid selection will increase the proportion of female offspring and will thus spread when the resident sex ratio is male biased ($BSR > 1/2$). Thus, heightened or weakened gametic selection may be favored, in a manner that brings the birth sex ratio closer to 50:50.

With a nearly even sex ratio ($BSR \approx 1/2$), mothers would again evolve to alter gametic selection according to Eq. 1 (see *SI Text* for δq and δW). Although a sex-linked antagonistic locus tends to select for reduced gametic selection, as was found for an autosomal locus, increased gametic selection can be favored when selection is sexually antagonistic and the haploid-beneficial allele is also female

beneficial (*SI Text*). In such cases, we would expect maximal gametic selection, regardless of the deleterious mutation rate.

Paternal Control of Haploid Selection

We now consider a model where fathers can modify the phenotype of their gametes and hence control the degree of haploid selection. In animals, such control can occur during gametogenesis, depending on the extent of sharing of RNAs, proteins, and cellular signals across the syncytium connecting haploid sperm. In plants, paternal control can be exerted by supplying the pollen grain with more diploid gene products from the microsporophyte. We continue to assume that selection occurs after the gametes are released from the father.

Specifically, we allow the provisioning of diploid gene products to be adjusted, depending on the father's genotype (ij) at a modifier locus (**M**), with gametes exhibiting a proportion p_{ij} of gene products reflecting their own haploid genome and $1 - p_{ij}$ reflecting the diploid genome of the father. For homozygous AA (or aa) fathers, we assume that such provisioning has no effect on the gamete, as all transcripts involve the A (or a) allele. Fathers that are Aa , however, produce gametes whose fitnesses are functions of the provisioning: $g_A(p_{ij})$ or $g_a(p_{ij})$, depending on whether the gamete carries allele A or a , respectively. These functions can take any form, although we assume that allele a is selected against in haploids ($g_A(p_{ij}) \geq g_a(p_{ij})$) and that complete provisioning causes all gametes of Aa fathers to have equal fitness ($g_A(0) = g_a(0)$).

We then track the spread of a new modifier allele m introduced into a population at either (i) mutation–selection balance or (ii) an equilibrium under antagonistic selection (see *SI Text* for recursions and equilibrium frequencies). In either case, the new modifier allele spreads at rate

$$\lambda = 1 + (\bar{g}_{Mm} - \bar{g}_{MM}) \hat{q}(1 - \hat{q}), \quad [8]$$

where $\bar{g}_{ij} = (g_A(p_{ij}) + g_a(p_{ij}))/2$ is the average fitness of gametes produced by an Aa father with modifier genotype ij . Thus, assuming weak selection, fathers evolve solely to increase the fertilization success of their gametes, regardless of the subsequent impacts on offspring fitness. Again, the net effect of selection summed over all loci that are expressed in the haploid stage would be $S_{\text{net}} = \lambda_{\text{net}} - 1 = \sum (\lambda_i - 1)$.

As a result, modifiers that reduce the degree of haploid expression ($p_{Mm} < p_{MM}$) spread whenever mixing of gene products increases the average fitness of gametes, e.g., by protecting them from poorly functioning alleles. Essentially, when $\bar{g}_{Mm} > \bar{g}_{MM}$, diploid fathers that better mask their own gametes have higher siring success. This condition requires that the fitter allele is partially dominant to the less fit allele with respect to gamete fitness when both gene products are present within the gamete. Although this need not always be true, empirical evidence suggests that such dominance is common for diploids (43), and we assume this pattern carries over to gene mixing in haploids, for loci subject to both mutation–selection balance and antagonistic selection (see *Mathematica* package for explorations of other cases).

Coevolution of Maternal and Paternal Control

Whereas mothers typically evolve to ensure some degree of selection among pollen (Fig. 1), fathers evolve to minimize this selection. Selection on the fathers to mask their gametes is, however, stronger than that acting on mothers, the former being proportional to the strength of selection (Eq. 8) and the latter to the square of selection (assuming no sex linkage or an unbiased sex ratio). This asymmetry occurs because the evolution of maternal control requires that mothers change the efficacy of selection among pollen and that this change has subsequent fitness consequences to their diploid offspring (both δq and δW in Eq. 1 being proportional to selection). As a result, our analysis predicts an overwhelming paternal drive to provision gametes with

Fig. 1. Evolution of the selective arena experienced by haploids. (A) When the degree of gametic selection is maternally controlled, evolution drives the level of selection in the haploid phase toward the ESS, c^* , given by the solid curves (dashed curves are repelling). As the deleterious mutation rate per antagonistic locus (Υ) rises along the x axis, selection favors higher levels of gametic selection among mothers. On the other hand, as ploidally antagonistic selection becomes stronger in the haploid phase (larger τ), mothers evolve to reduce the degree of gametic selection. (B) The resulting effects on the fitness load experienced by diploid offspring at the ESS. Diploid mean fitness is reduced both by recurrent mutations ("mutation load" in dark gray) and by ploidally antagonistic selection (light gray) as mutation rate Υ increases. Because gametic selection eliminates deleterious mutations, the mutation load (dark gray) is much lower than it would be in the absence of gametic selection (dashed line). Nevertheless, the total diploid load (ploidally antagonistic and mutation load) is often higher at the ESS, because the degree of gametic selection is also shaped by fitness variation in haploids. Other parameters: $t = 0.1$, $s^k = 0.2$, $h^k = 0.1$, $\sigma^k = -0.1$, $\eta^k = 0.9$, for both sexes.