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# Conflict between heterozygote advantage and hybrid incompatibility in haplodiploids (and sex chromosomes)

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## Running title:

Heterosis *versus* hybrid breakdown

## 1 Abstract

2 In many diploid species the sex chromosomes play a special role in mediating reproductive  
3 isolation. In haplodiploids, [where](#) females are diploid and males haploid, the whole genome  
4 behaves [similarly](#) to the X/Z chromosomes of diploids. Therefore, haplodiploid systems can  
5 serve as a model for the role of sex chromosomes in speciation and hybridization. A pre-  
6 viously described population of Finnish *Formica* wood ants displays genome-wide signs of  
7 ploidy and sexually antagonistic selection resulting from hybridization. Here, hybrid fe-  
8 males have increased survivorship but hybrid males are inviable. [To understand how the](#)  
9 [unusual hybrid population may be maintained, we developed a mathematical model with hy-](#)  
10 [brid incompatibility, female heterozygote advantage, recombination, and assortative mating.](#)  
11 [The rugged fitness landscape resulting from the co-occurrence of heterozygote advantage and](#)  
12 [hybrid incompatibility results in a sexual conflict in haplodiploids, which is caused by the](#)  
13 [ploidy difference. Thus, whereas heterozygote advantage always promotes long-term poly-](#)  
14 [morphism in diploids, we find various outcomes in haplodiploids in which the population](#)  
15 [stabilizes either in favor of males, females, or via maximizing the number of introgressed](#)  
16 [individuals. We discuss these outcomes with respect to the potential long-term fate of the](#)  
17 [Finnish wood ant population, and provide approximations for the extension of the model to](#)  
18 [multiple incompatibilities. Moreover, we highlight the general implications of our results for](#)  
19 [speciation and hybridization in haplodiploids versus diploids, and how the described fitness](#)  
20 [relationships could contribute to the outstanding role of sex chromosomes as hotspots of](#)  
21 [sexual antagonism and genes involved in speciation.](#)

## 22 Introduction

23 Haplodiploids are an emerging system for speciation genetics (Koevoets and Beukeboom,  
24 2009; Kulmuni and Pamilo, 2014; Lohse and Ross, 2015; Knecht et al., 2017). Although  $\approx 20\%$   
25 of animal species are haplodiploid (comprising most *Hymenoptera*, some arthropods, thrips

26 and *Hemipterans*, and several clades of beetles and mites; Crozier and Pamilo, 1996; Evans  
27 et al., 2004; de la Filia et al., 2015), little evolutionary theory has been developed specifically  
28 for speciation in haplodiploids (Koevoets and Beukeboom, 2009). Under haplodiploidy with  
29 arrhenotoky (hereafter simply haplodiploidy; Suomalainen et al., 1987), males develop from  
30 the mother’s unfertilized eggs and are haploid, whereas eggs fertilized by fathers result in  
31 diploid females. Since this mode of inheritance is, from a theoretical viewpoint, similar to  
32 that of the X/Z chromosome, most work on speciation of haplodiploids [draws on](#) the rich  
33 literature of sex chromosome evolution (Jablonka and Lamb, 1991; Presgraves, 2008; Johnson  
34 and Lachance, 2012; Lohse and Ross, 2015). An important similarity between haplodiploids  
35 and X/Z chromosomes is that recessive mutations in the haploid sex are exposed to selec-  
36 tion, but they are masked in diploids. This is expected to lead to faster evolution in the sex  
37 chromosomes (Charlesworth et al., 1987) that may partly underlie the large-X effect (Pres-  
38 graves, 2008). The large-X effect refers to the observation that the sex chromosomes seem  
39 to play a special role in speciation by acting as the strongest barrier for gene flow between  
40 hybridizing lineages across different species (Höllinger and Hermisson, 2017). Similarly, hap-  
41 lodiploid species have been suggested to acquire reproductive isolation earlier and speciate  
42 faster than diploid species (Lohse and Ross, 2015; Lima, 2014). Although the factors influ-  
43 encing haplodiploid and X/Z chromosome evolution are not expected to be exactly the same  
44 (e.g. movement of sexually antagonistic genes to the sex chromosomes, dosage compensation  
45 between the sex chromosomes and autosomes, and turnover of sex chromosomes cannot occur  
46 in haplodiploids; Abbott et al., 2017), by studying haplodiploid models we can both improve  
47 our understanding of how speciation happens in the large subgroup of the animal kingdom  
48 that is haplodiploid, and gain new insights into the role of X/Z chromosomes in speciation  
49 for diploid species.

50       Recent studies have shown that hybridization and resulting gene flow between diverging  
51 populations may be important players in the speciation process since signs of hybridiza-  
52 tion and introgression are being observed ubiquitously in natural populations (Mallet, 2005;  
53 Dieckmann and Doebeli, 1999; Schluter, 2009; Schluter and Conte, 2009; Seehausen et al.,  
54 2014). When a hybrid population is formed, various selective forces may act simultaneously  
55 to either increase or decrease hybrid fitness, which dictate the fate of the population. One  
56 commonly documented finding is hybrid incompatibility (Presgraves, 2008; Fraïsse et al.,

2014; Chen et al., 2016), where combinations of alleles at different loci interact to confer poor fitness when **combined** in a hybrid individual (Bateson, 1909; Dobzhansky, 1936; Muller, 1942; Orr, 1995). In a hybrid population, the existence of hybrid incompatibility reduces the mean population fitness. This deficit can be resolved either through reinforcement (evolution of increased premating isolation to avoid production of unfit hybrids; Servedio and Noor, 2003) **or** by purging (demographic swamping leading to extinction of one of the local populations/species **or reinstatement of the ancestral allele combinations**; Wolf et al., 2001). On the other hand, hybridization can transfer adaptive genetic variation from one lineage to another (Heliconius Genome Consortium, 2012; Song et al., 2011; Whitney et al., 2010) and may result in overall heterosis (also known as hybrid vigor): a higher fitness of hybrids as compared to their parents (Schwarz et al., 2005; Chen, 2013; Bernardes et al., 2017). Heterosis can stabilize polymorphisms by conferring a fitness advantage to hybrids and thereby favor the maintenance of hybridization either through the improved exploitation of novel ecological niches or the masking of recessive deleterious mutations. Therefore hybrid incompatibility acts to avert ongoing hybridization while heterosis favors the maintenance of hybrids.

One example of the simultaneous action of hybridization-averse and hybridization-favoring forces is found in a hybrid population of *Formica polyctena* and *F. aquilonia* wood ants in Finland (Kulmuni et al., 2010; Kulmuni and Pamilo, 2014; Beresford et al., 2017). Here, it has been reported that hybrid (haploid) males do not survive to adulthood, whereas (diploid) females have higher survivorship when they carry many introgressed alleles as heterozygotes (i.e., heterozygous for alleles originating from one of the parental species in a genomic background otherwise from the other parental species). Thus, a combination of hybrid incompatibility and heterosis seems to dictate the dynamics of the population **in a ploidy-specific manner**: hybrid haploid males suffer a fitness cost while diploid hybrid females can have a selective advantage over parental ones. **Here, the differences in ploidy create an apparent sexual conflict between haploid males and diploid females (sensu Arnqvist and Rowe, 2005), because their fitness landscapes (i.e., the complex relationship between genotypes and fitness created via hybrid incompatibility and heterozygote advantage) are different. This conflict is absent if the same rugged fitness landscape occurs in diploid autosomes.**

When both hybridization-averse and hybridization-favoring forces are acting, the long-term resolution of a hybridizing population is difficult to foresee: will hybridization eventually

88 result in either complete speciation or extinction of one of the populations involved? Alter-  
89 natively, can it represent an equilibrium maintained stably on an evolutionary time scale?  
90 Furthermore, will the probability of these outcomes depend on ploidy? In other words, is  
91 one of these outcomes more probable when interacting genes are found on a “haplodiploid”  
92 X/Z chromosome than when they exist on a “diploid” autosome?

93 We here develop and analyze a population-genetic model of an isolated hybrid popula-  
94 tion in which both hybridization-averse and hybridization-favoring forces are acting, and we  
95 study the evolutionary outcomes in both haplodiploid and (fully) diploid genetic systems.  
96 The rich dynamics of the haplodiploid model can result in four possible evolutionary stable  
97 states depending on the strength of heterozygote advantage *versus* hybrid incompatibility,  
98 the strength of recombination, and the degree of assortative mating. This includes a case of  
99 symmetric coexistence (where all diversity is maintained) in which both alleles can be main-  
100 tained [despite the segregating hybrid incompatibility](#), and in which long-term hybridization  
101 is favored. We find that the dynamics differ between haplodiploid and diploid systems and  
102 that, unlike in previous models of sexual conflict in haplodiploid populations (Kraaijeveld,  
103 2009; Albert and Otto, 2005), the conflict is not necessarily resolved in favor of the females.  
104 Indeed, a compromise may be reached at which the average fitness of females is decreased to  
105 rescue part of the fitness of males. Moreover, [evaluation of the model using](#) the data from  
106 the natural hybrid population suggests that, under the assumption of an equilibrium, the  
107 Finnish ant population may represent an example of compromise between male costs and  
108 female benefits through asymmetric coexistence. We discuss our findings with respect to the  
109 long-term effects of hybridization, the potential for speciation in haplodiploid versus diploid  
110 species, and with respect to their relevance for X- or Z-linked alleles in diploid individuals.

## 111 **Materials and Methods**

### 112 **The model**

113 We model an isolated haplodiploid or diploid hybrid population with individuals from  
114 two founder populations  $P_+$  and  $P_-$ . Note that throughout the manuscript, we preferen-  
115 tially refer to (sub-)populations rather than species; in those instances in which we use the  
116 term ‘species’ it is in order to emphasize that the two populations have diverged sufficiently

117 for (potentially strong) hybrid incompatibility to exist. We assume discrete generations and  
118 consider two loci, **A** and **B**. Each locus has two alleles, the ‘+’ allele ( $A_+$  or  $B_+$ ) inherited  
119 from population  $P_+$  and the ‘-’ allele ( $A_-$  or  $B_-$ ) inherited from population  $P_-$ . We refer  
120 to ‘hybrids’ as individuals that carry two alleles from each of the two parental populations  
121 and cannot be assigned to either parental background. We refer to ‘introgressed’ individuals  
122 as those genotypes for which three of the four alleles are from the same parental population;  
123 these genotypes are identical to those produced by hybridization followed by backcrossing.  
124 We ignore new or recurrent mutation and genetic drift . Thus, male and female popula-  
125 tions are of effectively infinite size; selection modifies the relative abundance of the different  
126 haplotypes/genotypes but not the number of individuals (soft selection). The life cycle is as  
127 follows (Fig. 1; see also Table 1 for a list of model parameters); consistent with the recursions  
128 defined below, we begin the life cycle at the adult stage:

- 129 1. mating, either randomly or via genotype matching with assortment strength  $\alpha$  as de-  
130 tailed below;
- 131 2. recombination (in diploid individuals) at rate  $\rho$ ;
- 132 3. viability (or survival) selection, where heterosis is modeled as a heterozygote advan-  
133 tage,  $\sigma$ , and hybrid incompatibility is modeled as a fully recessive negative epistasis,  $\gamma_1$   
134 and  $\gamma_2$  (further details are provided below and in Figure 2).

### 135 Viability selection

136 The fitness landscape described here (Fig. 2) is inspired by the situation observed in  
137 Finnish *Formica* ants (Kulmuni et al., 2010; Kulmuni and Pamilo, 2014; Beresford et al.,  
138 2017). There, the authors discovered heterosis in the diploid females but recessive incompat-  
139 ibilities expressed in the haploid males. This creates a situation in which the same alleles  
140 that are favored in heterozygous females are selected against in hybrid haploid males, and  
141 homozygous hybrid females. In the haplodiploid genetic system, males possess only one copy  
142 of each locus so they cannot be heterozygous and, therefore, cannot experience heterozygote  
143 advantage (Fig. 2(b)). Therefore, the fitness landscape with heterozygote advantage and re-

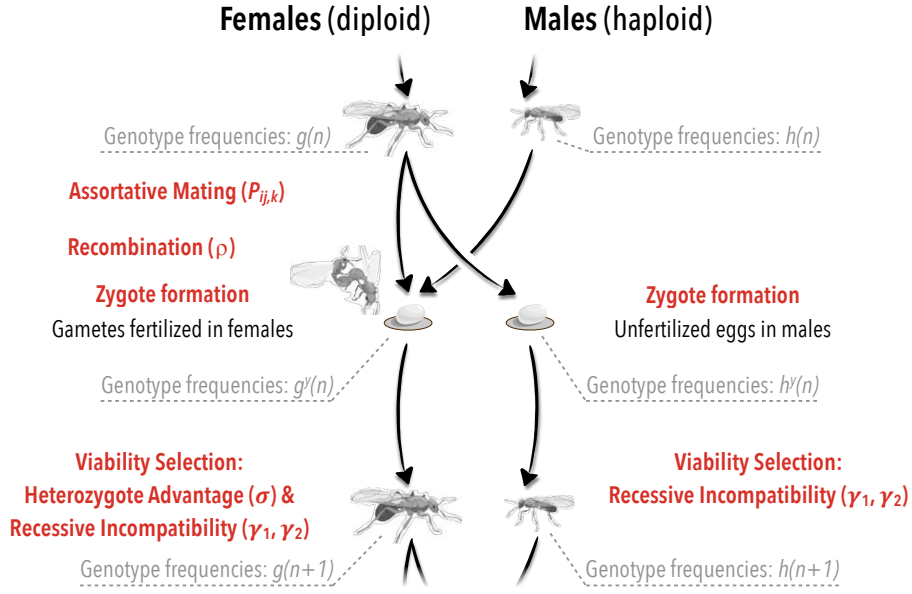


Figure 1: Illustration of the haplodiploid life cycle and its parametrization

Table 1: List of model parameters.

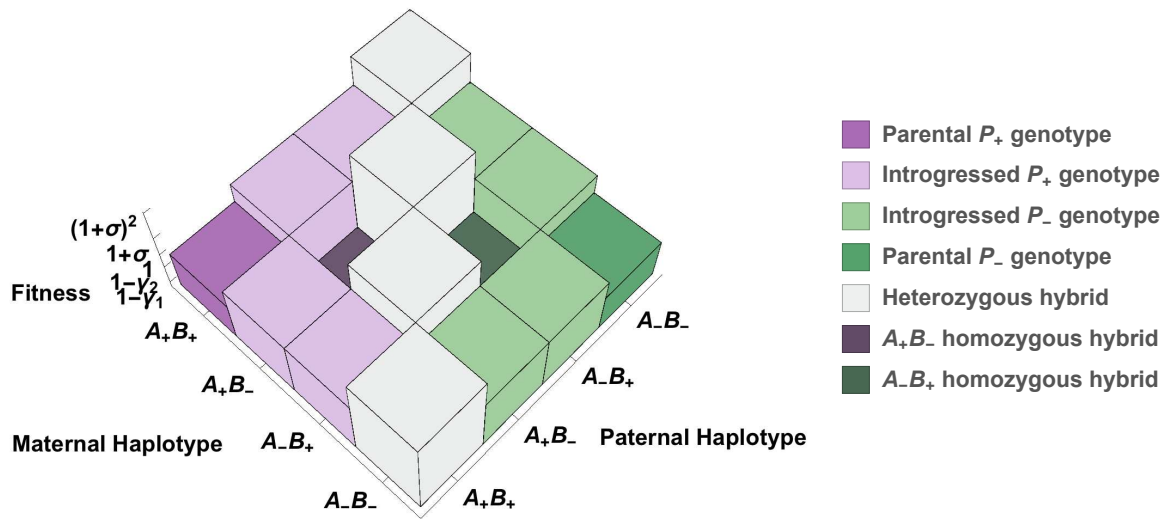
Symbol	Parameter	Limits
$\sigma, \omega$	<b>Strength of heterozygote advantage</b> , resulting in fitness $\omega = (1 + \sigma)$ or $\omega^2 = (1 + \sigma)^2$ of introgressed or double heterozygous diploid hybrids, respectively.	$\omega - 1 = \sigma > 0$
$\gamma_1, \gamma_2$	<b>Strength of fully recessive negative epistasis</b> , resulting in fitness $(1 - \gamma_1)$ for $A_+B_-$ homozygous diploid hybrids and $A_+B_-$ hybrid haploid males, and $(1 - \gamma_2)$ for $A_-B_+$ homozygous diploid hybrids and $A_-B_+$ hybrid haploid males.	$0 \leq \gamma_1, \gamma_2 \leq 1$
$\rho$	<b>Recombination rate</b> between locus <b>A</b> and <b>B</b> .	$0 \leq \rho \leq 0.5$
$\alpha$	<b>Strength of assortment</b> via genotype matching, where $\alpha = 0$ represents random mating, $\alpha > 0$ represents assortative mating among conspecifics, and $\alpha < 0$ represents assortative mating between heterospecifics.	$-1 \leq \alpha \leq 1$

144 cessive hybrid incompatibility expresses itself as an apparent sexual conflict when sexes differ  
145 in ploidy, as in haplodiploids or for X/Z chromosomes.

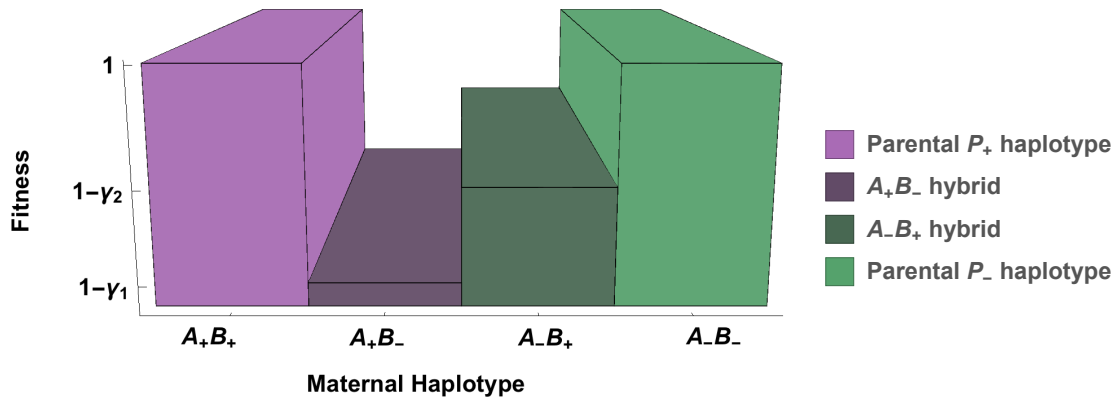
146 In our model, selection for heterozygous individuals is multiplicative with respect to  
147 the number of heterozygous loci: introgressed individuals with one heterozygous locus have  
148 fitness  $1 + \sigma$ , whereas diploid hybrid individuals are heterozygous at both loci and have  
149 survivorship  $(1 + \sigma)^2$  (Fig. 2(a)). Finally, the recessive epistatic incompatibility parameter  
150  $\gamma_1$  acts on individuals homozygous or haploid for the  $A_+B_-$  haplotype, and  $\gamma_2$  acts on  
151 individuals homozygous or haploid for the  $A_-B_+$  haplotype (without loss of generality, we  
152 assume  $\gamma_1 \geq \gamma_2$ ). Thus, epistasis in this model can be asymmetric, reflecting, for example,  
153 two Dobzhansky-Muller incompatibilities of different strength that have accumulated at a  
154 negligible recombination distance between the same chromosome pairs. Note that when  
155  $\gamma_1 = \gamma_2 = 1$ , haploid hybrid males and homozygous hybrid zygotes are produced but do not  
156 survive to adulthood and that the classical case of a single Dobzhansky-Muller incompatibility  
157 is recovered when  $\gamma_2 = 0$ .

## 158 Assortative mating

159 Prezygotic isolation via assortative mating is an important mechanism that could me-  
160 diate the detrimental effects to the population caused by the co-occurrence of heterozygote  
161 advantage and epistasis modeled here. In the Finnish wood ant population that inspired our  
162 model (Kulmuni and Pamilo, 2014), almost all egg-laying queens collected had been inse-  
163 mated by males of the same genetic group, indicating that prezygotic isolation barriers are  
164 likely operating to result in assortative mating. In this case, assortative mating could arise  
165 via choosiness of mating partners, via genotype-dependent development times, or via other  
166 post-mating prezygotic mechanisms. We implemented assortment via genotype matching  
167 (reviewed in Kopp et al. (2017)), where the proportion of matings depends on the genetic  
168 distance between two mating partners (and their respective frequencies in the population).  
169 We define the genetic distance between the genotypes of a mating pair as the average Ham-  
170 ming distance, i.e. the number of differences between 2 aligned sequences of characters,  
171 between all possible pairs of haplotypes with one partner from each sex. We use quadratic  
172 assortment (e.g., De Cara et al., 2008), which results in assortative mating without costs of  
173 choosiness but with sexual selection. The mating probability of a pair of male and female



(a) Fitness Landscape for Diploid Individuals



(b) Fitness Landscape for Haploid Males

Figure 2: Three-dimensional fitness landscapes for the (a) diploid and (b) haploid genotypes. Panel a) corresponds to females in the haplodiploid model and all individuals in the diploid model. Individuals heterozygous at both loci (heterozygous hybrids) reside on a high fitness ridge (in white), whereas individuals homozygous at both loci (homozygous hybrids) suffer from reduced fitness due to negative epistasis. Panel b) shows the fitness landscape for haploid individuals (i.e. males) in the haplodiploid model. This landscape is identical to a transect from Panel a) for genotypes homozygous at both loci.

174 genotypes,  $P_{ij,k}$  depends on the genetic distance between the two mates, the choosiness of  
 175 the female, and the abundance of the different haplotype and genotypes as detailed below.

## 176 Mathematical modeling and analysis

177 In a given generation  $n$ , the frequencies of the male and female adults are given by  $h_k(n)$   
 178 and  $g_{ij}(n)$ , respectively, with  $i$  and  $k$  indicating the haplotype received maternally and  $j$  the  
 179 one of paternal origin. Without loss of generality, we assign index  $i = 1$  to haplotype  $A_+B_+$ ,  
 180 index  $i = 2$  to haplotype  $A_+B_-$ ,  $i = 3$  to haplotype  $A_-B_+$  and,  $i = 4$  to  $A_-B_-$ . Below,  
 181 we describe the modeled life cycle (illustrated in Fig. S1) which determines how frequencies  
 182 change from one generation to the next.

- 183 1. As detailed in figure 1 the first step of the life cycle is the mating between two individ-  
 184 uals. The mating probability between an  $ij$  female and a  $k$  male is given by:

$$P_{ij,k}(n) = \frac{(1 - \alpha^{\frac{d_{i,k} + d_{j,k}}{2}})g_{ij}(n)h_k(n)}{\sum_i \sum_j \sum_k (1 - \alpha^{\frac{d_{i,k} + d_{j,k}}{2}})g_{ij}(n)h_k(n)} \quad (1)$$

185 with  $d_{i,k}$  the Hamming distance between two haplotypes. Note that for  $\alpha = 0$ , this  
 186 simplifies to random mating and thus becomes equivalent to the dynamics described in  
 187 Supplementary material (S7).

- 188 2. The next step is the formation of the zygote. Recombination happens only in females.  
 189 We denote the frequency of newly born females as  $g_{ik}^y(n+1)$ .

$$\begin{cases} g_{ik}^y(n+1) = \frac{1}{2} \sum_{j=1}^4 (P_{ij,k}(n) + P_{ji,k}(n)) - \frac{\rho}{2} \Delta_k(n) & \text{if } i \in \{1, 4\} \\ g_{ik}^y(n+1) = \frac{1}{2} \sum_{j=1}^4 (P_{ij,k}(n) + P_{ji,k}(n)) + \frac{\rho}{2} \Delta_k(n) & \text{if } i \in \{2, 3\} \end{cases} \quad (2)$$

190 with  $\Delta_k(n) = P_{14,k}(n) + P_{41,k}(n) - P_{23,k}(n) - P_{32,k}(n)$ .

191 Males are composed from unfertilized females' gametes, which have undergone recom-  
 192 bination. The frequencies of newborn males are given by  $h_k^y(n)$ :

$$\begin{aligned} h_k^y(n_y) &= \frac{1}{2} \sum_{j=1}^4 (g_{kj}(n) + g_{jk}(n)) - \frac{\rho}{2} \tau(n) & \text{if } k \in \{1, 4\} \\ h_k^y(n_y) &= \frac{1}{2} \sum_{j=1}^4 (g_{kj}(n) + g_{jk}(n)) + \frac{\rho}{2} \tau(n) & \text{if } k \in \{2, 3\} \end{aligned} \quad (3)$$

193 with  $\tau(n) = g_{14}(n) + g_{41}(n) - g_{23}(n) - g_{32}(n)$ .

194 3. Individuals of both sexes are under viability selection. The frequencies of male and  
 195 female adults of the next generations are given by

$$h_k(n+1) = \frac{w_k^m h_k^y(n)}{\sum_{k=1}^4 w_k^m h_k^y(n)} \quad (4)$$

196 with  $w_i^m$  the fitness of haplotype  $i$  in males and

$$g_{ij}(n+1) = \frac{w_{ij}^f g_{ij}^y(n)}{\sum_{i=1}^4 \sum_{j=1}^4 w_{ij}^f g_{ij}^y(n)} \quad (5)$$

197 where  $w_{ij}^f$  denotes the fitness of the  $ij$  genotype. Note that there are no parental effects:  
 198  $w_{ij}^f = w_{ji}^f$ ; we maintain the distinction only for modeling convenience.

199 The complete recursion for females is obtained by substituting  $g_{ij}^y(n)$  by its expression  
 200 given in (2) in (5) and  $P_{ij,k}(n)$  by (1). The complete recursion for males is given by substi-  
 201 tuting  $h_i^y$  by its expression given in (3) in (4). For  $\alpha = 0$ , the detailed recursion is given in  
 202 Supplement (S7). Note that we use a different point of the life cycle (the gamete frequencies)  
 203 as this is more easily tractable due to the reduced number of variables.

204 The diploid model can be obtained by applying equations (2) and (5) to males as well,  
 205 with the corresponding relevant substitutions.

206 For the analysis, we focus on the equilibrium of the system defined by:

$$\forall \{i, j, k\} \in \{1, 2, 3, 4\}^3, g_{ij}(n+1) = g_{ij}(n) \text{ and } h_k(n+1) = h_k(n). \quad (6)$$

207 These equilibria can either be obtained by solving the system of equations presented  
 208 above numerically, or by focusing on some of the known and potentially biological relevant  
 209 equilibria, like fixation of a given haplotype. The stability of the equilibria is then obtained  
 210 by computing the Eigenvalues of the Jacobian matrix at the focal equilibrium. If the absolute  
 211 value of all Eigenvalues are below 1, the equilibrium is locally stable. For a more detailed  
 212 explanation, see Otto and Day (2007, Chap. 7). We use this method to derive necessary and  
 213 sufficient conditions for the existence and stability of the different evolutionary outcomes.

## 214 Simulations

215 Derivations, simulations, and data fitting were performed in *Mathematica* (v 10.4.1.0;  
216 Wolfram Research, Inc., 2016). [To enable complete reproducibility of the results, we provide](#)  
217 [an Online Supplement that documents all steps of the analysis as well as the code used for](#)  
218 [simulations and figures](#). Equilibrium genotype frequencies were obtained numerically when  
219 possible, or based on simulations until the differences between genotype frequencies of two  
220 consecutive generations were smaller than  $10^{-8}$  (or stopped after  $10^5$  generations without  
221 convergence).

## 222 Fitting the model to a natural ant population

223 To compare our model with data from the natural, hybridizing Finnish ant population, we  
224 estimated the different genotype frequencies of parental *F. polycтена*-like and *F. aquilonia*-  
225 like individuals from the data. Assuming that the natural population is at equilibrium, we  
226 fit the data (Table S2) to the model by calculating the sum of squared differences between  
227 the observed data and predicted equilibrium frequencies. [Complete details of data estimation](#)  
228 [and model fitting are given in the Supplementary Methods and Supplementary Results](#).

## 229 Results

230 In this section, we describe the dynamics of a hybrid population under our model, with  
231 a particular focus on quantifying the differences between the haplodiploid and the diploid  
232 model. Two parameter [domains](#) are of particular interest:

- 233 1. The case of free recombination and strong epistasis (i.e., large  $\gamma_1, \gamma_2$ ) most likely re-  
234 sembles that of the natural ant hybrid population that inspired the model. Here, the  
235 [hybrid incompatibility loci are located on different chromosomes, and epistasis is](#) strong  
236 enough to erase a large fraction of male zygotes during development.
- 237 2. The case of low recombination is most relevant for the effects of a fitness landscape  
238 with epistasis (i.e., a “rugged” landscape) in X or Z chromosomes. Here, epistasis could  
239 arise, for example, through interactions between regulatory regions and their respective  
240 genes.

## 241 **Evolutionary scenarios**

242 Below, we describe four different types of evolutionary stable states (i.e., equilibrium sce-  
243 narios) of the model, which represent long-term solutions to the [opposing selective pressures](#)  
244 [of](#) the hybridization-averse force of recessive negative epistasis and the hybridization-favoring  
245 heterozygote advantage. The population will attain these equilibria if no further pre- or  
246 post-zygotic [barriers](#) or other functional mutations appear. Next, we provide various neces-  
247 sary and sufficient analytical conditions for these scenarios. Figure 3 illustrates the potential  
248 equilibria by means of phase diagrams.

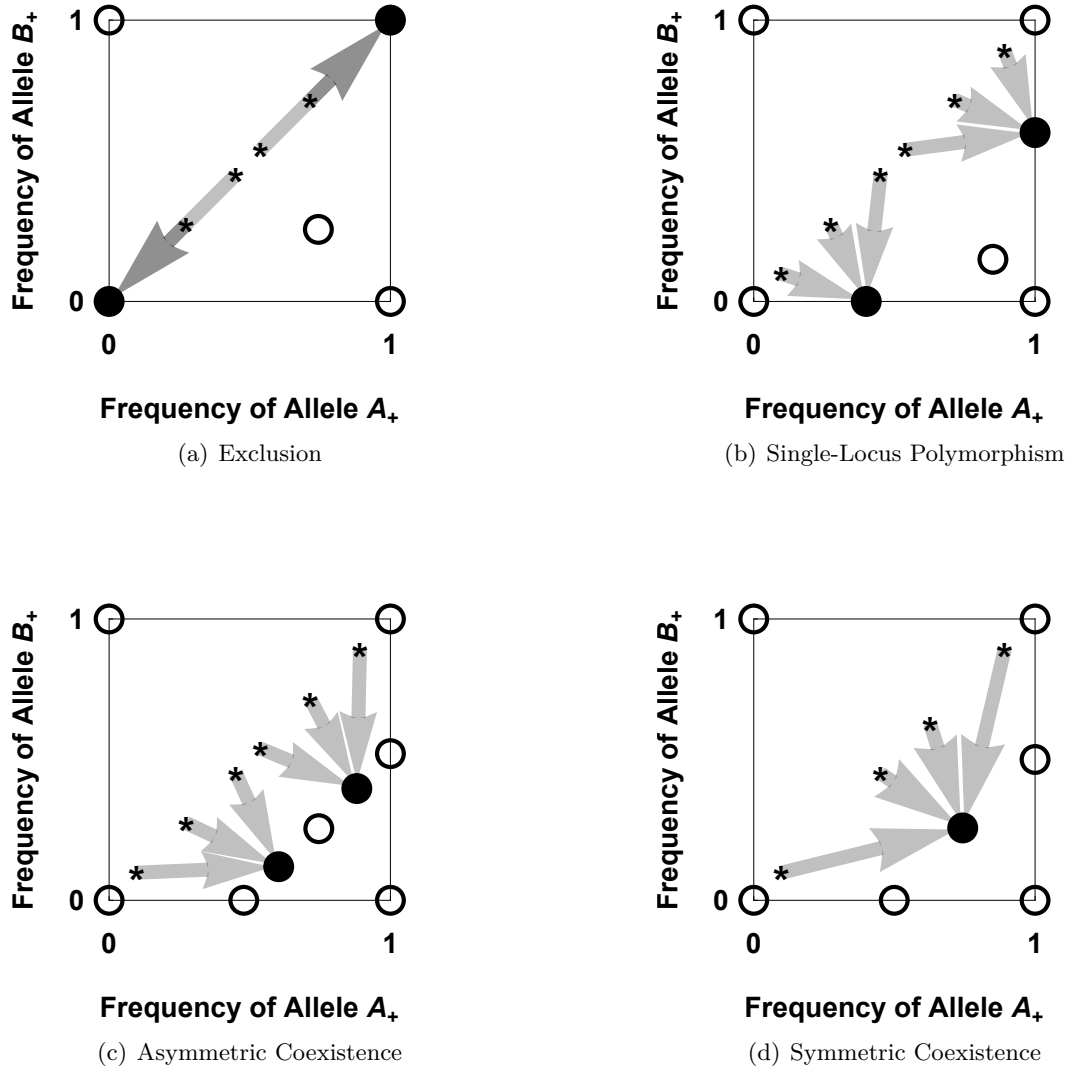


Figure 3: Phase-plane diagrams illustrating possible evolutionary scenarios in the haplodiploid model. The filled black dots show locally stable equilibria and the empty dots show unstable ones. The gray arrows show the basin of attraction starting from secondary contact scenarios (black asterisks on the line at  $p_{B_+} = p_{A_+}$ ). Panel (a) illustrates exclusion: There are 2 external locally stable equilibria, each corresponding to the fixation of a parental population haplotype. (Here,  $\sigma = 0.02$ ,  $\gamma_1 = 0.9$ ,  $\gamma_2 = 0.11$ ,  $\rho = 0.5$ , and  $\alpha = 0$ .) Panel (b) represents a single-locus polymorphism. Only one locus is polymorphic, leading to the maintenance of the weaker of the two incompatibilities (the  $A_-B_+$  interaction). (Here,  $\sigma = 0.009$ ,  $\gamma_1 = 0.11$ ,  $\gamma_2 = 0.002$ ,  $\rho = 0.5$ , and  $\alpha = 0$ .) Panel (c) corresponds to asymmetric coexistence. Two internal equilibria are locally stable, with one allele close to fixation. This scenario minimize the expression of the strongest interaction  $A_+B_-$ . (Here,  $\sigma = 0.03$ ,  $\gamma_1 = 0.11$ ,  $\gamma_2 = 0.0013$ ,  $\rho = 0.5$ , and  $\alpha = 0$ .) Panel (d) shows symmetric coexistence. Frequencies of alleles  $A_-$  and  $B_-$  are symmetric around 0.5, with  $p_{B_+} = 1 - p_{A_+}$ . This scenario maximizes the formation of female heterozygous hybrids. (Here,  $\sigma = 0.09$ ,  $\gamma_1 = 0.3$ ,  $\gamma_2 = 10^{-4}$ ,  $\rho = 0.5$ , and  $\alpha = 0$ .)

## 249 Exclusion

250 The *exclusion* scenario corresponds to the hybrid population becoming identical to one  
251 of the two parental populations, either  $P_+$  or  $P_-$ , and the other parental population being  
252 therefore excluded. It occurs when both alleles from one of the founder subpopulations are  
253 purged, leading to a monomorphic stable state of the population (Fig. 3(a)). In this case, the  
254 initial frequency of  $A_+B_+$  versus  $A_-B_-$  individuals mainly determines the outcome (i.e., the  
255 population is swamped by the majority subpopulation). As a rule of thumb, this outcome  
256 is observed when recombination is frequent and when the hybridization-averse force of neg-  
257 ative epistasis is strong as compared with the hybridization-favoring heterozygote advantage  
258 ( $\gamma_1, \gamma_2 \gg \sigma$ ).

259 With regard to the [apparent sexual/ploidy](#) conflict in the haplodiploid model, exclusion  
260 can be interpreted as a victory of the [haploid males](#) because all polymorphism is lost and  
261 no low-fitness hybrid males are produced. Conversely, since all polymorphism is lost, [diploid](#)  
262 [females](#) “lose” in this case and neither high-fitness introgressed (i.e., those individuals carrying  
263 only one ‘foreign’ allele) nor highest-fitness heterozygous hybrid females are produced. [As](#)  
264 [discussed below, exclusion is never a possible outcome in the diploid model, in which there](#)  
265 [are no differences in ploidy.](#)

## 266 Single-locus polymorphism

267 A *single-locus polymorphism* occurs when one allele is purged from the population but the  
268 other locus remains polymorphic at equilibrium (Fig. 3(b)). Because this is possible for either  
269 of the two loci, two such equilibria exist simultaneously, which are reached depending on the  
270 initial haplotype frequencies. This outcome is observed when recombination is frequent, epis-  
271 tasis is asymmetric ( $\gamma_1 \neq \gamma_2$ ), and heterozygote advantage is small ( $\gamma_1 \gg \sigma$ ). Like asymmetric  
272 coexistence below, this case represents a compromise between the hybridization-averse and  
273 hybridization-favoring forces of negative epistasis and heterozygote advantage, and is reached  
274 by maximizing the number of introgressed individuals of one founder subpopulation.

275 In the haplodiploid model, this [scenario](#) can be seen as a [haploid-dominated](#) compromise.  
276 Since one locus is fixed, one epistatic interaction has disappeared and few low-fitness hybrid  
277 males are produced. In females, high-fitness introgressed female frequencies are maximized

278 but, since one locus is fixed, the highest-fitness heterozygous hybrid female **genotypes are no**  
279 **longer available.**

280 **The single-locus polymorphism is never stable in the diploid model, i.e., when the ploidy**  
281 **difference is removed from the model.** In a diploid population that resides transiently at  
282 single-locus polymorphism, a rare mutant at the second locus will always begin as heterozy-  
283 gote and therefore reap the advantage of being a heterozygote hybrid long before it suffers  
284 the epistatic cost of being a homozygote hybrid.

### 285 **Asymmetric coexistence**

286 *“Asymmetric” coexistence* occurs when all four haplotypes remain in the population  
287 and the frequency of introgressed individuals of one founder subpopulation is maximized  
288 (Fig. 3(c)). Because this can be achieved in two ways, two possible equilibria reside off the  
289 diagonal line  $p_B = 1 - p_A$  (where  $p_A$  and  $p_B$  denote the allele frequencies of the ‘-’ allele at  
290 the respective locus), and the initial contribution of different haplotypes determines which  
291 equilibrium will be attained. Like the single-locus polymorphism, this equilibrium represents  
292 a compromise between hybridization-averse and hybridization-favoring forces that is reached  
293 by maximizing the number of introgressed individuals. Our simulations demonstrate that  
294 this scenario is rarely present in haplodiploids, and it generally involves asymmetric epistasis  
295 and intermediate-strength heterozygote advantage.

296 In the haplodiploid model, asymmetric coexistence can be seen as a compromise **that**  
297 **is dominated by the diploids.** Unlike in the single-locus polymorphism scenario, both loci  
298 are polymorphic and some double-heterozygous hybrid females are produced. But, unlike  
299 the symmetric coexistence scenario described below, females are not victorious over males  
300 because such high-fitness hybrid females are produced only at low frequencies.

### 301 **Symmetric coexistence**

302 *Symmetric coexistence* occurs when a locally stable equilibrium exists on the diagonal  
303  $p_B = 1 - p_A$ , such that the number of heterozygous hybrids is maximized (Fig. 3(d)). Our  
304 notion of “symmetric” refers to the total fraction of alleles from the  $P_+$  and  $P_-$  founder pop-  
305 ulations segregating at equilibrium, which is equal in this case. Here, prolonged hybridization  
306 is a mutual best-case scenario for both populations. This equilibrium is most likely when

307 recombination is weak or when the hybridization-favoring force of heterozygote advantage  
308 is strong as compared with the hybridization-averse negative epistasis ( $\sigma \geq \gamma_1, \gamma_2$ ). In the  
309 haplodiploid model, symmetric coexistence represents a victory for the **diploids**, because they  
310 maximize their own fitness without regard to the production of unfit hybrid **haploids**.

311

312 The four evolutionary stable states described above usually result in either a single, glob-  
313 ally stable **equilibrium** (in the case of symmetric coexistence) or a bistable system, in which  
314 two locally stable equilibria exist. In rare cases and close to bifurcation points, we observe  
315 cases of tristability, which are further described in Figure S2.

## 316 **Stability analysis of the model**

317 Although the model dynamics are too complex to derive general analytical solutions, we  
318 were able to perform stability analyses for specific cases, which yield information about the  
319 general behavior of the model. In the following, our use of ‘>’ and ‘<’ does not necessarily  
320 imply strict inequalities; we merely did not explicitly study the limiting cases. For ease of  
321 notation, we refer to heterozygote advantage in terms of  $\omega$  below; recall that  $\omega = 1 + \sigma$ .

## 322 **Conditions for symmetric coexistence when epistasis is lethal**

323 We begin by describing the equilibrium structure when epistasis is lethal, i.e.  $\gamma_1 = \gamma_2 = 1$ ;  
324 this case may resemble that in the natural ant population, in which most hybrid males do  
325 not survive to reproduce. For the haplodiploid model, we obtain a full analytic solution  
326 of the identity, existence and stability of equilibria. Here, only two outcomes are possible:  
327 symmetric coexistence and exclusion (Fig. 4(a)). As necessary and sufficient criterion for  
328 exclusion, we obtain

$$\rho > \frac{\omega^2 - 1}{\omega^2}. \quad (7)$$

329 Thus, exclusion is only possible if heterozygote advantage is not too strong, and if recombina-  
330 tion is breaking up gametes sufficiently often to significantly harm the **haploid** males.

331 For the diploid model, we can show that no boundary equilibrium is ever stable; asym-  
332 metric and symmetric coexistence are the only two possible outcomes. Although it was not  
333 possible to perform a stability analysis on the internal equilibria, we were able to propose a

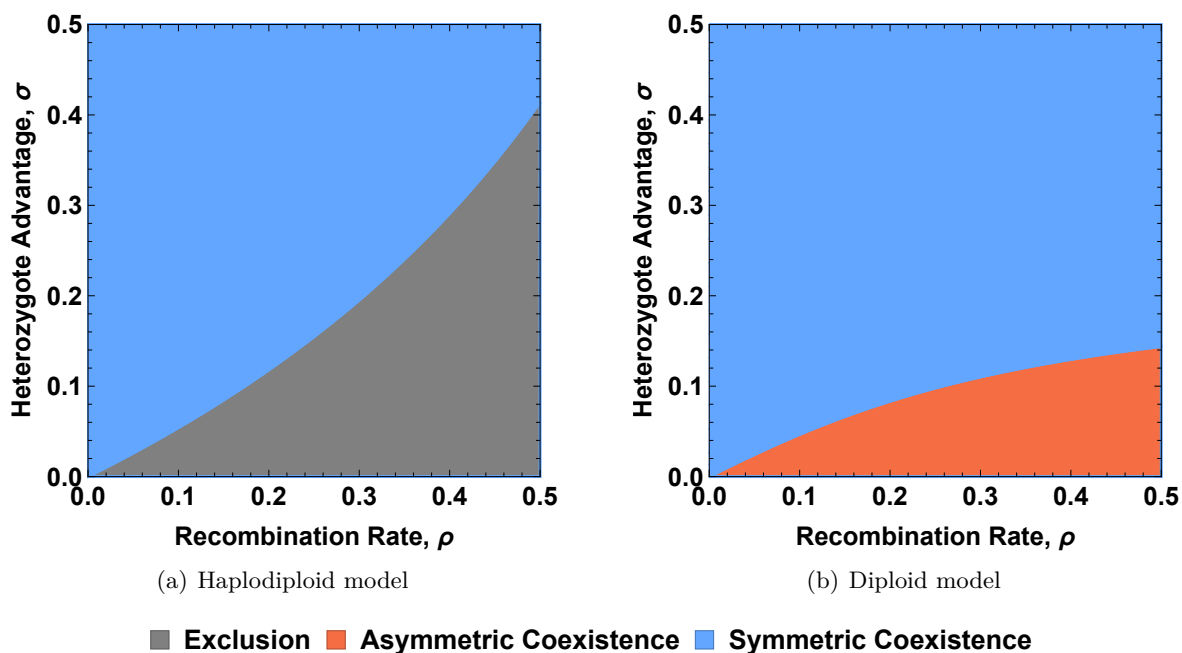


Figure 4: Symmetric coexistence can be locally stable if the heterozygote advantage,  $\sigma$ , is strong enough to compensate for recombination breaking up the parental haplotypes. Here we assume that epistasis is symmetric and lethal ( $\gamma_1 = \gamma_2 = 1$ ). Panel (a) is an illustration of the condition for haplodiploids given in equation (7) and panel (b) of equation (8) for diploids.

334 condition for asymmetric coexistence, which has been evaluated numerically:

$$\rho > \frac{(\omega^2 - 1)(2\omega^4 - 6\omega^3 + \omega^2 + 6\omega - 2)}{\omega^2(2\omega^2 - 4\omega + 1)(2\omega^2 - 3)} + 2\sqrt{\frac{(\omega - 1)^5(\omega + 1)^2(\omega^3 - \omega^2 - 3\omega + 1)}{\omega^4(2\omega^2 - 4\omega + 1)^2(2\omega^2 - 3)^2}}. \quad (8)$$

335 Although this expression is not very telling, its illustration in Figure 4(b) demonstrates how  
 336 different this criterion is from that of the haplodiploid model. *In the diploid model, males  
 337 and females evolve on the same fitness landscape. Therefore, both males and females benefit  
 338 from heterozygote advantage. This reduces the influence of the hybrid incompatibility on  
 339 the optimal location of the population in genotype space, which thereby makes asymmetric  
 340 coexistence less likely.* Indeed, a heterozygote advantage of  $\omega - 1 = \sigma > \approx 0.14$  is sufficient to  
 341 ensure symmetric coexistence for all recombination rates, whereas in the haplodiploid model,  
 342  $\sigma > \sqrt{2} - 1 \approx 0.41$  is necessary for symmetric coexistence independent of the recombination  
 343 rate.

344 **General stability conditions in the haplodiploid model**

345 Using the results derived for the case of lethal epistasis, and by means of critical exam-  
 346 ination of the existence and stability conditions that we were able to compute analytically,  
 347 we arrived at several illustrative conjectures delimiting the evolutionary outcomes in the  
 348 haplodiploid model when epistasis is not lethal ( $\gamma_1, \gamma_2 \neq 1$ ). These were all confirmed by ex-  
 349 tensive numerical simulations (see Mathematica Online Supplement). Note that assortative  
 350 mating was not considered here.

351 Firstly, strong heterozygote advantage can always override the effect of epistasis. Specif-  
 352 ically, if

$$\omega > \sqrt{2}, \tag{9}$$

353 the evolutionary outcome is always symmetric coexistence, regardless of the values of  $\gamma_1$   
 354 and  $\gamma_2$ . This is true not only for a single pair of interacting loci, but also for an arbitrary  
 355 number of independent incompatibility pairs, because the [detrimental effects caused by each](#)  
 356 [incompatibility pair are](#) eventually resolved independently (see also the section on multiple  
 357 loci below). [This result can be deduced from equation \(7\) for  \$\rho = 0.5\$  and therefore corre-](#)  
 358 [sponds to an upper bound: if heterozygote advantage is very strong, recombination no longer](#)  
 359 [affects the outcome.](#)

360 Secondly, recombination is a key player to determine whether compromise or exclusion  
 361 can occur. In particular,

$$\rho < \frac{\omega^2 - 1}{\omega^2} \tag{10}$$

362 is a sufficient condition for the observation of symmetric coexistence, independent of the  
 363 strength and symmetry of epistasis. This makes intuitive sense, because [hybrid incompati-](#)  
 364 [bility is masked until](#) gametes are broken up by recombination.

365 Thirdly, for symmetric epistasis ( $\gamma_1 = \gamma_2$ ), there are three possible equilibrium patterns:  
 366 symmetric coexistence, exclusion, and tristability of the two former types of equilibria. A  
 367 necessary and sufficient condition for observation of anything but symmetric coexistence is

$$\omega < \sqrt{2} \quad \text{and} \quad \rho > \frac{\omega^2 - 1}{\omega^2} \quad \text{and} \quad \gamma_1 = \gamma_2 > \frac{2(\omega - 1)}{\omega}. \tag{11}$$

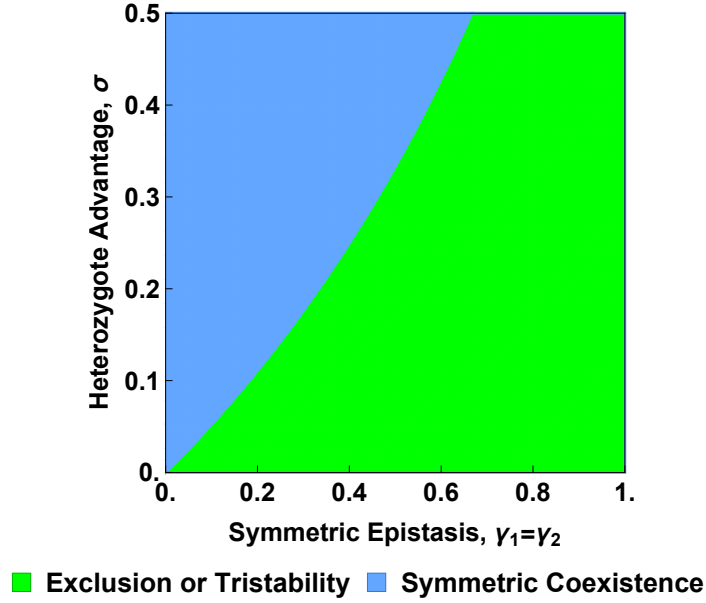


Figure 5: In haplodiploids, symmetric coexistence requires that heterozygote advantage,  $\sigma$ , is strong enough to both compensate for recombination such that the condition in equation 10 is fulfilled (see also Fig. 4(a)), and to overcome the deleterious effects of epistasis, as expressed by condition 11 for symmetric epistasis.

368 If the recombination rate  $\rho$  and the epistatic effects  $\gamma_1, \gamma_2$  are very close to this limit,  
 369 there is tristability; if they are far away, there is exclusion (cf. Fig. 5).

370 Finally, for asymmetric epistasis ( $\gamma_1 \neq \gamma_2$ ), the dynamics display the whole range of  
 371 possible evolutionary outcomes: symmetric coexistence, asymmetric coexistence, single-locus  
 372 polymorphism, exclusion, as well as tristability of exclusion *and* symmetric coexistence, and  
 373 single-locus polymorphism *and* symmetric coexistence. The local stability criterion for the  
 374 stability of the monomorphic equilibria (i.e., the criterion for exclusion, or tristability of  
 375 exclusion and symmetric coexistence) is

$$\omega < \sqrt{2} \quad \text{and} \quad \rho > \frac{\omega^2 - 1}{\omega^2} \quad \text{and} \quad \gamma_2 > \frac{2(\omega - 1)}{\omega}. \quad (12)$$

376 Thus, if epistasis is strong as compared with heterozygote advantage, no degree of asym-  
 377 metry is sufficient to promote a compromise between males and females (i.e., single-locus  
 378 polymorphism or asymmetric coexistence). In fact, we observe the following necessary (but  
 379 not sufficient) condition for a single-locus polymorphism:

$$\omega < \sqrt{2} \quad \text{and} \quad \rho > \frac{\omega^2 - 1}{\omega^2} \quad \text{and} \quad \gamma_1 > \frac{2(\omega - 1)}{\omega} \quad \text{and} \quad \gamma_2 < \frac{2(\omega - 1)}{\omega}. \quad (13)$$

380 Hence, only a tight balance between the selective pressures of epistasis and heterozygote  
381 advantage in combination with asymmetry of the hybrid incompatibility promotes a long-  
382 term equilibrium with compromise.

### 383 **An extension to multiple loci**

#### 384 **Incompatibilities involving four loci**

385 Above, we have demonstrated that recombination is an essential player when determining  
386 whether exclusion or coexistence is the long-term outcome in the haplodiploid dynamics. In  
387 order to see how our results change in the (biologically relevant) case of multiple hybrid  
388 incompatibilities, we implemented the dynamics for four loci. Given the complexity of the  
389 system, we considered only lethal incompatibilities, i.e.  $\gamma_i = 1$  for all interactions  $i$ . With  
390 this extension, we consider two scenarios. Firstly, in the “*pairwise*” case we consider pairs  
391 of independent hybrid incompatibilities, where we assume that the incompatible loci are  
392 located next to each other (locus **A** interacts with locus **B** at recombination distance  $\rho_{12}$ ,  
393 and locus **C** with locus **D** at recombination distance  $\rho_{34}$ ), which leaves four viable male  
394 haplotypes ( $A_+B_+C_+D_+$ ,  $A_+B_+C_-D_-$ ,  $A_-B_-C_+D_+$  and  $A_-B_-C_-D_-$ ). Secondly, in the  
395 “*network*” case we assume that all loci interact such that only two viable male haplotypes  
396 exist  $A_+B_+C_+D_+$  and  $A_-B_-C_-D_-$ . In both cases, heterozygote advantage is defined as  
397 before, now acting on all four loci multiplicatively.

398 Under this model, we derived the conditions under which exclusion (the purging of all  
399 foreign alleles resulting in a monomorphic equilibrium) is locally stable (cf. Mathematica  
400 Online Supplement). For the pairwise case, exclusion is stable only if heterozygote advantage  
401 is relatively weak:

$$\omega < \min \left[ \frac{1}{\sqrt{1 - \rho_{12}}}, \frac{1}{\sqrt{1 - \rho_{34}}} \right], \quad (14)$$

402 where  $\rho_{ij}$  is the recombination rate between neighboring loci  $i$  and  $j$ . Note that this is in-  
403 dependent of the recombination rate between non-interacting loci, here  $\rho_{23}$ . If  $\rho_{12} = \rho_{34}$ ,  
404 this expression is equivalent to equation 7 (Fig. 4(a)). Overall, this condition indicates that  
405 exclusion, which we define as the fixation of one of the parental haplotypes, is less likely with  
406 four interacting loci than with two. [This is because the fate of the two pairs of incompati-](#)

407 bilities is decided independently, and exclusion requires that both pairs of incompatibilities fix  
 408 for the same parental haplotype.

409 For the network case, the condition for stability of exclusion (see also Fig. S3) is

$$\omega < ((1 - \rho_{12})(1 - \rho_{23})(1 - \rho_{34}))^{-\frac{1}{4}}. \quad (15)$$

410 In this scenario, exclusion is a more likely outcome with two pairs of incompatibilities than  
 411 with one. This is because there are more unfit intermediate types in this scenario as com-  
 412 pared with the pairwise model. Specifically in males, 14 out of the 16 possible haplotypes do  
 413 not survive to adulthood. To compensate for this fitness cost, any alternative evolutionary  
 414 outcome requires strong heterozygote advantage.

#### 415 **Incompatibilities involving an arbitrary number of loci**

416 From the results for two and four loci, we derived a conjecture that generalizes to an  
 417 arbitrary number of loci. For the pairwise case, equation 14 can be generalized to

$$\omega < \min \left[ \frac{1}{\sqrt{1 - \rho_{ij}}} \right], \quad (16)$$

418 with  $i$  and  $j$  representing neighboring interacting loci. Note that this result holds only if  
 419 interacting loci are next to each other on the same chromosome, or if all loci are unlinked (in  
 420 which case it simplifies to  $\omega < \sqrt{2}$ ).

421 For the network case, equation (15) generalizes to

$$\omega < \left( \prod_{\substack{i=1 \\ j=i+1}}^{n-1} (1 - \rho_{ij}) \right)^{-\frac{1}{n}}, \quad (17)$$

422 with  $i$  and  $j$  neighboring loci and  $n$  the total number of loci in the network. Unlike in the  
 423 pairwise case, the results for the network case do not depend on the genetic architecture  
 424 (here, the ordering of loci along the genome).

425 We can therefore deduce that, for the pairwise case, exclusion becomes increasingly un-  
 426 likely as the number of pairs of independent hybrid incompatibilities involved in the genetic  
 427 barrier increases. Conversely, the opposite result is observed for the network case: more

428 loci make exclusion a more likely outcome, but each additional interaction contributes less  
429 (cf. Fig. S3).

### 430 **Increased assortative mating counteracts recombination and heterozygote** 431 **advantage**

432 Increasing the strength of assortative mating,  $\alpha > 0$ , counteracts the hybridization-  
433 favoring effect of heterozygote advantage, because matings between individuals with the  
434 same genotype are more common under stronger, positive assortment. Under sufficiently  
435 large positive  $\alpha$ , exclusion is unavoidable. In general, increasing  $\alpha$  leads to less mainte-  
436 nance of polymorphism in the population (Fig. S4). Conversely, when  $\alpha < 0$ , which means  
437 that individuals prefer to mate with those whose genotype is most different from their own,  
438 polymorphism is more likely to be maintained in the population.

439 Also with assortative mating, recombination remains a key player in determining the  
440 evolutionary outcome. When  $\alpha < 0$  and recombination is small, symmetric coexistence is  
441 possible even in the absence of heterozygote advantage (i.e.,  $\sigma = 0$ ; Fig. S4). Indeed, under  
442 these conditions and assuming epistasis is very strong, (almost) all hybrid males are dead  
443 and only parental males survive. This ‘disassortative’ mating ( $\alpha < 0$ ) creates a bias for the  
444 rare male haplotype. For example, if one female genotype increases in frequency, it will seek  
445 mainly the males of the other parental haplotype to reproduce with (which are currently rare,  
446 as their frequency is directly tied to the frequency of the females in the previous generation.  
447 This will increase their reproductive success, which leads to an increase of this haplotype  
448 frequency. Therefore, under this mate choice regime, we would observe a stable population  
449 composed almost exclusively of the  $A_+B_+$  and  $A_-B_-$  haplotypes.

### 450 **Differences between the haplodiploid and the diploid systems**

451 As described above and illustrated in Figure 6, the resulting haplodiploid dynamics display  
452 a wider range of possible evolutionary outcomes than the diploid dynamics. Because both  
453 males and females profit from heterozygote advantage in the diploid model, polymorphism  
454 is always maintained; in other words, even the smallest amount of heterozygote advantage  
455 promotes the creation or maintenance of diversity in diploids (Table S3). Conversely, in  
456 the haplodiploid model, polymorphism can be lost either at one or both loci, resulting in

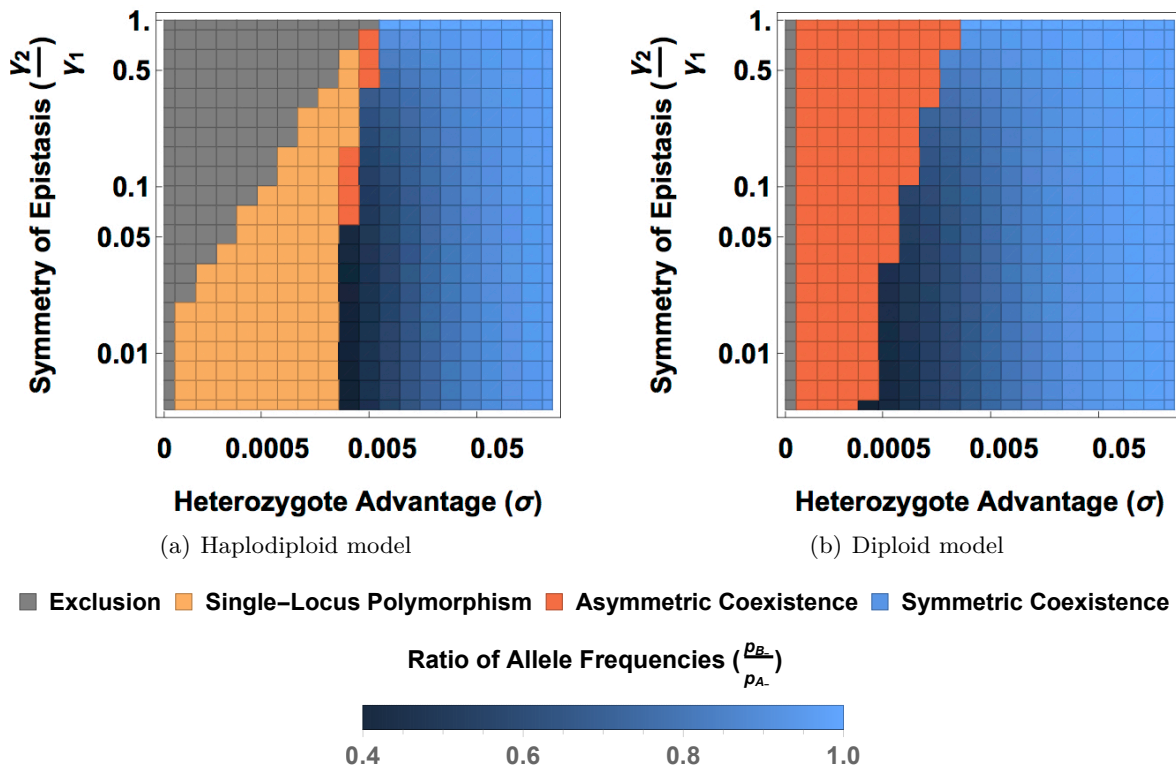


Figure 6: More evolutionary outcomes are possible in (a) the haplodiploid than (b) the diploid model. The y-axis shows the degree of asymmetry of epistasis, displayed as the ratio of the two epistasis parameters ( $\frac{\gamma_2}{\gamma_1}$ ) for a constant value of  $\gamma_1 = 0.01$ . For symmetric coexistence, the locally stable equilibrium can be at any point on the diagonal  $p_{B-} = 1 - p_{A-}$ , where  $p_{A-}$  and  $p_{B-}$  denote the allele frequencies of the  $-$  allele at the respective locus. Blue shading illustrates the location of the equilibrium at symmetric coexistence: darker shades correspond to a bigger disparity in allele frequencies. This is the case when the asymmetry of the two epistasis parameters is large (i.e. smaller values on the y-axis) because smaller values of  $\gamma_2$  favor the  $A_-B_+$  haplotype over the  $A_+B_-$  haplotype. (Here,  $\gamma_1 = 0.01$ ,  $\rho = 0.5$ ,  $\alpha = 0$ .)

457 a single-locus polymorphism or exclusion. Thus, alleles responsible for incompatibilities are  
 458 more effectively purged in the haplodiploid model.

459 In the diploid model, a single-locus polymorphism is never stable: Assume locus  $A$  is  
 460 polymorphic and locus  $B$  is fixed for allele  $B_+$ . Then, a new mutant carrying allele  $B_-$  will  
 461 always have a selective advantage regardless of the genotype in which it first appears (Table  
 462 S3). In contrast, in the haplodiploid model, this is no longer true as the mutant carrying  
 463 allele  $B_-$  will have a much lower fitness in males when associated to allele  $A_+$ . Therefore, if  
 464 the cost of generating this unfit haplotype in males overrides the advantage in females, and  
 465 allele  $A_+$  is at high frequency, then invasion of the  $B_+$  mutant may be prevented, leading to  
 466 the stability of the single-locus polymorphism.

467 When polymorphism is maintained at both loci at equilibrium (i.e., asymmetric and sym-  
468 metric coexistence), epistasis creates associations between the compatible alleles which results  
469 in elevated linkage disequilibrium (LD). Recombination breaks the association between al-  
470 leles, thus high recombination decreases normalized LD ( $D'$ , where  $D' = \frac{LD}{D_{max}}$  (Lewontin,  
471 1964); Fig. S5).  $D'$  increases with the strength of heterozygote advantage at low recombi-  
472 nation rates because it maximizes the discrepancy between highly fit double-heterozygote  
473 females [on the one hand](#) that can, under low recombination rate, still produce many fit male  
474 offspring and introgressed females [on the other](#), who are less fit and produce many unfit  
475 hybrid males

476 In Figure S6, we compare the normalized LD (i.e.  $D'$ ) between the haplodiploid and  
477 diploid models. When polymorphism is maintained at both loci in both the haplodiploid and  
478 diploid model, normalized LD is always larger in haplodiploids than diploids. The difference  
479 in normalized LD between haplodiploids and diploids is maximized for intermediate recombi-  
480 nation rates, where recombination is strong enough to [create unfit hybrid genotypes](#), but not  
481 efficient enough to break the associations that are [generated](#). Due to the increased selection  
482 against hybrid incompatibility in haploid males in the haplodiploid model, the normalized  
483 LD is usually 2-3 times higher in the haplodiploid as compared with the diploid model.

484 Thus, the hybrid incompatibility leaves a statistical signature in a population, even if the  
485 population finds itself at an equilibrium. The increased association across the genome, exhib-  
486 ited if the interacting loci are on the same chromosome, may also result in an underestimate  
487 of the recombination rate. Although both the diploid and the haplodiploid models display the  
488 elevated LD signal, it is much more pronounced in the haplodiploid scenario. This is because  
489 only an eighth of the possible diploid male genotypes suffer the cost of the incompatibility as  
490 compared to half of the possible haploid male genotypes.

## 491 Discussion

492 Multiple recent studies have highlighted the pervasive nature of hybridization and its  
493 potential consequences for diversification and speciation (Abbott et al., 2013; Runemark et al.,  
494 2017; Montecinos et al., 2017). We here modeled the fate of a hybrid population in a scenario  
495 in which hybridization is simultaneously favored and selected against, inspired by a natural

496 population of hybrid ants that simultaneously displays heterosis and hybrid incompatibility.  
497 In addition, both adaptive introgression and hybrid incompatibilities have been identified in  
498 natural systems (Heliconius Genome Consortium, 2012; Whitney et al., 2015; Corbett-Detig  
499 et al., 2013) and it is **therefore** likely that both processes may occur simultaneously during  
500 a single hybridization event. Furthermore, we were interested in comparing the long-term  
501 **evolution of populations exposed to these opposing selective pressures** under different ploidies  
502 (haplodiploid versus diploid), since it has been argued that haplodiploids might speciate more  
503 easily than diploids (Lohse and Ross, 2015). Finally, the comparison of ploidies can also be  
504 transferred to the case of diploid species **with sex chromosomes**, in which the described fitness  
505 landscape results in the diploid dynamics on the autosomes, and in the haplodiploid dynamics  
506 on the X/Z chromosome.

507 Our model considers a population in which heterozygote advantage and hybrid incompat-  
508 ibility act simultaneously on the same pair of loci, which creates a rugged fitness landscape  
509 with a ridge of high-fitness heterozygote genotypes, adjacent to which there are holes of in-  
510 compatible double homozygotes (Fig. 2(a)). In haplodiploids, **haploid** males cannot profit  
511 from heterozygote advantage but suffer strongly from hybrid incompatibility (Fig. 2(b)). This  
512 results in a conflict of ploidies/sexes over the optimal location in the fitness landscape, be-  
513 cause haploid males survive best if one parental haplotype is fixed whereas diploid females  
514 profit from maximum heterozygosity. Although females suffer from the same incompatibility  
515 as males, their presence is mainly masked in the diploid individuals because of the recessivity  
516 of the hybrid incompatibility. This is similar to Haldane’s rule (Charlesworth et al., 1987;  
517 Koevoets and Beukeboom, 2009).

518

## 519 **How ploidy matters**

520 We found that, in the haplodiploid model, there exist four different stable outcomes **of**  
521 **the conflict** over hybrid status (Fig. 3): exclusion, where “males/haploids win”; symmetric  
522 coexistence, where “females/**diploids** win”; and two outcomes, single-locus polymorphism and  
523 asymmetric coexistence, where a compromise between male costs and female benefits is me-  
524 diated by high frequencies of introgressed females. In fact, since low-frequency heterozygotes  
525 are favored both in males and in females in the diploid model, while only suffering the hybrid

526 cost if introgressed alleles rise to high frequencies, exclusion and single-locus polymorphism  
527 never occur in the diploid model, which reduces the number of possible outcomes to asymmet-  
528 ric and symmetric coexistence. Therefore, consistent with Pamilo (1979); Pamilo and Crozier  
529 (1981); Patten et al. (2015), we found that introgression and maintenance of polymorphism,  
530 and thus long-term hybridization, are less likely in haplodiploids as compared to diploids.

531 Prior work has found that in haplodiploid species traditional sexual conflict tends to be  
532 resolved in favor of females because genes spend two thirds of their time in females (Albert  
533 and Otto, 2005). In our model, the [co-occurrence of heterozygote advantage and hybrid](#)  
534 [incompatibility also creates an apparent sexual conflict that is caused by the difference in](#)  
535 [ploidy between the sexes](#). For several scenarios, we here derived the conditions for whether  
536 this conflict is resolved in favor of diploid females or haploid males. We find, that in addition  
537 to the strength of selection, recombination is a major player (cf. Fig. 4 and equation 12);  
538 [only if recombination breaks up gametes, the hybrid incompatibility is expressed](#). With free  
539 recombination, i.e., if the interacting genes are found on separate chromosomes, heterozygote  
540 advantage has to be very strong to counteract the hybrid incompatibility. We find that it  
541 has to be on the same order of magnitude [as](#) the strength of the incompatibility, but can be  
542 slightly lower in its absolute value. For example, heterozygote advantage [with](#) strength 41%  
543 is sufficient to result in symmetric coexistence even if the incompatibility is lethal (Fig. 4B).  
544 Thus, under consideration of absolute magnitude [across the full parameter range](#), our results  
545 are consistent with prior work. However, reported cases and potential mechanisms of hybrid  
546 incompatibility indicate that large effects are feasible, whereas observed cases of heterozygote  
547 advantage or heterosis of large effect are relatively rare (Hedrick, 2012). Therefore, it may  
548 well be that under natural circumstances, the conflict modeled here may indeed be likely to  
549 be resolved via purging of at least one incompatible allele and thus in favor of males/[haploids](#).

550 As expected in the presence of epistasis, we observed that linkage disequilibrium (LD)  
551 is elevated at all polymorphic stable states (i.e., for symmetric and asymmetric coexistence)  
552 both in the diploid and haplodiploid models, especially at intermediate recombination rates.  
553 This is particularly true for haplodiploids, which display about 2-3 times the LD of the diploid  
554 model with the same parameters. Transferred to the context of X/Z chromosomes, this is  
555 consistent with observations of larger LD on the X chromosome as compared with autosomes  
556 ([Wall et al., 2002; Sandor et al., 2006; Li and Merilä, 2010](#)). It has been argued that this is

557 because selection is more effective on X-linked loci: recessive deleterious mutations are more  
558 visible to selection in haploid individuals (Charlesworth et al., 1987). However, a hybrid  
559 incompatibility accompanied by heterosis/heterozygote advantage as in our model may not  
560 be purged but create a continuous high-LD signal in an equilibrium population. This can  
561 potentially result in less efficient recombination and in underestimates of recombination rates  
562 on X chromosomes (because recombined individuals are not observed).

563

## 564 **Generalization to multiple incompatibilities**

565 Exclusion remains a stable solution when we extend the model to multiple loci and in-  
566 compatibilities. We describe an interesting difference between multiple independent pairs  
567 of incompatibilities, and multiple loci that all interact with each other: in the latter case,  
568 exclusion becomes increasingly probable because the number of viable males decreases. This  
569 scenario of higher-order epistasis has recently received attention with regards to speciation  
570 (Paixão et al., 2014; Fraïsse et al., 2014; Kulmuni and Westram, 2017), and it will be interest-  
571 ing [in the future](#) to identify molecular scenarios (for example, involving biological pathways)  
572 that could result in such incompatibilities. In contrast, exclusion becomes less likely in the  
573 case of independent incompatibility pairs, where each incompatibility has to be purged inde-  
574 pendently, [and](#) in the same direction, for exclusion to occur. Here, mechanisms that reduce  
575 the recombination rate, such as inversions, could potentially invade and tilt the balance to-  
576 wards coexistence and thus maintenance of polymorphism in the hybrid population. It is  
577 important to [note that the independent purging of incompatibilities, which leads to a de-](#)  
578 [creasing probability of exclusion with increasingly many incompatibility pairs, is only true in](#)  
579 [effectively infinite-sized populations. In small populations,](#) we expect that exclusion becomes  
580 a more likely scenario, especially if lethal incompatibility pairs are present.

## 581 **Model assumptions**

582 We chose a classical population-genetic modeling approach (Bürger, 2000; Nagylaki et al.,  
583 1992) to study how [the co-occurrence of heterozygote advantage and hybrid incompatibility](#)  
584 [affect the long-term dynamics of a hybrid population.](#) By treating the problem in a determin-  
585 istic framework and considering only two loci throughout most of the manuscript, we [greatly](#)  
586 oversimplify the situation in the natural population that [inspired](#) our model. However, at the

587 same time this allowed us to gain a general insight, (often by means of analytical expressions),  
588 into how opposing selective pressures in genomes may be resolved, and to contrast these out-  
589 comes between haplodiploid and diploid systems. In addition to some obvious mechanisms  
590 at play in natural populations, which we ignore in our model (e.g., random genetic drift),  
591 some extensions of the model could be interesting to elaborate on in the future. For example,  
592 the ant populations represent networks of interacting nests with many queens per nest, but  
593 potentially different mating flight timing that depends, for example, on sun exposure in the  
594 spring. Thus, for the purpose of population-genetic inference of the evolutionary history (and  
595 potential evolutionary fate) of the hybrid ant population in Finland, it would be desirable  
596 to incorporate population structure, uneven sex ratios at birth, and sex-biased dispersal into  
597 the model, and obtain population-genomic data to infer evolutionary parameters.

### 598 **Is the natural population at an equilibrium of asymmetric coexistence?**

599 Model fitting results (see Supplementary Methods, Results, and Discussion) are incon-  
600 clusive about the fate of the natural ant population that inspired our model. Our results  
601 suggest that the natural population might be approaching an evolutionary outcome that al-  
602 lows a compromise between male and female interests; either as single-locus polymorphism or  
603 via asymmetric coexistence. In particular, our model is able to explain the unusual skew in  
604 the population, where *F. aquilonia*-like parental genotypes far outnumber *F. polyctena*-like  
605 genotypes (see Supplement). Furthermore, the high recombination rates and strong prezy-  
606 gotic mechanisms operating in the natural population (Kulmuni et al., 2010; Kulmuni and  
607 Pamilo, 2014), are consistent with a parameter domain in our models at which asymmetric  
608 coexistence can be stably maintained over a wide range of values of female hybrid advantage.  
609 More complex models, for example including more than two incompatibility loci, may be  
610 better able to explain the high frequencies of introgressed as compared to parental females  
611 observed in the natural hybrid population. As argued in the Results, interactions at or be-  
612 tween multiple loci should result in steeper differences of introgressed-allele frequencies across  
613 life stages than our model is able to produce.

## 614 Implications for hybrid speciation

615 Our model illustrates how [the co-occurrence of heterozygote advantage and hybrid in-](#)  
616 [compatibility affects](#) haplodiploid and diploid populations. We can hypothesize how these  
617 different outcomes may provide an engine to hybrid speciation, or which other long-term  
618 evolutionary scenarios we expect to arise. The case of exclusion, which is possible only in  
619 the haplodiploid model, will lead to loss of diversity in the hybrid population, and, in the  
620 two-locus case, should result in the reversion of the hybrid population into one of its parental  
621 species. However, if multiple pairs of interacting loci are resolved independently, they may be  
622 purged randomly towards either parent, which could result in a true hybrid species that is iso-  
623 lated from both its parental species (Buerkle et al., 2000; Butlin and Ritchie, 2013; Schumer  
624 et al., 2015). In fact, our finding that exclusion is less likely to occur in populations with  
625 multiple pairs of interacting loci may result from exactly this mechanism, but it is beyond  
626 the scope of this manuscript to explore this further.

627 The long-term fate of the population is less straightforward to anticipate in the case of  
628 polymorphic stable equilibria. For any of these, heterozygote advantage is strong enough  
629 to stabilize the polymorphism either at one or both loci. Without further occurrence of  
630 functional mutations, males (in the haplodiploid model) and double-homozygotes for the  
631 incompatible alleles will continue to suffer a potentially large fitness cost. Mechanisms that  
632 could reduce this cost would be increased assortative mating or decreased recombination.  
633 However, [neither](#) of these would necessarily cause isolation from the parental species, unless  
634 they involved additional hybrid incompatibilities which isolate the hybrid population from  
635 its parental species. Alternatively, mutations that lower the hybrid fitness cost could invade,  
636 which [would](#) result in a weakening of species barriers and promote further introgression from  
637 the parental species. This indicates that any scenario in which polymorphic equilibria are  
638 stable may indeed be an unlikely candidate for hybrid speciation. Considering that such  
639 stable polymorphism (either as symmetric or asymmetric coexistence) is the only possible  
640 outcome in the diploid model, this results in the prediction that hybrid speciation would be  
641 more likely in a haplodiploid scenario. This is an interesting observation that is in line with  
642 other predictions that haplodiploids speciate more easily, that X/Z chromosomes are engines  
643 of speciation (Lima, 2014), and that hybrid speciation is rare (Schumer et al., 2014).

## 644 **Relevance of the model for sex chromosomes**

645 Haplodiploids and X/Z chromosomes have a similar mode of inheritance, where one sex  
646 carries a single copy of the chromosome, and the other carries two copies. Therefore, our  
647 results apply equally to cases of X-to-X or Z-to-Z hybrid incompatibilities (Lohse and Ross,  
648 2015). Although haplodiploid systems do not include all of the unique evolutionary phenom-  
649 ena exhibited by sex chromosomes (Abbott et al., 2017), our results for haplodiploids are  
650 relevant for sex chromosomes. Our model predicts [the long-term evolution of a population](#)  
651 [under the simultaneous influence of heterozygote advantage and hybrid incompatibility](#), and  
652 indicates the signatures that this type of fitness landscape could leave depending on whether  
653 it finds itself on an X chromosome or an autosome.

654 [Firstly, the complex selection pressure imposed by the co-occurrence of heterozygote ad-](#)  
655 [vantage and hybrid incompatibility manifests itself as an apparent sexual conflict on the](#)  
656 [X chromosome/in haplodiploids. This conflict is caused by the ploidy difference between the](#)  
657 [sexes.](#) Here, the same fitness landscape that would be masked on an autosome and result in a  
658 stable polymorphism, creates a signal of sexually antagonistic selection on an X chromosome.  
659 Most importantly, this signal is created without the need for direct sexually antagonistic  
660 selection on single functional genes that have a sex-specific antagonistic effect. Thus, our  
661 model proposes an additional mechanism by which sex chromosomes can appear as hotspot  
662 of sexual conflict (e.g., Gibson et al., 2002; Pischedda and Chippindale, 2006).

663 Secondly, we find that purging of incompatibilities is more likely in the haplodiploid model,  
664 and thus on X/Z chromosomes. This is consistent with the faster-X theory (Charlesworth  
665 et al., 1987). However, only if recombination is strong enough, incompatibilities will be-  
666 come visible to selection and purged in the presence of heterozygote advantage. If they are  
667 not purged, they may persist [as](#) a long-term polymorphism, invisible to most empirical ap-  
668 proaches, and confound population-genetic inference by creating signals of elevated linkage  
669 disequilibrium.

## 670 **Conclusion**

671 Hybridization is observed frequently in natural populations, and can have both deleterious  
672 and advantageous effects. We here show how diverse outcomes [can be](#) produced even under

673 a rather simple model of a single hybrid population, in which heterozygote advantage and  
674 hybrid incompatibility are occurring at the same time. Consistent with previous theory on  
675 haplodiploids and X/Z chromosomes, we found that incompatible alleles are more likely to be  
676 purged in a haplodiploid than in a diploid model. Nevertheless, our results suggest that long-  
677 term hybridization can occur even in the presence of hybrid incompatibility, and if there are  
678 many incompatible pairs or many loci involved in the incompatibility. The evolutionary fate  
679 of the Finnish hybrid *ant* population that [inspired](#) our model is difficult to predict; further  
680 population-genetic analysis will be necessary to gain a more complete picture of its structure  
681 and evolutionary history.

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## 689 **Data Accessibility**

690 The complete documentation of all steps of the analysis is available as a Mathematica  
691 Online Supplement. *Ant* colony data is provided as Supplementary Table S1; genotype  
692 frequency data were obtained from Kulmuni and Pamilo (2014).

## 693 **Author Contributions**

694 CB, JK, and RB designed research, AB and CB developed the models, AHG performed  
695 simulations and data analysis, all authors interpreted the results and wrote the manuscript.

## Bibliography

- 696
- 697 Abbott, J., Nordén, A., and Hansson, B. (2017). Sex chromosome evolution: Historical  
698 insights and future perspectives. *Proceedings of the Royal Society of London B: Biological*  
699 *Sciences*, 284(1854):20162806.
- 700 Abbott, R., Albach, D., Ansell, S., Arntzen, J. W., Baird, S. J. E., Bierne, N., Boughman, J.,  
701 Brelsford, A., Buerkle, C. A., Buggs, R., Butlin, R. K., Dieckmann, U., Eroukhmanoff, F.,  
702 Grill, A., Cahan, S. H., Hermansen, J. S., Hewitt, G., Hudson, A. G., Jiggins, C., Jones,  
703 J., Keller, B., Marczewski, T., Mallet, J., Martinez-Rodriguez, P., Möst, M., Mullen, S.,  
704 Nichols, R., Nolte, A. W., Parisod, C., Pfennig, K., Rice, A. M., Ritchie, M. G., Seifert,  
705 B., Smadja, C. M., Stelkens, R., Szymura, J. M., Väinölä, R., Wolf, J. B. W., and Zinner,  
706 D. (2013). Hybridization and speciation. *Journal of Evolutionary Biology*, 26(2):229–246.
- 707 Albert, A. and Otto, S. (2005). Sexual selection can resolve sex-linked sexual antagonism.  
708 *Science*, 310(5745):119–121.
- 709 Arnqvist, G. and Rowe, L. (2005). *Sexual conflict*.
- 710 Bateson, W. (1909). Heredity and variation in modern lights. *Darwin and modern science*,  
711 pages 85–101.
- 712 Beresford, J., Elias, M., Pluckrose, L., Sundström, L., Butlin, R., Pamilo, P., and Kulmuni,  
713 J. (2017). Widespread hybridization within mound-building wood ants in Southern Fin-  
714 land results in cytonuclear mismatches and potential for sex-specific hybrid breakdown.  
715 *Molecular Ecology*, 26(15):4013–26.
- 716 Bernardes, J., Stelkens, R., and Greig, D. (2017). Heterosis in hybrids within and between  
717 yeast species. *Journal of Evolutionary Biology*, 30(3):538–548.
- 718 Buerkle, C. A., Morris, R. J., Asmussen, M. A., and Rieseberg, L. H. (2000). The likelihood  
719 of homoploid hybrid speciation. *Heredity*, 84(4):441–451.
- 720 Bürger, R. (2000). *The mathematical theory of selection, recombination, and mutation*, vol-  
721 ume 228. Wiley Chichester.
- 722 Butlin, R. K. and Ritchie, M. G. (2013). Pulling together or pulling apart: hybridization in  
723 theory and practice. *Journal of Evolutionary Biology*, 26(2):294–298.
- 724 Charlesworth, B., Coyne, J., and Barton, N. (1987). The relative rates of evolution of sex  
725 chromosomes and autosomes. *The American Naturalist*, 130(1):113–146.
- 726 Chen, C., Zhiguo, E., and Lin, H.-X. (2016). Evolution and molecular control of hybrid  
727 incompatibility in plants. *Frontiers in Plant Science*, 7:1208.
- 728 Chen, Z. (2013). Genomic and epigenetic insights into the molecular bases of heterosis. *Nature*  
729 *Review Genetics*, 14(7):471–482.
- 730 Corbett-Detig, R. B., Zhou, J., Clark, A. G., Hartl, D. L., and Ayroles, J. F. (2013). Genetic  
731 incompatibilities are widespread within species. *Nature*, 504(7478):135–7.
- 732 Crozier, R. and Pamilo, P. (1996). *Evolution of social insect colonies: Sex allocation and kin*  
733 *selection*. Oxford University Press, Oxford, UK.

- 734 De Cara, M., Barton, N., and Kirkpatrick, M. (2008). A model for the evolution of assortative  
735 mating. *The American Naturalist*, 171(5):580–596.
- 736 de la Fila, A., Bain, S., and Ross, L. (2015). Haplodiploidy and the reproductive ecology of  
737 arthropods. *Current Opinion in Insect Science*, 9:36–43.
- 738 Dieckmann, U. and Doebeli, M. (1999). On the origin of species by sympatric speciation.  
739 *Nature*, 400(6742):354–357.
- 740 Dobzhansky, T. (1936). Studies on hybrid sterility. II. Localization of sterility factors in  
741 *Drosophila pseudoobscura* hybrids. *Genetics*, 21(2):113.
- 742 Evans, J., Shearman, D., and Oldroyd, B. (2004). Molecular basis of sex determination in  
743 haplodiploids. *Trends in Ecology and Evolution*, 19(1):1–3.
- 744 Fraïsse, C., Elderfield, J., and Welch, J. (2014). The genetics of speciation: are complex  
745 incompatibilities easier to evolve? *Journal of Evolutionary Biology*, 27(4):688–99.
- 746 Gibson, J., Chippindale, A., and Rice, W. (2002). The X chromosome is a hot spot for  
747 sexually antagonistic fitness variation. *Proceedings of the Royal Society of London B:  
748 Biological Sciences*, 269(1490):499–505.
- 749 Hedrick, P. W. (2012). What is the evidence for heterozygote advantage selection? *Trends  
750 in Ecology & Evolution*, 27(12):698–704.
- 751 Heliconius Genome Consortium (2012). Butterfly genome reveals promiscuous exchange of  
752 mimicry adaptations among species. *Nature*, 487(7405):94.
- 753 Höllinger, I. and Hermisson, J. (2017). Bounds to parapatric speciation: A Dobzhan-  
754 sky–Muller incompatibility model involving autosomes, X chromosomes, and mitochondria.  
755 *Evolution*, 71(5):1366–1380.
- 756 Jablonka, E. and Lamb, M. J. (1991). Sex Chromosomes and Speciation. *Proceedings of the  
757 Royal Society B: Biological Sciences*, 243(1308):203–208.
- 758 Johnson, N. A. and Lachance, J. (2012). The genetics of sex chromosomes: evolution and  
759 implications for hybrid incompatibility. *Annals of the New York Academy of Sciences*,  
760 1256(1):E1–E22.
- 761 Knecht, B., Potter, T., Pearson, N., Sato, Y., Staudacher, H., Schimmel, B., Kiers, E., and  
762 Egas, M. (2017). Detection of genetic incompatibilities in non-model systems using simple  
763 genetic markers: hybrid breakdown in the haplodiploid spider mite *tetranychus evansi*.  
764 *Heredity*, 118(4):311.
- 765 Koevoets, T. and Beukeboom, L. (2009). Genetics of postzygotic isolation and Haldane’s rule  
766 in haplodiploids. *Heredity*, 102(1):16–23.
- 767 Kopp, M., Servedio, M. R., Mendelson, T. C., Safran, R. J., Rodríguez, R. L., Hauber,  
768 M. E., Scordato, E. C., Symes, L. B., Balakrishnan, C. N., Zonana, D. M., et al. (2017).  
769 Mechanisms of assortative mating in speciation with gene flow: Connecting theory and  
770 empirical research. *The American Naturalist*, 191(1).
- 771 Kraaijeveld, K. (2009). Male genes with nowhere to hide; sexual conflict in haplodiploids.  
772 *Animal Biology*, 59(4):403–415.

- 773 Kulmuni, J. and Pamilo, P. (2014). Introgression in hybrid ants is favored in females but  
774 selected against in males. *Proceedings of the National Academy of Sciences*, 111(35):12805–  
775 10.
- 776 Kulmuni, J., Seifert, B., and Pamilo, P. (2010). Segregation distortion causes large-scale  
777 differences between male and female genomes in hybrid ants. *Proceedings of the National*  
778 *Academy of Sciences*, 107(16):7371–6.
- 779 Kulmuni, J. and Westram, A. M. (2017). Intrinsic incompatibilities evolving as a by-product  
780 of divergent ecological selection: Considering them in empirical studies on divergence with  
781 gene flow. *Molecular Ecology*, 26(12):3093–3103.
- 782 Lewontin, R. (1964). The interaction of selection and linkage. i. general considerations;  
783 heterotic models. *Genetics*, 49–67(1):49.
- 784 Li, M.-H. and Merilä, J. (2010). Sex-specific population structure, natural selection, and  
785 linkage disequilibrium in a wild bird population as revealed by genome-wide microsatellite  
786 analyses. *BMC evolutionary biology*, 10(1):66.
- 787 Lima, T. G. (2014). Higher levels of sex chromosome heteromorphism are associated with  
788 markedly stronger reproductive isolation. *Nature Communications*, 5:4743.
- 789 Lohse, K. and Ross, L. (2015). What haplodiploids can teach us about hybridization and  
790 speciation. *Molecular Ecology*, 24(20):5075–5077.
- 791 Mallet, J. (2005). Hybridization as an invasion of the genome. *Trends in Ecology and Evolution*,  
792 20(5):229–237.
- 793 Montecinos, A. E., Guillemin, M.-L., Couceiro, L., Peters, A. F., Stoeckel, S., and Valero, M.  
794 (2017). Hybridization between two cryptic filamentous brown seaweeds along the shore:  
795 analysing pre- and postzygotic barriers in populations of individuals with varying ploidy  
796 levels. *Molecular Ecology*, 26(13):3497–3512.
- 797 Muller, H. (1942). Isolating mechanisms, evolution and temperature. In *Biology Symposium*,  
798 volume 6, pages 71–125.
- 799 Nagylaki, T. et al. (1992). *Introduction to theoretical population genetics*, volume 142.  
800 Springer-Verlag Berlin.
- 801 Orr, H. (1995). The population genetics of speciation: The evolution of hybrid incompatibil-  
802 ities. *Genetics*, 139(4):1805–1813.
- 803 Otto, S. P. and Day, T. (2007). *A biologist's guide to mathematical modeling in ecology and*  
804 *evolution*, volume 13. Princeton University Press.
- 805 Paixão, T., Bassler, K. E., and Azevedo, R. B. R. (2014). Emergent speciation by multiple  
806 Dobzhansky-Muller incompatibilities. *bioRxiv*, page 8268.
- 807 Pamilo, P. (1979). Genic variation at sex-linked loci: Quantification of regular selection  
808 models. *Hereditas*, 91(1):129–133.
- 809 Pamilo, P. and Crozier, R. H. (1981). Genic variation in male haploids under deterministic  
810 selection. *Genetics*, 98(1):199–214.

- 811 Patten, M., Carioscia, S., and Linnen, C. (2015). Biased introgression of mitochondrial and  
812 nuclear genes: A comparison of diploid and haplodiploid systems. *Molecular Ecology*,  
813 24(20):5200–5210.
- 814 Pischedda, A. and Chippindale, A. K. (2006). Intralocus sexual conflict diminishes the ben-  
815 efits of sexual selection. *PLoS biology*, 4(11):e356.
- 816 Presgraves, D. (2008). Sex chromosomes and speciation in *Drosophila*. *Trends in Genetics*,  
817 24(7):336–343.
- 818 Runemark, A., Trier, C. N., Eroukhmanoff, F., Hermansen, J. S., Matschiner, M., Ravinet,  
819 M., Elgvin, T. O., and Saetre, G.-P. (2017). Variation and constraints in hybrid genome  
820 formation. *bioRxiv*, page 107508.
- 821 Sandor, C., Farnir, F., Hansoul, S., Coppieters, W., Meuwissen, T., and Georges, M. (2006).  
822 Linkage disequilibrium on the bovine x chromosome: characterization and use in quanti-  
823 tative trait locus mapping. *Genetics*, 173(3):1777–1786.
- 824 Schluter, D. (2009). Evidence for ecological speciation and its alternative. *Science*,  
825 323(5915):737–741.
- 826 Schluter, D. and Conte, G. (2009). Genetics and ecological speciation. *Proceedings of the*  
827 *National Academy of Sciences*, 106(Supplement 1):9955–9962.
- 828 Schumer, M., Cui, R., Rosenthal, G. G., and Andolfatto, P. (2015). Reproductive isolation  
829 of hybrid populations driven by genetic incompatibilities. *PLOS Genetics*, 11(3):1–21.
- 830 Schumer, M., Rosenthal, G., and Andolfatto, P. (2014). How common is homoploid hybrid  
831 speciation? *Evolution*, 68(6):1553–1560.
- 832 Schwarz, D., Matta, B., Shakir-Botteri, N., and McPheron, B. (2005). Host shift to an  
833 invasive plant triggers rapid animal hybrid speciation. *Nature*, 436(7050):546–9.
- 834 Seehausen, O., Butlin, R., Keller, I., Wagner, C., Boughman, J., Hohenlohe, P., Peichel, C.,  
835 Saetre, G.-P., Bank, C., Brännström, Å., Brelsford, A., Clarkson, C., Eroukhmanoff, F.,  
836 Feder, J., Fischer, M., Foote, A., Franchini, P., et al. (2014). Genomics and the origin of  
837 species. *Nature Reviews Genetics*, 15(3):176–192.
- 838 Servedio, M. and Noor, M. (2003). The role of reinforcement in speciation: theory and data.  
839 *Annual Review of Ecology, Evolution, and Systematics*, 34(1):339–364.
- 840 Song, Y., Endepols, S., Klemann, N., Richter, D., Matuschka, F.-R., Shih, C.-H., Nachman,  
841 M., and Kohn, M. (2011). Adaptive introgression of anticoagulant rodent poison resistance  
842 by hybridization between old world mice. *Current Biology*, 21(15):1296–1301.
- 843 Suomalainen, E., Saura, A., and Lokki, J. (1987). *Cytology and evolution in parthenogenesis*.  
844 CRC Press, Boca Raton, Florida.
- 845 Wall, J. D., Andolfatto, P., and Przeworski, M. (2002). Testing models of selection and  
846 demography in *Drosophila simulans*. *Genetics*, 162(1):203–216.
- 847 Whitney, K., Randell, R., and Rieseberg, L. (2010). Adaptive introgression of abiotic toler-  
848 ance traits in the sunflower *Helianthus annuus*. *New Phytologist*, 187(1):230–239.

- 849 Whitney, K. D., Broman, K. W., Kane, N. C., Hovick, S. M., Randell, R. A., and Riese-  
850 berg, L. H. (2015). Quantitative trait locus mapping identifies candidate alleles involved  
851 in adaptive introgression and range expansion in a wild sunflower. *Molecular Ecology*,  
852 24(9):2194–2211.
- 853 Wolf, D., Takebayashi, N., and Rieseberg, L. (2001). Predicting the risk of extinction through  
854 hybridization. *Conservation Biology*, 15(4):1039–1053.
- 855 Wolfram Research, Inc. (2016). Mathematica v. 10.4.1.0. Champaign, Illinois, USA.  
856 <https://www.wolfram.com>.