



**HAL**  
open science

## Interactions between Genetic and Ecological Effects on the Evolution of Life Cycles

Marie Rescan, Thomas Lenormand, Denis Roze

► **To cite this version:**

Marie Rescan, Thomas Lenormand, Denis Roze. Interactions between Genetic and Ecological Effects on the Evolution of Life Cycles. *The American Naturalist*, 2016, 187 (1), pp.19-34. 10.1086/684167 . hal-03642391

**HAL Id: hal-03642391**

**<https://hal.science/hal-03642391>**

Submitted on 15 Apr 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



CHICAGO JOURNALS

---

Interactions between Genetic and Ecological Effects on the Evolution of Life Cycles

Author(s): Marie Rescan, Thomas Lenormand and Denis Roze

Source: *The American Naturalist*, Vol. 187, No. 1 (January 2016), pp. 19-34

Published by: [University of Chicago Press](#) for [American Society of Naturalists](#)

Stable URL: <http://www.jstor.org/stable/10.1086/684167>

Accessed: 15-01-2016 19:53 UTC

---

Your use of the JSTOR archive indicates your acceptance of the Terms & Conditions of Use, available at <http://www.jstor.org/page/info/about/policies/terms.jsp>

JSTOR is a not-for-profit service that helps scholars, researchers, and students discover, use, and build upon a wide range of content in a trusted digital archive. We use information technology and tools to increase productivity and facilitate new forms of scholarship. For more information about JSTOR, please contact [support@jstor.org](mailto:support@jstor.org).



*American Society of Naturalists* and *University of Chicago Press* are collaborating with JSTOR to digitize, preserve and extend access to *The American Naturalist*.

<http://www.jstor.org>

# Interactions between Genetic and Ecological Effects on the Evolution of Life Cycles

Marie Rescan,<sup>1,\*</sup> Thomas Lenormand,<sup>2</sup> and Denis Roze<sup>1</sup>

1. CNRS, Unité Mixte Internationale 3614, Evolutionary Biology and Ecology of Algae, Roscoff, France; and Sorbonne Universités, Université Pierre et Marie Curie, University of Paris 6, Roscoff, France; 2. Centre d'Ecologie Fonctionnelle et Evolutive Unité Mixte de Recherche 5175, CNRS, Université de Montpellier, Université Paul-Valéry Montpellier, École Pratique des Hautes Études, 1919 Route de Mende, F-34293 Montpellier, Cedex 5, France

Submitted February 25, 2015; Accepted July 20, 2015; Electronically published November 25, 2015

Online enhancement: appendix. Dryad data: <http://dx.doi.org/10.5061/dryad.40qp5>.

**ABSTRACT:** Sexual reproduction leads to an alternation between haploid and diploid phases, whose relative length varies widely across taxa. Previous genetical models showed that diploid or haploid life cycles may be favored, depending on dominance interactions and on effective recombination rates. By contrast, niche differentiation between haploids and diploids may favor biphasic life cycles, in which development occurs in both phases. In this article, we explore the interplay between genetical and ecological factors, assuming that deleterious mutations affect the competitiveness of individuals within their ecological niche and allowing different effects of mutations in haploids and diploids (including antagonistic selection). We show that selection on a modifier gene affecting the relative length of both phases can be decomposed into a direct selection term favoring the phase with the highest mean fitness (due to either ecological differences or differential effects of mutations) and an indirect selection term favoring the phase in which selection is more efficient. When deleterious alleles occur at many loci and in the presence of ecological differentiation between haploids and diploids, evolutionary branching often occurs and leads to the stable coexistence of alleles coding for haploid and diploid cycles, while temporal variations in niche sizes may stabilize biphasic cycles.

**Keywords:** evolution of life cycles, density dependence, deleterious mutations, multilocus model, evolutionary branching.

## Introduction

Alternation of meiosis and syngamy in sexual eukaryotes results in the alternation of haploid and diploid generations, whose relative duration and degree of development vary largely among taxa. Most animals and some protists (e.g., diatoms, oomycetes) have diploid life cycles: the haploid phase is reduced to a single cell, the gamete. Other organisms (e.g., ascomycetes, charophytes, dinoflagellates) have

haploid cycles, where the diploid phase is reduced to the zygote, which undergoes meiosis before any mitotic development. Finally, many species present haploid-diploid life cycles, where somatic development occurs in both haploid and diploid phases. While the relative development of the haploid (gametophytic) generation is rather limited in seed plants (spermatophytes)—with only a few cell divisions to form the pollen grain and the embryo sac—it is much more important in many fungi, mosses, and macroalgae. In particular, the life cycle of many red algae involves an alternation between haploid and diploid individuals (which may have very different morphologies), while many different life cycles are observed among brown algae, from the isomorphic, haploid-diploid cycle of Dictyotales to the diploid cycle of Fucales.

The limited development and/or short duration of one phase may strongly limit the opportunity for selection. For instance, in many female animals, there is virtually no haploid phase (since the last meiotic division of the egg takes place only at fertilization). By contrast, much selection can occur among male gametes, even though they have very limited development (Joseph and Kirkpatrick 2004). As a consequence, the problem of the evolution of life cycles (i.e., the relative degrees of development of the haploid and diploid phases) is often recast in terms of the opportunity of selection within each phase. From the early nineties, different theoretical studies have explored how genetical or ecological factors may affect the evolution of life cycles (for reviews, see, e.g., Valero et al. 1992; Mable and Otto 1998; Otto and Gerstein 2008). From a genetical perspective, diploids may benefit from more efficient repair of DNA damage because of the presence of a homologous chromosome that may serve as a template (Michod and Wojciechowski 1994). In addition, diploids may benefit from an increased fitness as a result of the masking of deleterious mutations: for this, the fitness effect of mutations in the heterozygous state must be sufficiently low to compensate for the fact that a diploid

\* Corresponding author; e-mail: [marie.rescan@sb-roscoff.fr](mailto:marie.rescan@sb-roscoff.fr).

tends to carry twice as many mutations as a haploid. Under random mating, and assuming that mutations have the same effect in haploids and homozygous diploids, this requires only that deleterious alleles are partially recessive on average (Perrot et al. 1991), which seems to be the case (Halligan and Keightley 2009; Manna et al. 2011). However, mutations increasing the relative length of the diploid phase may not necessarily be favored in this situation. In particular, Otto and Goldstein (1992) showed that modifier alleles coding for a longer diploid phase tend to be associated with more heavily loaded genomes because selection is less efficient among diploids. If linkage is sufficiently tight, this effect may favor modifier alleles increasing the haploid phase, while diploidy is favored under looser linkage because of the masking effect (as long as deleterious alleles are partially recessive). As a consequence, reproductive systems that reduce the effective recombination rate (inbreeding, partial asexuality) tend to increase selection for haploidy (Otto and Marks 1996). Similar results are obtained when considering the spread of beneficial alleles within a population: selection should generally be more efficient in haploids (which was confirmed by evolution experiments on *Saccharomyces cerevisiae*; e.g., Zeyl et al. 2003; Gerstein et al. 2010), but partially dominant beneficial alleles may favor diploidy in sexual populations (Orr and Otto 1994). Finally, Nuismer and Otto (2004) proposed that host-parasite interactions should favor diploidy in the host (because of the benefit of a higher number of recognition alleles) and haploidy in the parasite (for the opposite reason). In general, these genetic models predict evolution toward either haploidy or diploidy (depending, for example, on the degree of dominance of deleterious mutations or on the mating system) but cannot explain the evolutionary stability of haploid-diploid life cycles unless considering additional mechanisms directly favoring biphasic cycles.

Importantly, most of these previous models assume that deleterious alleles have the same fitness effect in haploids and in homozygous diploids. However, haploids and diploids often differ in terms of physiology, morphology, or ecology (Thorner 2006). Transcriptomic studies on haploid-diploid species show that a fraction of genes is expressed in one phase only (Coelho et al. 2007; Von Dassow et al. 2009; Rokitta et al. 2011), and mutations in these genes should thus have no effect on fitness in the other phase. More generally, selective pressures on different genes may differ quantitatively in both phases, leading to different selection coefficients of mutations in both phases. The fact that mutations may have different fitness effects in haploids and diploids is illustrated by several experimental studies on yeast: in particular, Szafraniec et al. (2003) found that ethyl methanesulfonate-induced spontaneous mutations were more deleterious in haploids than in homozygous diploids, while Gerstein (2013) showed that mutations conferring tolerance to nystatin often

have larger fitness effects in haploids than in homozygous diploids. Furthermore, Thompson et al. (2006) observed that beneficial mutations fixed during the adaptation of haploid and diploid mutator populations have different properties, with the mutations fixed in diploids being more generalist. One can also imagine that selection at some loci may favor different alleles in haploids and diploids; such ploidy antagonistic selection can maintain stable polymorphism (Ewing 1977; Immler et al. 2012) and was recently shown to have the potential to drive (in combination with sexually antagonistic selection) the evolution of ploidy differences between sexes (Immler and Otto 2014). However, the overall impact of quantitative and qualitative variations of mutational effects across phases on the evolution of the relative duration of these phases has received very limited attention.

One reason why selection may differ among phases is that haploids and diploids may not be ecologically equivalent. These differences may be cryptic and occur even among morphologically similar haploids and diploids, such as in the isomorphic red alga *Gracilaria gracilis* (Destombe et al. 1993; Hughes and Otto 1999) or the nearly isomorphic brown alga *Ectocarpus crouaniorum*, where sporophytes and gametophytes are typically found on different substrata (rock/shells versus other algal species; Couceiro et al. 2015). In addition, temporal variations of the relative abundance (Bolton and Joska 1993; Otaiza et al. 2001; Dyck and De Wreede 2006) or fecundity (Santos and Duarte 1996) of haploids and diploids have been reported, suggesting that environmental fluctuations may favor alternatively diploid sporophytes or haploid gametophytes. As shown by Hughes and Otto (1999) using a model incorporating density dependence effects, differentiation between the haploid and the diploid ecological niches may favor biphasic life cycles over purely haploid or diploid cycles (since a mutant using a relatively empty niche tends to increase in frequency). This model thus provides a plausible mechanism for the maintenance of biphasic cycles, given that many haploid-diploid species (such as algae or mosses) are often found in dense populations, in which individuals may be strongly affected by intraspecific competition (e.g., Reed 1990; Paalme et al. 2013). However, in the presence of genetic variability for fitness, ecological differentiation between phases may also affect the relative importance of purging and masking effects, depending in particular on the level of competition within and between phases. For example, the masking advantage associated with diploidy (when deleterious alleles are partially recessive) should vanish when the haploid and diploid niches are fully separated (i.e., when haploids do not compete against diploids) and when selection is soft within each niche, so that the total reproductive output from a niche is not affected by selection (e.g., Wallace 1975; Agrawal 2010). Furthermore, different experimental studies (to which we will return in the discussion) suggest that the overall strength of selection against deleterious

alleles may increase with density, in which case ecological differences between haploids and diploids may affect the relative efficiency of selection in the two phases.

In this article, we explore the interplay between ecological and genetic effects on the evolution of life cycles. As in Hughes and Otto (1999), our ecological model is based on a logistic model of population growth, with a variable degree of overlap between the haploid and diploid niches. We assume that deleterious alleles affect the efficiency with which individuals compete for resources within each niche and allow them to have different effects in haploids and homozygous diploids (including ploidy antagonistic selection). In the following, we first use a two-locus model to derive analytical results on the strength of selection on a modifier gene affecting the probability of developing as a diploid or as a haploid (using the approach of Otto and Goldstein 1992), and we explore the effects of niche differentiation and differences in mutational effects between phases. In general, we will see that selection on the modifier can be decomposed into a term stemming from differences in mean fitness between ploidy levels (short-term effect, due to differences in niche availability and in the fitness effect of mutations between phases) and terms involving linkage disequilibria between the modifier and selected locus (indirect selection), favoring the phase in which natural selection is most efficient. We will then extrapolate from our two-locus model to consider deleterious alleles occurring at a large number of loci and check our analytical predictions using multilocus, individual-based simulations. These simulations show that in the absence of deleterious mutation, many different strategies may coexist in the population, provided that the haploid and diploid niches are sufficiently differentiated (in agreement with predictions from Hughes and Otto 1999). With deleterious mutations, however, only extreme strategies (corresponding to purely haploid or purely diploid cycles) are maintained, either alone or coexisting. Finally, in both cases (with or without deleterious mutation), adding temporal fluctuations in the relative sizes of ecological niches may lead to the fixation of biphasic life cycles, in agreement with bet-hedging theory (e.g., Philippi and Seger 1989).

### Model

#### Analytical Model

Our model represents a panmictic population undergoing a biphasic life cycle with nonoverlapping generations. The first event of each generation corresponds to gamete union, assumed to be random. As in the study by Otto and Goldstein (1992), diploid zygotes can either enter meiosis immediately to form new haploid individuals or develop as diploids. The probability to develop as a diploid or as a haploid is controlled by a modifier locus with two alleles,  $M$  and  $m$ : zygotes  $MM$ ,  $Mm$ , and  $mm$  develop as diploids with proba-

bilities  $d$ ,  $d + h_m\delta$ , and  $d + \delta$ , respectively;  $h_m$  thus measures dominance of allele  $m$  (the different parameters and variables of the model are summarized in table 1). The population follows a discrete-time logistic model of population growth. The fitness of the different genotypes in the different phases depends on several parameters. We first consider the fitness of haploids ( $W_h$ ) and diploids ( $W_d$ ), defined as the number of offspring—or half the number of gametes—that will participate to the next generation, in the absence of deleterious mutation. It is given by

$$\begin{aligned} W_h &= 1 + r_h \left( 1 - \frac{N_h + \gamma_{hd}N_d}{K_h} \right), \\ W_d &= 1 + r_d \left( 1 - \frac{N_d + \gamma_{dh}N_h}{K_d} \right), \end{aligned} \quad (1)$$

where  $N_h$  and  $N_d$  are the numbers of parental haploids and diploids (haploid individuals produce gametes by mitosis, while diploids produce gametes by meiosis). As can be seen from equation (1),  $K_h$  and  $K_d$  correspond to the carrying capacities of a purely haploid ( $d = 0$ ) and purely diploid ( $d = 1$ ) population, which depends on resource abundance within the haploid and diploid niches and on the efficiency with which individuals use those resources. Coefficient  $\gamma_{dh}$  (respectively,  $\gamma_{hd}$ ) measures the efficacies by which haploids (diploids) compete for the diploid (haploid) resources (Hughes and Otto 1999). If  $\gamma_{dh} = \gamma_{hd} = 1$ , both phases use the same resources and thus compete directly against each other, while  $\gamma_{dh} = \gamma_{hd} = 0$  corresponds to the case where haploids and diploids occupy different ecological niches. As shown by Hughes and Otto (1999), haploid-diploid life cycles (i.e., intermediate values of  $d$ ) may be favored when  $\gamma_{dh}\gamma_{hd} < 1$ . Finally, note that the baseline reproductive factors  $1 + r_h$  and  $1 + r_d$  (corresponding to the fitness of haploids and diploids in the absence of intraspecific competition) incorporate all effects of the environment on fertility and mortality (e.g., gamete or zygote mortality) that do not depend on density.

We then introduce a second locus affecting the sensitivity of individuals to competition. Following Christiansen and Loeschcke (1980), we consider two different forms of selection. In the first scenario, genotypes differ in their efficiency in using limited resources, so that individuals carrying more deleterious alleles need more resources to produce offspring. This may be represented by multiplying the coefficients  $K_d$  and  $K_h$  in equation (1) by factors that depend on the genotype of the individual. Note that selection affects demography under this scenario because it changes carrying capacities. The second scenario corresponds to a situation where genotypes differ in their competitiveness for resources: individuals suffer more from competition with genotypes carrying fewer deleterious alleles and less from

**Table 1:** Parameters and variables used in the model

Symbol	Definition
$N$	Population size
$d$	Probability that a zygote with genotype $MM$ at the modifier locus develops as a diploid
$\delta$	Change in the probability to develop as a diploid caused by the modifier allele $m$ in the homozygous state
$h_m$	Dominance coefficient of allele $m$
$W_h^i, \overline{W}_h$	Fitness (number of offspring at the next generation) of a haploid individual with genotype $i$ and average fitness of haploids
$W_d^i, \overline{W}_d$	Fitness of a diploid with genotype $i$ and average fitness of diploids
$r_h, r_d$	Baseline growth rate of haploids and diploids ( $W_h = 1 + r_h$ and $W_d = 1 + r_d$ in the absence of competition)
$K_h, K_d$	Haploid and diploid carrying capacities
$\gamma_{hd}, \gamma_{dh}$	Competitive effect of diploids on haploids ( $\gamma_{hd}$ ) and of haploids on diploids ( $\gamma_{dh}$ )
$C_h, C_d$	Strength of density-dependent competition acting on haploids and diploids (see eq. [7])
$\lambda, \tau$	Amplitude ( $\lambda$ ) and period ( $\tau$ ) of the temporal fluctuations of $K_h$ and $K_d$
$\omega_h^i, \overline{\omega}_h$	Sensitivity to competition of a haploid with genotype $i$ and average sensitivity to competition of haploids
$\omega_d^i, \overline{\omega}_d$	Sensitivity to competition of a diploid with genotype $i$ and average sensitivity to competition of diploids
$\beta$	Degree of softness of selection on sensitivity to competition
$\alpha$	Effect of allele $a$ on the sensitivity to competition of homozygous diploids
$h$	Dominance coefficient of allele $a$
$\rho\alpha$	Effect of allele $a$ on the sensitivity to competition of haploids ( $\rho$ is thus the ratio between the effect of allele $a$ in haploids and diploids)
$s_h, s_d$	Strength of selection against allele $a$ in haploids and diploids (see eq. [10])
$u$	Mutation rate from allele $A$ to allele $a$
$r_{ma}$	Recombination rate between the ( $M, m$ ) and ( $A, a$ ) locus
$p_m, p_a, D_{ma}$	Frequencies of alleles $m$ and $a$ and linkage disequilibrium between these alleles
$U$	Genomic deleterious mutation rate (multilocus model)
$R$	Genome map length (multilocus model)

competition with genotypes carrying more deleterious alleles. Under this scenario, selection may not affect demography (soft selection): indeed, the fact that some individuals leave fewer offspring (because they are poor competitors) may be compensated by the fact that better competitors leave more offspring. If we consider for a moment that haploids and diploids do not compete against each other ( $\gamma_{dh} = \gamma_{hd} = 0$ ), the fitnesses of haploids with genotype  $i$  for the two scenarios just mentioned may be written as

$$W_h^i = 1 + r_h \left( 1 - \frac{N_h}{K_h} \frac{\omega_h^i}{1 - \beta + \beta \overline{\omega}_h} \right). \quad (2)$$

The same equation holds for diploids, with all h subscripts replaced by d subscripts. In this equation,  $\omega_h^i$  represents the sensitivity to competition of haploid genotype  $i$ , and  $\overline{\omega}_h$  is the average sensitivity to competition of the different haploid genotypes. When  $\beta = 1$ , the genotype with the lowest sensitivity is favored by selection. However, the overall demography is not affected by variation in sensitivities, since the decrease in net growth rate of high-sensitivity genotypes is exactly compensated by the opposite increase in growth rate of low-sensitivity genotypes (the division by  $\overline{\omega}_h$  ensures this behavior). This situation thus represents the soft selection regime mentioned above (selection through difference in competitiveness). When  $\beta = 0$ , the genotype with the lowest

sensitivity is still favored by selection, but selection now affects the overall demography, as the carrying capacity of genotype  $i$  becomes  $K_h/\omega_h^i$ . This situation represents variation among genotypes in their efficiency in using resources, as mentioned above. In fact, changing the parameter  $\beta$  allows one to tune the softness of selection and consider selective scenarios that are intermediate between the two extreme scenarios just described (selection through differences in competitiveness for  $\beta = 1$  or differences in efficiency of using resources for  $\beta = 0$ ).

Now, genetic variation in sensitivity to competition can be combined with partial competition between haploids and diploids introduced in equation (1), yielding the full fitness functions

$$\begin{aligned} W_h^i &= 1 + r_h \left[ 1 - \frac{\omega_h^i}{K_h} \left( \frac{N_h}{1 - \beta + \beta \overline{\omega}_h} + \gamma_{hd} \frac{N_d}{1 - \beta + \beta \overline{\omega}_d} \right) \right], \\ W_d^i &= 1 + r_d \left[ 1 - \frac{\omega_d^i}{K_d} \left( \gamma_{dh} \frac{N_h}{1 - \beta + \beta \overline{\omega}_h} + \frac{N_d}{1 - \beta + \beta \overline{\omega}_d} \right) \right], \end{aligned} \quad (3)$$

where  $W_h^i$  and  $W_d^i$  are the fitnesses of haploids and diploids with genotype  $i$ . Overall, fitness is density dependent as in a classical logistic model but also depends on (1) the degree of competition between haploid and diploids ( $\gamma_{dh}, \gamma_{hd}$  mea-

suring the degree of niche overlap); (2) individual sensitivity to competition, which is genotype dependent ( $\omega_h^i, \omega_d^i$ ); and (3) the degree of softness of selection against individuals with higher sensitivities ( $\beta$ ). In our two-locus model, sensitivities depend on genotype at a single locus with two alleles  $A$  and  $a$  (located at recombination distance  $r_{ma}$  from the modifier locus) and are written as

$$\begin{aligned} \omega_d^{AA} &= 1, \\ \omega_d^{Aa} &= 1 + h\alpha, \\ \omega_d^{aa} &= 1 + \alpha, \\ \omega_h^A &= 1, \\ \omega_h^a &= 1 + \rho\alpha. \end{aligned} \tag{4}$$

The parameter  $\alpha$  thus measures the effect of allele  $a$  in homozygous diploids,  $h$  is the dominance coefficient of  $a$ , and  $\rho$  measures the effect of  $a$  in haploids relative to homozygous diploids. We will treat separately situations where  $\rho > 0$  (selection has the same direction in both phases) and  $\rho < 0$  (ploidy antagonistic selection).

In the two-locus analysis, we assume that the modifier effect and the strength of selection against the deleterious allele are weak ( $\alpha, \delta$  small), so that selection acting at both loci has a weak effect on population size at equilibrium. Assuming that both population size and the frequency of allele  $a$  have reached equilibrium, we express the change in frequency of the modifier  $\Delta p_m$  as a function of the frequencies of alleles  $a$  and  $m$  ( $p_a$  and  $p_m$ ) and of the linkage disequilibrium  $D_{ma}$  ( $D_{ma} = p_m - p_a p_m$ , where  $p_{ma}$  is the frequency of  $ma$  haplotypes). In a second step, we use a quasi-linkage equilibrium (QLE) approximation to express the linkage disequilibrium in terms of allele frequencies; this approximation assumes that selection is weak relative to recombination, so that  $D_{ma}$  equilibrates quickly relative to the rate of change of allele frequencies.

As we will see, these two-locus results can be extrapolated to obtain an expression for the change in frequency of the modifier when deleterious mutations ( $\alpha > 0, \rho > 0$ ) occur at a large number of loci, assuming that the effects of different deleterious alleles on sensitivity to competition are multiplicative (see ‘‘Multilocus Simulations’’). When selection affects the efficiency of resource use ( $\beta = 0$ ), mutations may have a strong effect on population size, which must be taken into account. As shown in the appendix, available online, the equilibrium population size and mean number of deleterious alleles per genome can be obtained by solving numerically a system of equations.

### Multilocus Simulations

We used individual-based simulations (C++ program available in the Dryad Digital Repository: <http://dx.doi.org/10.5061/dryad.40qp5>; Rescan et al. 2015) to test predictions from our analytical model when deleterious mutations ( $\alpha > 0, \rho > 0$ ) segregate at a large number  $L$  of loci. Each individual carries either one or two copies of a chromosome (depending on its ploidy level) represented by a modifier locus (located at the midpoint of the chromosome) and a sequence of  $L$  bits (0 or 1) corresponding to the different loci. Mutations occur at a rate  $U$  per generation: the number of new mutations per chromosome is sampled from a Poisson distribution with parameter  $U$  and are distributed randomly; alleles at mutant loci are switched from 0 to 1 or from 1 to 0. Mutation and back mutation thus occur at the same rate, but back mutations should generally have negligible effects under the parameter values that we use (as deleterious alleles remain at low frequencies). We assume that all deleterious alleles have the same effects on sensitivity to competition ( $\alpha, h, \rho$ ) and that these effects multiply across loci: the sensitivity of a haploid carrying  $n$  deleterious alleles is given by  $\omega_h = (1 + \rho\alpha)^n$ , while the sensitivity of a diploid carrying  $n_{he}$  deleterious alleles in the heterozygous state and  $n_{ho}$  in the homozygous state is given by  $\omega_d = (1 + h\alpha)^{n_{he}}(1 + \alpha)^{n_{ho}}$ .

At the start of each generation, diploid zygotes undergo meiosis or not with probabilities depending on their alleles at the modifier locus. We assume additivity among modifier alleles (which can take any value between 0 and 1): a zygote with alleles coding for rates of diploidy  $d_1$  and  $d_2$  develops as a diploid with probability  $(d_1 + d_2)/2$ . If the individual develops as a haploid, meiosis occurs to produce a recombinant haplotype: the number of crossovers is sampled from a Poisson distribution with parameter  $R$ , while the position of each crossover is sampled from a uniform distribution. The next generation of zygotes is then generated as follows: the number of successful gametes (gametes that will participate to the next generation) produced by each individual is sampled from a Poisson distribution with parameter set to twice the fitness of the individual (calculated as explained above; see also appendix). If the individual is diploid, a recombinant haplotype is generated for each of these gametes, while gametes produced by haploid parents carry the same genotype as the parent. Finally, gametes fuse randomly to form the next generation of zygotes.

During the first few preliminary generations (generally 200), the modifier locus is fixed for an allele coding for an initial diploidy rate  $d_{init}$ , while all selected loci are fixed for allele 0, so that the population can reach its ecological equilibrium in the absence of mutation. Then, deleterious mutations are introduced at rate  $U$  per chromosome (the diploidy rate being still fixed to  $d_{init}$ ), so that the population reaches mutation-selection equilibrium (after generally 2,000 generations). After that, mutations at the modifier locus are introduced at a rate  $\mu_M$  per generation. When a mutation occurs, the rate of diploidy coded by the mu-

tant allele is sampled from a uniform distribution between  $d_{\text{old}} - 0.1$  and  $d_{\text{old}} + 0.1$ , where  $d_{\text{old}}$  is the value of the parent allele; if the new value is negative or higher than 1, it is set to 0 or 1, respectively. Simulations generally lasted 20,000 generations, which was sufficient in most cases for the rate of diploidy to reach equilibrium.

Finally, in additional simulations, we explored the effect of temporal fluctuations in the relative niche sizes of haploids and diploids. For this, we set  $K_d = \overline{K_d}[1 + \lambda \sin(\pi t/\tau)]$  and  $K_h = \overline{K_h}[1 - \lambda \sin(\pi t/\tau)]$  (where  $t$  is time in generations), so that both  $K_d$  and  $K_h$  undergo oscillations with amplitude  $\lambda$  ( $\in [0, 1]$ ) and period  $\tau$ , while the ratio  $K_d/K_h$  also fluctuates over time.

By default, growth rates  $r_h$  and  $r_d$  were set to 1.8 so that population size reaches a stable equilibrium and the population remains viable for values of the deleterious mutation rate  $U$  up to 1 or 2. Carrying capacities  $K_h$  and  $K_d$  were set to 15,000, so that population size reaches values that are compatible to what may be observed in real populations (in particular, large enough so that drift is not too strong). The degree of softness of selection was set to either 0 or 1, in order to contrast the two scenarios mentioned above concerning the effect of selection on demography. Finally, the default values of  $\alpha$  and  $h$  (0.05 and 0.3) generate selection and dominance coefficients of deleterious alleles that are in the range of estimated values from mutation accumulation studies (e.g., Halligan and Keightley 2009; Manna et al. 2011).

### Results

The change in frequency of a modifier allele affecting the probability to undergo selection as a diploid depends on population size, the frequency of allele  $a$  (that may be deleterious in both phases or under antagonistic selection), and linkage disequilibrium between the two loci. We first compute the equilibrium population size and equilibrium frequency of allele  $a$  and then use a QLE approximation to express linkage disequilibrium  $D_{ma}$ . Details of the mathematical derivations are given in the appendix.  $\overline{W}_d$  and  $\overline{W}_h$  stand for the mean fitnesses of diploids and haploids (averages of  $W_d^i$  and  $W_h^i$  given by eq. [3] over all diploids and haploids). All results are derived under the assumption that the modifier effect ( $\delta$ ) and selection acting on allele  $a$  (through its effect  $\alpha$  on sensitivity to competition) are weak.

#### Equilibrium Population Size

Neglecting the effect of the modifier, population size at the next generation is given by  $N' = N[d\overline{W}_d + (1-d)\overline{W}_h]$ . At equilibrium, we thus have

$$d\overline{W}_d + (1-d)\overline{W}_h = 1. \quad (5)$$

Neglecting the effect of selection acting on allele  $a$  and the modifier effect, we have from equation (3)

$$\begin{aligned} \overline{W}_d &= 1 + r_d - NC_d, \\ \overline{W}_h &= 1 + r_h - NC_h, \end{aligned} \quad (6)$$

where  $C_d$  and  $C_h$  measure the strength of competition acting on diploids and haploids:

$$\begin{aligned} C_d &= \frac{r_d}{K_d} \left[ d + (1-d)\gamma_{dh} \right], \\ C_h &= \frac{r_h}{K_h} \left[ (1-d) + d\gamma_{hd} \right]. \end{aligned} \quad (7)$$

In absence of genetic variation for the rate of diploidy and the sensitivity to competition ( $\delta = \alpha = 0$ ), population size reaches an equilibrium value  $\hat{N}_0$ :

$$\hat{N}_0 = \frac{dr_d + (1-d)r_h}{dC_d + (1-d)C_h}. \quad (8)$$

Population size increases with the diploid and haploid carrying capacities  $K_d$  and  $K_h$  and is maximized for intermediate levels of diploidy  $d$  when the haploid and diploid niches are at least partly separated ( $\gamma_{dh}\gamma_{hd} < 1$ ).

#### Equilibrium Frequency of Allele $a$

As discussed in ‘‘Model,’’ we consider two different situations: (1) allele  $a$  is deleterious in both phases ( $\alpha > 0, \rho > 0$ ) and (2) allele  $a$  is beneficial in one phase but deleterious in the other (ploidy antagonistic selection;  $\rho < 0$ ). In the first case, we assume that allele  $a$  is generated by mutation from allele  $A$  at a rate  $u$  per generation (and neglect back mutation), while in the second case, we focus on situations where polymorphism is maintained by selection only, and we neglect mutation. In both situations, we assume that population size is sufficiently large so that genetic drift can be ignored. As shown in the appendix, a first-order approximation for the change in frequency of  $a$  over one generation is given by

$$\Delta p_a \approx \{d s_d [h + (1-2h)p_a] + (1-d)s_h\} p_a q_a + u q_a, \quad (9)$$

where  $s_d$  and  $s_h$  measure the strength of selection against allele  $a$  in haploids and diploids, respectively, and  $q_a = 1 - p_a$ . To the first order in  $\alpha$ ,  $s_d$  and  $s_h$  are given by

$$\begin{aligned} s_h &= \rho \alpha NC_h, \\ s_d &= \alpha NC_d. \end{aligned} \quad (10)$$



As expected, density-dependent selection becomes more intense when competition is harsher (as measured by  $NC_h$ ,  $NC_d$ ); however, for a given value of  $N$ ,  $s_h$  and  $s_d$  are not affected by the degree of softness of selection ( $\beta$ ).

From equation (9), one obtains three possible equilibria for  $p_a$ . The first,  $p_a = 1$ , is trivial and corresponds to the fixation of allele  $a$ . The second equilibrium corresponds to mutation-selection balance when  $a$  is deleterious in both phases. The third corresponds to polymorphism maintained by antagonistic selection ( $\rho < 0$ ).

*Mutation-Selection Balance.* Assuming that  $p_a$  is small at equilibrium, we can neglect terms in  $p_a^2$  in equation (9). Furthermore, we can replace  $N$  by  $\hat{N}_0$  in equation (10) to express  $\Delta p_a$  to the first order in  $\alpha$  at the demographic equilibrium, which yields

$$p_a^{\text{del}} = \frac{u}{dh s_d + (1-d)s_h} = \frac{u}{\hat{N}_0 \alpha [dh C_d + (1-d)\rho C_h]} \quad (11)$$

This equilibrium frequency takes the same form as in Otto and Goldstein's (1992) model and decreases as the intensity of competition among individuals increases. In a purely haploid population ( $d = 0$ ), we have  $p_a^{\text{del}} = u/s_h$  with  $s_h = \rho \alpha r_h$ , while in a purely diploid population ( $d = 1$ ),  $p_a^{\text{del}} = u/h s_d$ , with  $s_d = \alpha r_d$  (note that baseline fecundities  $r_h$  and  $r_d$  determine the intensity of competition among haploid or diploid offspring in populations at demographic equilibrium).

The previous expressions neglect the effect of the deleterious allele on population size at equilibrium. While this is legitimate in the case of a single mutation, deleterious alleles occurring at many loci are more likely to affect population size (in particular when selection acts through differences in the efficiency of resource use, i.e., small  $\beta$ ). In the appendix, we consider a situation where all deleterious alleles have the same effect ( $\alpha, \rho, h$ ) and where epistasis is absent. Neglecting linkage disequilibria among loci, the equilibrium values of population size and of the mean number of mutations per haploid genome can be obtained by solving numerically a system of two equations. As expected, genetic variation in competitiveness ( $\beta = 1$ ) has virtually no effect on population size. On the contrary, variation in the efficiency of resource use ( $\beta = 0$ ) has much stronger effects, which are reasonably well captured by our analytical results (fig. A1, available online).

*Antagonistic Selection.* Ploidally antagonistic selection may maintain polymorphism in the absence of recurrent mutation. From equation (9), we have at equilibrium

$$p_a^{\text{anta}} = \frac{dh C_d + (1-d)\rho C_h}{(2h-1)d C_d} \quad (12)$$

This equilibrium is biologically relevant (i.e., between 0 and 1) if

$$-\frac{d C_d}{(1-d)C_h} \max(1-h, h) < \rho < -\frac{d C_d}{(1-d)C_h} \min(1-h, h).$$

It is stable if the allele that is disfavored in diploids ( $a$  if  $\alpha > 0$ ,  $A$  if  $\alpha < 0$ ) is partially recessive. If allele  $a$  is totally recessive (dominant if  $\alpha < 0$ ) and if the population is mainly diploid, the parameter range allowing a stable polymorphism is wide, while it tends to shrink when the proportion of haploids increases (small  $d$ ), when competition in haploids is stronger ( $C_h > C_d$ ), or when mutations become more additive ( $h$  close to  $1/2$ ), which corroborates previous results by Ewing (1977) and Immler et al. (2012).

### Evolution of the Ploidy Level

*Change in Frequency at the Modifier Locus.* To leading order in the effects of alleles  $m$  and  $a$  ( $\delta$  and  $\alpha$ ), the change in frequency of the modifier allele  $m$  can be decomposed into two terms (for derivation, see appendix):

$$\Delta p_m = \delta h_m^* (\overline{W}_d - \overline{W}_h) p_m q_m + [d s_d h_a^* + (1-d)(1-r_{ma})s_h] D_{ma}, \quad (13)$$

where  $q_m = 1 - p_m$ ,  $h_m^* = h_m(1 - p_m) + (1 - h_m)p_m$  (simplifying to  $1/2$  when  $h_m = 1/2$ ), and  $h_a^* = h(1 - p_a) + (1 - h)p_a$  (which is approximately  $h$  when  $p_a$  is small). The first term of equation (13) is proportional to the difference in mean fitness between haploids and diploids and favors diploidy when  $\overline{W}_d > \overline{W}_h$ . The second term is proportional to  $D_{ma}$  and represents indirect selection on  $m$  through its association with allele  $a$ ; when the direction of selection on allele  $a$  is the same in both phases, this term disfavors the modifier allele that tends to be associated with the deleterious allele. Following previous models (e.g., Cailleau et al. 2010), we will denote the first term direct selection (selection to produce more of the phase that has the highest mean fitness), while the second term will be denoted indirect selection (effect of the linkage disequilibrium).

*Direct Selection.* Direct selection in turn decomposes into two terms: a term of order  $\delta$  representing differences in mean fitness between haploids and diploids due to different ecological parameters, and a term of order  $\delta \alpha p_a q_a$  representing additional differences in mean fitness due to the selection acting at the locus affecting the sensitivity to competition, for example, increased mean fitness of diploids due to the fact that recessive deleterious alleles are partially masked (Otto and Goldstein 1992; Cailleau et al. 2010). This second term is generally negligible relative to the first when only a single

locus segregates for a deleterious allele (as shown by eq. [11],  $\alpha p_a q_a$  is of order  $u$  at mutation-selection balance); however, we will see that the overall effect of deleterious alleles on mean fitnesses may become more important when they segregate at many loci.

*Effect of ecological differences between haploids and diploids.* In the absence of selection at the second locus ( $\alpha = 0$  or  $p_a q_a = 0$ ), our model corresponds to a simplified version of Hughes and Otto's (1999) model and confirms that ecological differences between haploids and diploids generate direct selection on the modifier locus. From equations (6) and (7), one obtains

$$\overline{W}_d - \overline{W}_h = \frac{C_d C_h}{d C_d + (1-d) C_h} \left( \frac{r_h}{C_h} - \frac{r_d}{C_d} \right) = S_{eco}, \quad (14)$$

while the change in frequency of the modifier simplifies to  $\Delta p_m = \delta h_m S_{eco} p_m q_m$ . The term  $S_{eco}$  thus represents the strength of selection on the modifier generated by ecological differences between phases (favoring the phase where fecundity is highest and competition lowest). This term cancels when  $r_d/C_d = r_h/C_h$ , which occurs when the rate of diploidy  $d$  equals

$$d_0 = \frac{K_d - K_h \gamma_{dh}}{K_d(1 - \gamma_{hd}) + K_h(1 - \gamma_{dh})}. \quad (15)$$

In addition,

$$\left. \frac{d(S_{eco})}{d(d)} \right|_{d_0} < 0,$$

and  $d_0$  thus represents the evolutionarily stable rate of diploidy (evolutionarily stable strategy [ESS]; Maynard Smith 1982) when it is comprised between 0 and 1. We can note that the ratios  $r_d/C_d$  and  $r_h/C_h$  are independent of  $r_d$  and  $r_h$  (see eq. [7]); therefore, differences in the baseline fecundity of haploids and diploids do not affect the sign of  $S_{eco}$  or the ESS. Furthermore, carrying capacities  $K_d$  and  $K_h$  affect only  $d_0$  through the ratio  $K_d/K_h$ . With weak or no ecological differentiation ( $\gamma_{dh}$  and  $\gamma_{hd}$  close to 1), the population should evolve toward the phase with the highest carrying capacity (i.e., most efficient resource usage). Confirming Hughes and Otto's (1999) results, we predict that intermediate rates of diploidy may be maintained when the ecological niches of haploids and diploids are sufficiently differentiated (see fig. 1A). In this situation, Hughes and Otto (1999) showed that the population may consist of a mixture of genotypes coding for different rates of diploidy (as long as this combination of genotypes fully exploits the available resources). Indeed, figure 1B shows that when  $\gamma_{dh} = \gamma_{hd} = 0.5$  and

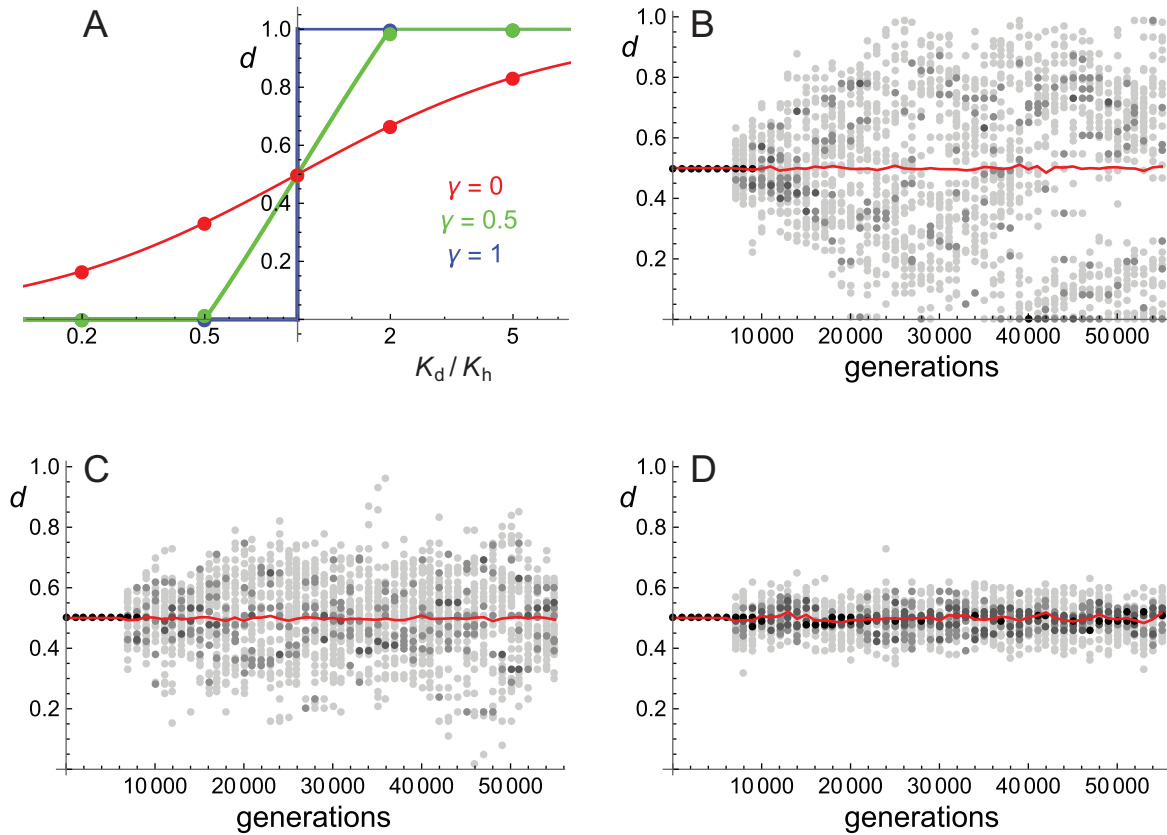
$K_d = K_h$  (so that the predicted ESS rate of diploidy is  $d_0 = 0.5$ ), a high level of polymorphism is maintained at the modifier locus: although the average value of  $d$  is 0.5, many alleles coding for values between 0 and 1 coexist in the population. In a stable environment, niche differentiation between haploids and diploids therefore does not lead to the fixation of a strategy corresponding to a biphasic life cycle (intermediate value of  $d$ ). However, results from bet-hedging theory (e.g., Philippi and Seger 1989) suggest that genotypes coding for intermediate values of  $d$  may be favored when the relative abundance of resources used by haploids and diploids fluctuate over time (indeed, producing both haploid and diploid offspring may be seen as a bet-hedging strategy). As shown in figure 1C and 1D, this prediction is confirmed by introducing fluctuations in the relative sizes of the haploid and diploid niches ( $K_d/K_h$ ) over time: as the amplitude of these fluctuations increases, the distribution of values of  $d$  in the population narrows around  $d = 0.5$  (decreasing the period of oscillations also reduces the variance in  $d$ ; simulations performed with  $\tau \in \{1, 2, 4, 8, 16, 64\}$  and  $\lambda = 1/15$ , not shown).

*Effect of genetic variation in the sensitivity to competition.* Genetic variation for fitness (e.g., due to recurrent deleterious mutations) may not have the same quantitative effect on the mean fitness of haploid and diploid individuals, generating direct selection on ploidy even in the absence of ecological difference between haploids and diploids (Otto and Goldstein 1992). This introduces a new component to the direct selection term, which becomes  $\delta h_m^* (S_{eco} + S_{a,direct}) p_m q_m$ , where  $S_{a,direct}$  is the effect of allele  $a$  on  $\overline{W}_d - \overline{W}_h$ . At mutation-selection balance,  $S_{a,direct}$  is given by

$$S_{a,direct} \approx \frac{\alpha(\rho - 2h)C_d C_h}{d C_d + (1-d)C_h} \times \left\{ (1 - \beta) + \beta \frac{d^2 \gamma_{hd} + (1-d)^2 \gamma_{dh} + 2d(1-d)\gamma_{dh}\gamma_{hd}}{(1-d + d\gamma_{hd})[d + (1-d)\gamma_{dh}]} \right\} \hat{N}_0 P_a^{del} \quad (16)$$

(see appendix).

Interestingly, the sign of  $S_{a,direct}$  is entirely determined by the sign of  $\alpha(\rho - 2h)$  (because  $d C_d + (1-d)C_h$  and the term within curly brackets are always positive), so that ecological parameters ( $\gamma_i$ ,  $\beta$ ,  $r_i$ , and  $K_i$ ) modulate only the strength of  $S_{a,direct}$ . Equation (16) bears some similarity with previous results on the benefits of diploidy stemming from masking of deleterious alleles (Otto and Goldstein 1992); in particular, when  $\rho = 1$  (so that allele  $a$  has the same effect on the sensitivity to competition of haploids and homozygous diploids), diploidy is favored when the deleterious allele is partially recessive ( $h < 1/2$ ). However, in Otto and Goldstein's model, the sign of direct selection is deter-



**Figure 1:** A, Evolutionarily stable strategy rate of diploidy ( $d_{eq}$ ) as a function of the ratio of carrying capacities  $K_d/K_h$  and for different levels of differentiation between phases ( $\gamma_{dh} = \gamma_{hd} = \gamma$ ). Lines, analytical prediction in the absence of deleterious mutations (eq. [15]). Circles, multilocus simulations in the absence of deleterious mutations. Blue,  $\gamma = 1$ ; green,  $\gamma = 0.5$ ; red,  $\gamma = 0$ . B–D, Distribution of alleles present at the modifier locus throughout the simulation, in the absence of deleterious mutation, with  $K_d = K_h = 15,000$ ,  $r_d = r_h = 1.8$ , and  $\gamma_{hd} = \gamma_{dh} = 0.5$ . Shading corresponds to the frequencies  $f$  of different ranges of values of  $d$  in the population, from light gray to black:  $f \in [1\%, 5\%]$ ,  $f \in [5\%, 10\%]$ ,  $f \in [10\%, 20\%]$ , and  $f \geq 20\%$ . B, When the environment stays constant, a large range of values of  $d$  is maintained in the population. C, Fluctuations of the relative sizes of the haploid and the diploid niches of low amplitude ( $\lambda = 1/15, \tau = 4$ ) narrow this range. D, Increasing the amplitude of fluctuations ( $\lambda = 1/2, \tau = 4$ ) further narrows the range around the ESS value of  $d$ . In all cases, the average value of  $d$  in the population stays near 0.5 (red lines).

mined by the fitness effect of the deleterious allele in haploids and heterozygous diploids:  $s_h - 2hs_d$ , which should thus depend on ecological parameters (given that  $s_h = \rho\alpha NC_h$  and  $s_d = \alpha NC_d$ ). By contrast, in our model, a deleterious allele may generate direct selection for a given ploidy phase even if it has a stronger fitness effect in that phase (provided that  $s_h - 2hs_d$  and  $\rho - 2h$  have opposite signs). This seemingly surprising result comes from the fact that in our model of density-dependent selection, there is not a simple correspondence between the fitness effect of adding a mutation in a given haploid or diploid ( $s_h$  or  $s_d$ , to the first order in  $\alpha$ ) and the mean fitness of haploids and diploids at equilibrium.

When polymorphism at the selected locus is maintained by ploidy antagonistic selection, terms in  $p_a^2$  cannot be neglected, and the term  $\rho - 2h$  in equation (16) is replaced

by  $\rho - 2h_a^* = \rho - h(1 - p_a) - (1 - h)p_a$ , which is always negative (recall that  $\rho < 0$  under antagonistic selection). Therefore,  $S_{a,direct}$  has the sign of  $-\alpha$ : direct selection favors the phase in which ploidy antagonistic selection increases mean fitness (haploidy if  $\alpha > 0$  and diploidy if  $\alpha < 0$ ).

Finally, as expected,  $S_{a,direct}$  vanishes when the ecological niches of haploids and diploids are fully disjoint ( $\gamma_{dh} = \gamma_{hd} = 0$ ) and selection is soft (selection through differences in competitiveness:  $\beta = 1$ ; see eq. [16]). When deleterious mutations impact resource use ( $\beta = 0$ ), however,  $S_{a,direct}$  does not depend on the degree of overlap between the haploid and diploid niches: mutations generate a direct selection component favoring the phase whose carrying capacity is least impacted by the presence of deleterious mutations. Between these two extreme situations, equation (16) indicates

that direct selection on the modifier decreases linearly with  $\beta$  (as long as  $\gamma_{hd}\gamma_{dh} \leq 1$ ).

*Indirect Selection.* Finally, genetic variation for fitness generates indirect selection (through the linkage disequilibrium between the modifier and the selected locus) favoring the ploidy phase in which selection is more efficient. From equation (13), the change in frequency of the modifier is affected by linkage disequilibrium ( $D_{ma}$ ) through the term

$$S_{a,\text{indirect}} = [ds_d h_a^* + (1-d)(1-r_{ma})s_h]D_{ma}. \quad (17)$$

At QLE, and to the first order in  $\alpha$  and  $\delta$ ,  $D_{ma}$  is given by

$$D_{ma} \approx \frac{\delta h_m^*}{r_{ma}} \left( \frac{s_h}{\bar{W}_h} - \frac{h_a^* s_d}{\bar{W}_d} \right) \bar{W}_h \bar{W}_d p q_{ma} \quad (18)$$

(for derivation, see appendix), where  $p q_{ma} = p_m q_m p_a q_a$ ,  $r_{ma}$  is the recombination rate, and  $\bar{W}_h$  and  $\bar{W}_d$  are given by equation (6) (replacing  $N$  by  $\bar{N}_0$ ). When allele  $a$  is deleterious in both phases, it thus tends to be associated with the modifier allele increasing the phase in which selection is less efficient (diploidy if  $h s_d / \bar{W}_d < s_h / \bar{W}_h$ , haploidy otherwise). When the rate of diploidy  $d$  is such that the direct selection term cancels (i.e., when  $\bar{W}_d = \bar{W}_h$ ),  $D_{ma}$  has the sign of  $\delta(s_h - h s_d)$ . Importantly, and in contrast to the direct selection term  $S_{a,\text{direct}}$  discussed in ‘‘Direct Selection,’’ the sign of indirect selection depends on ecological parameters  $r_b$ ,  $\gamma_b$ , and  $K_i$  (through  $s_d$  and  $s_h$ ): it is the effect of the deleterious allele on fitness (and not on sensitivity to competition) that matters.

Under ploidy antagonistic selection ( $\alpha < 0$ ), inserting the expression of the equilibrium frequency of  $a$  given by equation (12) into equation (18) yields

$$D_{ma} \approx \frac{\delta h_m^*}{d r_{ma}} s_h p q_{ma}, \quad (19)$$

indicating that the modifier allele increasing a given ploidy level tends to be associated with the allele that is favored in this ploidy level; that is,  $D_{ma} > 0$  if  $m$  increases diploidy and  $a$  is advantageous in diploids ( $s_h < 0$ ,  $s_d > 0$ ) or if  $m$  increases haploidy and  $a$  is advantageous in haploids ( $s_h > 0$ ,  $s_d < 0$ ). From equation (17), the indirect selection term is then

$$S_{a,\text{indirect}} \approx (1-d)r_{ma}s_h D_{ma}, \quad (20)$$

which has the sign of  $d_m$ ; therefore, indirect selection generated by ploidy antagonistic polymorphisms always favor modifier alleles that increase diploidy. This result can be understood as follows: during selection, each modifier allele benefits from the increase in frequency of the selected allele with which it is associated (within the ploidy phase where this allele is favored); however, this hitchhiking effect is weaker for the allele that increases haploidy, because

recombination occurs before haploid selection (reducing the linkage disequilibrium before selection).

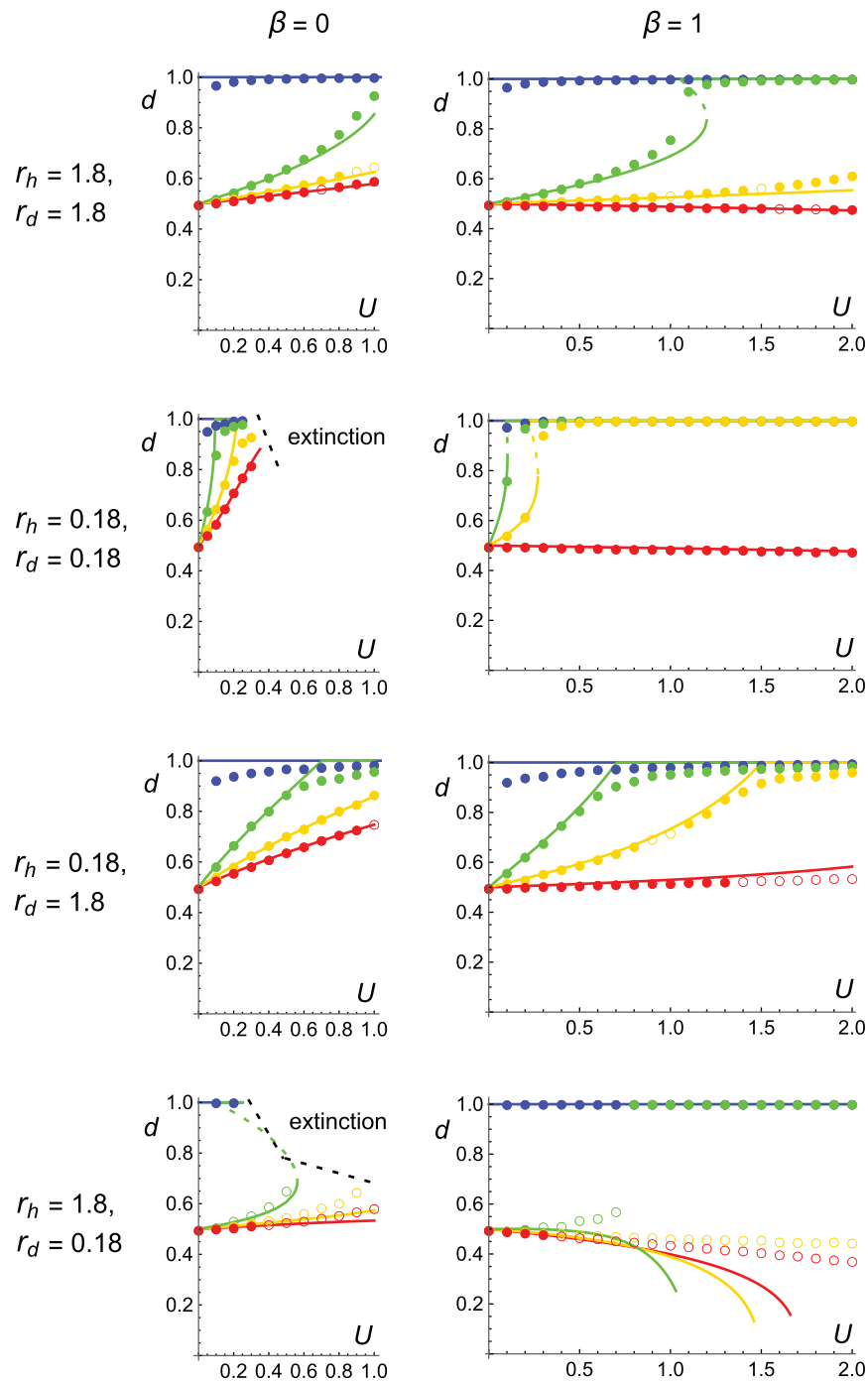
As can be seen from the equations above, indirect selection is not affected by the parameter  $\beta$  (indicating the degree of softness of selection). Under complete differentiation of the haploid and diploid niches ( $\gamma_{dh} = \gamma_{hd} = 0$ ) and soft selection ( $\beta = 1$ ), the selected locus therefore affects the evolution of the modifier through indirect selection only, since the direct selection term  $S_{a,\text{direct}}$  vanishes in this situation (eq. [16]). In other situations, the effect of indirect selection (of order  $\delta\alpha^2 p_a q_a$ ) is expected to be weak relative to direct selection ( $S_{a,\text{direct}}$ , of order  $\delta\alpha p_a q_a$ ). However, stronger effects of indirect selection may arise at mutation-selection balance either when linkage is tight (as shown previously in Otto and Goldstein 1992) or when ecological parameters of haploids and diploids (in particular, their baseline fecundities  $r_h$  and  $r_d$ ) are very different, so that density-dependent selection is much stronger in one phase than in the other (since the strength of indirect selection is proportional to  $\rho/C_d - h/C_h$ ).

#### *Extrapolation to Many Loci at Mutation-Selection Balance.*

As discussed previously, the effect of a single deleterious allele should generally be negligible compared with direct selection stemming from ecological differences between haploids and diploids (unless these ecological differences are very slight). However, the overall effect of deleterious alleles occurring at many loci could be more important. To explore that, we extrapolated results from our two-locus model to an arbitrary number of selected loci, assuming a deleterious mutation rate  $U$  per haploid genome per generation. Neglecting linkage disequilibria between loci at which deleterious alleles are segregating, the overall effect of all selected loci on the change in frequency of the modifier can be approximated by the sum of the individual effects of these loci (provided by the two-locus analysis above). When the average number of deleterious alleles per genome ( $n$ ) is large (so that  $s n$  may be of order 1), more accurate results can be obtained numerically as explained in the appendix.

Figure 2 compares the ESS rate of diploidy predicted by our analytical model with multilocus simulation results (with deleterious alleles occurring at 5,000 loci and a map length of 10 Morgans). Note that analytical extrapolations assume unlinked loci rather than a continuous genetic map, since our QLE results (eq. [18]) diverge for tightly linked loci. However, simulations indicate that linkage does not have much effect on the ESS rate of diploidy for the parameter values used in the figures (simulating free recombination yields very similar results; not shown).

In the absence of genetic variation for sensitivity to competition ( $U = 0$ ), the evolution of ploidy is only driven by ecological differences between haploids and diploids ( $S_{\text{eco}}$ ). Because  $K_d = K_h$  while  $\gamma_{dh} = \gamma_{hd} = \gamma$  for all graphs of



**Figure 2:** Evolutionarily stable strategy ploidy level as a function of the mutation rate  $U$  when mutations affect the efficiency of resource use ( $\beta = 0$ ) or the competitiveness ( $\beta = 1$ ). Lines, analytical results from equations (13), (A5), (A6), and (A7) (eqq. [A5], [A6], and [A7] in the appendix, available online); dashed lines correspond to unstable equilibria predicted by the model, while solid lines correspond to stable equilibria. Circles, multilocus simulations with 5,000 loci under selection and a map length of 10 Morgans. Simulations are run for 20,000 generations, with a mutation rate of  $10^{-2}$  at the modifier locus. Open circles correspond to cases where evolutionary branching occurred during the simulation. Blue,  $\gamma = 1$ ; green,  $\gamma = 0.5$ ; yellow,  $\gamma = 0.2$ ; red,  $\gamma = 0$ . Other parameters values:  $K_d = K_h = 15,000$ ,  $\rho = 1$ ,  $h = 0.3$ ,  $\alpha = 0.05$ . Error bars (computed using the spAMM1.2.4 R package [Rousset and Ferdy 2014] to deal with autocorrelated data) were smaller than the size of symbols in most cases and are thus not shown.

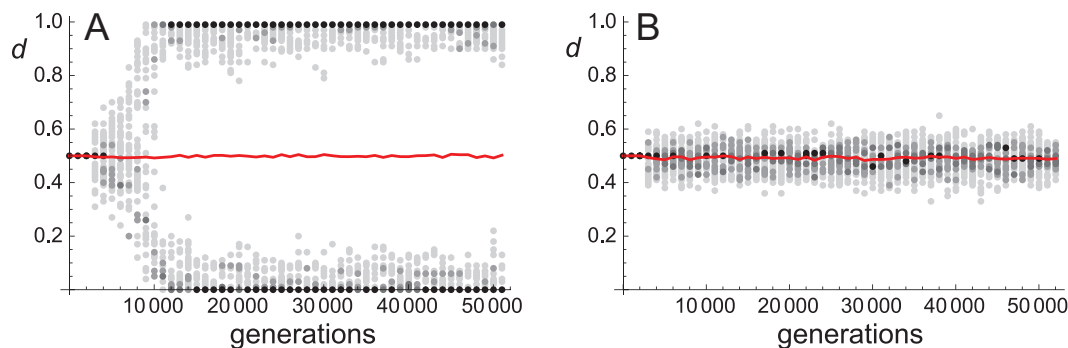
figure 2, the evolutionarily stable rate of diploidy is  $d = 0.5$  if  $\gamma < 1$ , while selection on ploidy vanishes when  $\gamma = 1$ . Indeed, we can see on figure 2 that  $d$  always converges to 0.5 as  $U$  tends to 0, as long as  $\gamma < 1$ .

When  $U > 0$ , we have seen that deleterious alleles generate direct selection for diploidy (term  $S_{a,direct}$ ) whenever  $\rho > 2h$  (and selection for haploidy otherwise), which vanishes when selection is soft ( $\beta = 1$ ) and haploids and diploids occupy totally separated niches ( $\gamma = 0$ ). In figure 2, deleterious alleles have the same effect on sensitivity to competition in haploids and homozygous diploids ( $\rho = 1$ ) and are partially recessive ( $h = 0.3$ ), generating direct selection for diploidy. Increasing the degree of niche overlap ( $\gamma$ ) or the mutation rate  $U$  generally increases the relative effect of deleterious alleles ( $S_{a,direct}$ ) over ecological differentiation ( $S_{eco}$ ) and displaces the ESS rate of diploidy  $d$  from 0.5 toward 1. Interestingly, lower baseline fecundities ( $r_d, r_h = 0.18$ ) also increase the relative effect of  $S_{a,direct}$ , leading to higher rates of diploidy. Indeed, decreasing baseline fecundities decreases the strength of the ecological component of selection  $S_{eco}$  by reducing competition between individuals (see eq. [14]), while the direct selection advantage generated by deleterious alleles ( $S_{a,direct}$ ) is less affected by  $r_d$  and  $r_h$  because of the fact that deleterious alleles are more frequent when fecundities are lower (eq. [11]).

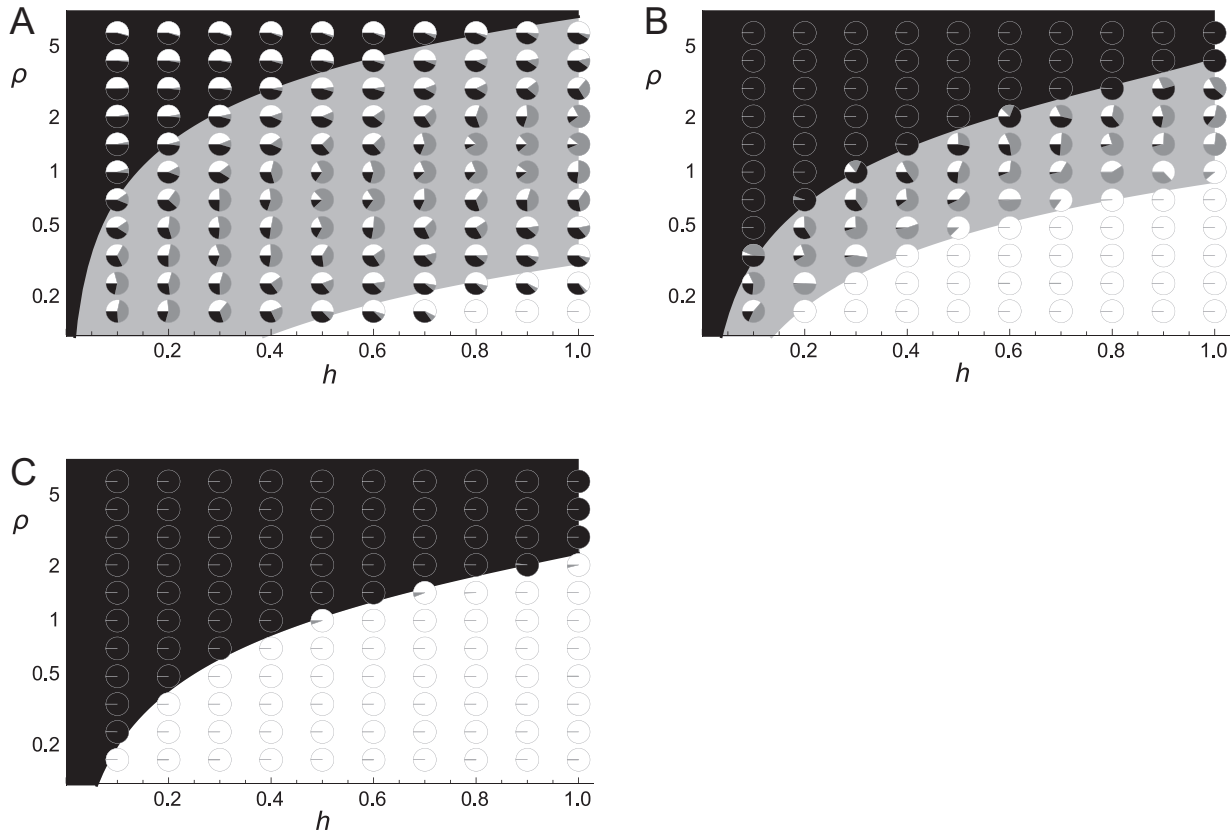
Finally, indirect selection generated by deleterious mutations ( $S_{a,indirect}$ ) is generally negligible but causes slight displacements from  $d = 0.5$  when  $S_{a,direct}$  vanishes; that is, selection is soft ( $\beta = 1$ ), and haploids and diploids occupy totally separated niches ( $\gamma = 0$ ; red lines in fig. 2). In this case, deleterious alleles tend to favor haploidy, unless selection is stronger in diploids ( $r_d \gg r_h$ ; see eqs. [7], [10]). Although our analytical model predicts stronger deviations

toward haploidy when  $r_d \ll r_h$  and  $U$  is large,  $d$  remains close to 0.5 in the simulations (this discrepancy may be due to the fact that our analytical model neglects higher-order associations between selected loci).

*Evolutionary Branching.* As we have seen before, high polymorphism may be maintained at equilibrium at the modifier locus under ecological selection alone ( $U = 0$ ; fig. 1B). A different pattern can be observed in the presence of deleterious alleles ( $U > 0$ ), however. An example is shown in figure 3A: in a stable environment ( $K_h, K_d$  constant), evolutionary branching occurs once the population has reached the ESS rate of diploidy  $d$  (here close to 0.5), and a proportion  $d$  of the modifier alleles evolves toward 1 (diploidy) while a proportion  $1 - d$  evolves toward 0 (haploidy); note that the average proportion of diploids in the population remains unchanged. As illustrated in figure 4, this evolutionary branching occurs more easily when selection against deleterious alleles is stronger in one phase than in the other ( $s_h - hs_d$  large in absolute value; upper left/lower right in fig. 4A). This effect may be understood as follows. A modifier allele coding for an intermediate value of  $d$  undergoes selection alternatively in the diploid and the haploid phases and therefore experiences periods of higher fitness (in the phase where mutations have a weaker effect) followed by periods of lower fitness (in the phase where mutations have a stronger effect). These temporal fluctuations reduce geometric mean fitness and favor modifiers that tend to stay in the same phase (so that selection is always weak or always strong). However, part of the benefit of this specialization is lost under random mating (since heterozygous genotypes at the modifier locus are produced each generation), suggesting that assortative mating should be favored under this sce-



**Figure 3:** Distribution of effects of alleles at the modifier locus through time (50,000 generations) when deleterious mutations occur at rate  $U = 1$  in a stable (A) or fluctuating (B) environment. In this example, deleterious mutations affect competitiveness ( $\beta = 1$ ), and there is limited niche overlap ( $\gamma_{dh} = \gamma_{hd} = 0.05$ ). In both cases, the average rate of diploidy at equilibrium is close to 0.5 (red lines). A, When the environment stays constant ( $\lambda = 0$ ), evolutionary branching occurs, and at equilibrium, only alleles coding for values of  $d$  close to either 0 or 1 are maintained in the population. B, Fluctuations of the relative sizes of the haploid and diploid niches ( $\lambda = 1/2, \tau = 4$ ) prevent this branching by favoring genotypes coding for intermediate rates of diploidy. Parameters values:  $U = 1, K_d = K_h = 15,000, r_d = 1.8, r_h = 1.8, \rho = 1, h = 0.3, \alpha = 0.05$ , mutation rate at the modifier locus:  $10^{-2}$ .



**Figure 4:** Evolution of the ploidy level when mutations have differential effects between phases and with different degrees of niche overlap under soft selection ( $\beta = 1$ ). *A*,  $\gamma_{dh} = \gamma_{hd} = 0.05$ . *B*,  $\gamma_{dh} = \gamma_{hd} = 0.5$ . *C*,  $\gamma_{dh} = \gamma_{hd} = 1$ . On the *X*-axes, dominance ( $h$ ) of deleterious mutations varies between 0 (mutations are fully recessive) and 1 (mutations are fully dominant). On *Y*-axes, the relative effect of mutations in haploids compared with homozygote diploids ( $\rho$ ) varies between 1/6 and 6 (shown on a log scale). Background color corresponds to analytical predictions: evolution toward diploidy (black), haploidy (white), or maintenance of an intermediate rate of diploidy (gray). Pie charts represent the distribution of modifier alleles in simulated populations after 20,000 generations of evolution, with a mutation rate of  $10^{-3}$  at the modifier locus (black,  $d < 0.1$ ; gray,  $d \in [0.1, 0.9]$ ; white,  $d > 0.9$ ). Other parameters values:  $U = 1$ ,  $K_d = K_h = 15,000$ ,  $r_d = r_h = 1.8$ ,  $\alpha = 0.05$ .

nario. For the parameter values used in figure 4, branching was not observed when the strength of selection against deleterious alleles was similar in haploids and diploids; however, in several cases, we ran simulations over larger numbers of generations and observed branching. Similarly, increasing the mutation rate at the modifier locus (so that evolution occurs more rapidly) greatly increases the number of cases where branching occurs, and this suggests that it may eventually occur in most cases where  $U > 0$  and where an intermediate value of  $d$  is predicted at the ESS. This is confirmed in figure 2 using a mutation rate of 0.01 at the modifier locus: evolutionary branching occurs in many cases when the average value of  $d$  in the population at equilibrium is intermediate, in particular when  $s_h - hs_d$  is higher in absolute value ( $r_d = 1.8$ ,  $r_h = 0.18$ ); it is possible that branching would occur in more cases if the simulations could run over larger numbers of generations. Finally, as we have seen in the ab-

sence of deleterious mutation (fig. 1), temporal fluctuations in the relative sizes of the haploid and diploid niches ( $K_h$ ,  $K_d$ ) may inhibit this branching phenomenon (as illustrated in fig. 3*B*) by favoring intermediate values of  $d$  (which may be seen as a bet-hedging strategy).

### Discussion

Different types of selective forces may affect the evolution of the relative degree of development of the haploid and diploid phases of the eukaryotic sexual life cycle. In the presence of genetic variation in fitness, changing the ploidy level of individuals may affect their mean fitness as a result of dominance interactions among selected alleles (in particular, diploidy benefits from an immediate advantage in the presence of partially recessive deleterious alleles). However, ploidy also affects the genetic variance among individuals

and thus the efficiency of natural selection: in general, selection is expected to be more efficient among haploids, in which all mutations are expressed. As shown by Otto and Goldstein (1992) and Otto and Marks (1996), either haploid or diploid life cycles are expected to be favored under the combined action of these two forces, depending in particular on the importance of recombination within genomes and on the mating system. However, an important assumption of these genetic models is that haploids and diploids have the same ecological properties, being fully equivalent in terms of survival, fecundity, and competition exerted on other individuals in the absence of genetic variation in fitness. As shown by Hughes and Otto (1999), relaxing this hypothesis introduces direct selection on life cycle variants and can explain the evolutionary stability of biphasic life cycles when haploids and diploids have different ecological niches: indeed, under density-dependent competition, an individual entering a more vacant niche has greater chances to survive and contribute to the next generation. Furthermore, ecological niche differences between haploids and diploids may affect relative fitness effect of deleterious mutations in the two phases, in turn affecting the predictions from the genetic models cited above (in which mutations are assumed to have the same fitness effect in haploids and homozygote diploids).

In this article, we used a simple demographic model to explore the interaction between the effects of ecological differentiation and of genetic variation in fitness on the evolution of ploidy cycles. We focused on a scenario where selection is density dependent, with deleterious alleles reducing the success of individuals when competing with conspecifics. This particular form of selection is certainly restricted to a subset of all possible deleterious alleles, with the effect of most mutations causing developmental abnormality or lethality being probably little affected by population density. Nevertheless, it appears likely that the deleterious effect of a substantial proportion of mutations may increase with the strength of intraspecific competition: in particular, several experimental studies (e.g., table 2 in Agrawal and Whitlock 2010) reported stronger average effects of deleterious alleles at higher density, while other studies measured stronger inbreeding depression at higher densities, which may possibly be due to stronger effects of deleterious alleles (e.g., Cheptou et al. 2000; Meagher et al. 2000). Exploring the effect of density-dependent selection appears particularly interesting in the context of models combining ecological and genetical effects, since the interplay between these different components is not intuitively obvious.

In our model, the evolution of a modifier gene affecting the ploidy of individuals is controlled by three different effects: (1) differences in mean fitness between ploidy levels generated by intrinsic ecological differences between haploid and diploid individuals (independently of their geno-

type); (2) additional differences in mean fitness caused by deleterious alleles, which may have different effects on the sensitivity to competition in haploids and homozygous diploids; and (3) differences among phases in the efficiency of selection against these deleterious alleles. As we have seen, the results show that these effects scale differently with the strength of competition within and between ploidy phases. In particular, at demographic equilibrium, the strength of ecological selection depends on differences in the carrying capacities of haploids and diploids (reflecting differences in the availability of resources and/or in the efficiency with which individuals use these resources), on the degree of overlap between their ecological niches, and on the average baseline fecundities of individuals ( $r_d$  and  $r_h$ , controlling the intensity of competition among offspring). By contrast, changing baseline fecundities has little effect on differences in mean fitness caused by deleterious alleles. As a consequence, the relative importance of effects 1 and 2 depends on these baseline fecundities, with effect 1 being relatively stronger when  $r_d$  and  $r_h$  are higher and relatively weaker when  $r_d$  and  $r_h$  are lower. Therefore, we predict that biphasic life cycles should be more easily maintained (by ecological differentiation among phases) when the intensity of competition among offspring is strong, while deleterious alleles affecting the sensitivity to competition of individuals may have stronger destabilizing effects (favoring either haploid or diploid life cycles) when lower fecundities reduce the intensity of competition (fig. 2). It would thus be interesting to test whether biphasic (haploid-diploid) life cycles tend to be associated with higher intensities of competition among offspring in phylogenetic groups where different types of life cycles coexist (such as algae).

Another result is that ecological differences between haploids and diploids may affect the relative importance of the two components of selection on ploidy generated by deleterious alleles (effects 2 and 3). In our model, the effect of deleterious alleles on the sensitivity of individuals to competition determines whether they generate a direct selection advantage for haploidy or diploidy (effect 2). By contrast, whether indirect selection (effect 3) favors haploidy or diploidy depends on the effect of deleterious alleles on the overall fitness of individuals (number of offspring produced), which under density-dependent selection is affected by the ecological parameters of haploids and diploids. As a consequence, a deleterious allele having the same effect on the competitiveness of haploids and homozygous diploids ( $\rho = 1$ ) would favor diploidy through a masking advantage if it is partially recessive ( $h < 1/2$ ) and could also favor diploidy through a purging advantage if competition is stronger among diploids, leading to stronger density-dependent selection ( $r_d h > r_h$ ). More generally, these results outline the fact that selection may not necessarily be more efficient among haploids when mutations have the same phenotypic effects in haploids and homozygous diploids, provided that



selection is affected by density and that haploids and diploids experience different degrees of density-dependent competition. This may explain the observation that purifying selection does not seem to be more efficient in haploid-expressed genes than in diploid-expressed genes of *Arabidopsis thaliana* and of the moss *Funaria hygrometrica* (Szoevenyi et al. 2013), and it outlines the need for more systematic measures of fitness effects of deleterious mutations at different population densities.

We also explored the case of antagonistic selection, where different alleles at the same locus are favored in haploids and in diploids. As with deleterious alleles, the direct competition term favors the phase with the highest mean fitness—a result also described in a recent article by Immler and Otto (2014). In addition, we found that independently of the ecological parameters, indirect selection always favors diploidy when the locus under antagonistic selection is at its polymorphic equilibrium, because of the fact that a modifier allele increasing diploidy tends to benefit more from hitchhiking than an allele increasing haploidy, whose association with the haploid-beneficial allele is broken by recombination before selection. In the case of heteromorphic species where haploid and diploid individuals occupy different niches, many loci may possibly be under ploidy antagonistic selection (because of morphological and physiological differences between ploidy phases), and this should thus tend to favor modifiers increasing the relative importance of the diploid phase.

Our simulations showed that in the absence of deleterious mutations, ecological differentiation between phases may lead to the stable coexistence of a high diversity of life cycles (from fully haploid to fully diploid cycles), in agreement with predictions by Hughes and Otto (1999). However, when deleterious alleles are introduced and when the ecological component of selection is sufficiently strong to favor biphasic life cycles (despite the destabilizing effect of deleterious alleles), eventually the population evolves to a state where alleles coding for fully haploid and fully diploid life cycles stably coexist. In this case, we expect that assortative mating should be favored, ultimately leading to the coexistence of a haploid and a diploid species. Therefore, ecological differentiation between phases does not seem sufficient to explain the stable maintenance of truly biphasic life cycles (involving an obligatory alternation between haploid and diploid individuals), unless additional factors favor such an alternation, for example, constraints due to the different biology of spores and gametes (e.g., Stebbins and Hill 1980; Bell 1997) or temporal variability of the environment, as explored here. Finally, we assumed a preexisting ecological differentiation between haploid and diploid individuals. It may be of interest to extend our model in order to explore the ecological and genetic factors that may drive this differentiation.

### Acknowledgments

We thank A. Agrawal, Y. Michalakakis, S. Otto, M. Valero, and two anonymous reviewers for helpful discussions and comments. M.R. and D.R. were funded by the Agence Nationale de la Recherche (project BiCycle ANR10-BLAN-1727).

### Literature Cited

- Agrawal, A. F. 2010. Ecological determinants of mutation load and inbreeding depression in subdivided populations. *American Naturalist* 176:111–122.
- Agrawal, A. F., and M. C. Whitlock. 2010. Environmental duress and epistasis: how does stress affect the strength of selection on new mutations? *Trends in Ecology and Evolution* 25:450–458.
- Bell, G. 1997. The evolution of the life cycle of brown seaweeds. *Biological Journal of the Linnean Society* 60:21–38.
- Bolton, J. J., and M. A. P. Joska. 1993. Population studies on a South African carrageenophyte: *Iridaea capensis* (Gigartinales, Rhodophyta). *Hydrobiologia* 261:191–195.
- Cailleau, A., P. O. Cheptou, and T. Lenormand. 2010. Ploidy and the evolution of endosperm of flowering plants. *Genetics* 184:439–453.
- Cheptou, P. O., E. Imbert, J. Lepart, and J. Escarre. 2000. Effects of competition on lifetime estimates of inbreeding depression in the outcrossing plant *Crepis sancta* (Asteraceae). *Journal of Evolutionary Biology* 13:522–531.
- Christiansen, F. B., and V. Loeschcke. 1980. Evolution and intraspecific exploitative competition. 1. One-locus theory for small additive gene effects. *Theoretical Population Biology* 18:297–313.
- Coelho, S. M., A. F. Peters, B. Charrier, D. Roze, C. Destombe, M. Valero, and J. M. Cock. 2007. Complex life cycles of multicellular eukaryotes: new approaches based on the use of model organisms. *Gene* 406:152–170.
- Couceiro, L., M. Le Gac, H. Hunsperger, S. Mauger, C. Destombe, M. Cock, S. Ahmed, et al. 2015. Evolution and maintenance of haploid-diploid life cycles in natural populations: the case of the marine brown alga *Ectocarpus*. *Evolution* 69:1808–1822.
- Destombe, C., J. Godin, M. Nocher, S. Richerd, and M. Valero. 1993. Differences in response between haploid and diploid isomorphic phases of *Gracilaria verrucosa* (Rhodophyta, Gigartinales) exposed to artificial environmental conditions. *Hydrobiologia* 261:131–137.
- Dyck, L. J., and R. E. De Wreede. 2006. Seasonal and spatial patterns of population density in the marine macroalga *Mazzaella splendens* (Gigartinales, Rhodophyta). *Phycological Research* 54:21–31.
- Ewing, E. P. 1977. Selection at haploid and diploid phases: cyclical variation. *Genetics* 87:195–207.
- Gerstein, A. C. 2013. Mutational effects depend on ploidy level: all else is not equal. *Biology Letters* 9:20120614.
- Gerstein, A. C., L. A. Cleathero, M. A. Mandegar, and S. P. Otto. 2010. Haploids adapt faster than diploids across a range of environments. *Journal of Evolutionary Biology* 24:531–540.
- Halligan, D. L., and P. D. Keightley. 2009. Spontaneous mutation accumulation studies in evolutionary genetics. *Annual Review of Ecology, Evolution, and Systematics* 40:151–172.
- Hughes, J. S., and S. P. Otto. 1999. Ecology and the evolution of biphasic life cycles. *American Naturalist* 154:306–320.
- Immler, S., G. Arnqvist, and S. P. Otto. 2012. Ploidally antagonistic selection maintains stable genetic polymorphism. *Evolution* 66:55–65.

- Immler, S., and S. P. Otto. 2014. Driven apart: the evolution of ploidy differences between the sexes under antagonistic selection. *American Naturalist* 183:96–107.
- Joseph, S. B., and M. Kirkpatrick. 2004. Haploid selection in animals. *Trends in Ecology and Evolution* 19:592–597.
- Kirkpatrick, M., T. Johnson, and N. Barton. 2002. General models of multilocus evolution. *Genetics* 161:1727–1750.
- Mable, B. K., and S. P. Otto. 1998. The evolution of life cycles with haploid and diploid phases. *Bioessays* 20:453–462.
- Manna, F., G. Martin, and T. Lenormand. 2011. Fitness landscape: an alternative theory for the dominance of mutations. *Genetics* 189: 923–937.
- Maynard Smith, J. 1982. The century since Darwin. *Nature* 296:599–601.
- Meagher, S., D. J. Penn, and W. K. Potts. 2000. Male-male competition magnifies inbreeding depression in wild house mice. *Proceedings of the National Academy of Sciences of the USA* 97:3324–3329.
- Michod, R. E., and M. F. Wojciechowski. 1994. DNA repair and the evolution of transformation. 4. DNA damage increases transformation. *Journal of Evolutionary Biology* 7:147–175.
- Nuismer, S. L., and S. P. Otto. 2004. Host-parasite interactions and the evolution of ploidy. *Proceedings of the National Academy of Sciences of the USA* 101:11036–11039.
- Orr, H. A., and S. P. Otto. 1994. Does diploidy increase the rate of adaptation? *Genetics* 136:1475–1480.
- Otaiza, R. D., S. R. Abades, and A. J. Brante. 2001. Seasonal changes in abundance and shifts in dominance of life history stages of the carrageenophyte *Sarcothalia crispata* (Rhodophyta, Gigartinales) in south central Chile. *Journal of Applied Phycology* 13:161–171.
- Otto, S. P., and A. C. Gerstein. 2008. The evolution of haploidy and diploidy. *Current Biology* 18:R1121–R1124.
- Otto, S. P., and D. B. Goldstein. 1992. Recombination and the evolution of diploidy. *Genetics* 131:745–751.
- Otto, S. P., and J. C. Marks. 1996. Mating systems and the evolutionary transition between haploidy and diploidy. *Biological Journal of the Linnean Society* 57:197–218.
- Paalme, T., J. Kotta, and P. Kersen. 2013. Does the growth rate of drifting *Furcellaria lumbricalis* and *Coccotylus truncatus* depend on their proportion and density? *Proceedings of the Estonian Academy of Sciences* 62:141–147.
- Perrot, V., S. Richerd, and M. Valero. 1991. Transition from haploidy to diploidy. *Nature* 351:315–317.
- Philippi, T., and J. Seger. 1989. Hedging ones evolutionary bets, revisited. *Trends in Ecology and Evolution* 4:41–44.
- Reed, D. C. 1990. An experimental evaluation of density dependence in a subtidal algal population. *Ecology* 71:2286–2296.
- Rescan, M., T. Lenormand, and D. Roze. 2015. Data from: Interactions between genetic and ecological effects on the evolution of life cycles. *American Naturalist*, Dryad Digital Repository, <http://dx.doi.org/10.5061/dryad.40qp5>.
- Rokitta, S. D., L. J. de Nooijer, S. Trimborn, C. de Vargas, B. Rost, and U. John. 2011. Transcriptome analyses reveal differential gene expression patterns between the life-cycle stages of *Emiliania huxleyi* (Haptophyta) and reflect specialization to different ecological niches. *Journal of Phycology* 47:829–838.
- Rousset, F., and J. B. Ferdy. 2014. Testing environmental and genetic effects in the presence of spatial autocorrelation. *Ecography* 37: 781–790.
- Santos, R., and P. Duarte. 1996. Fecundity, spore recruitment and size in *Gelidium sesquipedale* (Gelidiales, Rhodophyta). *Hydrobiologia* 327:223–228.
- Stebbins, G. L., and G. J. C. Hill. 1980. Did multicellular plants invade the land? *American Naturalist* 115:342–353.
- Szafraniec, K., D. M. Wloch, P. Sliwa, R. H. Borts, and R. Korona. 2003. Small fitness effects and weak genetic interactions between deleterious mutations in heterozygous loci of the yeast *Saccharomyces cerevisiae*. *Genetical Research* 82:19–31.
- Szoevenyi, P., M. Ricca, Z. Hock, J. A. Shaw, K. K. Shimizu, and A. Wagner. 2013. Selection is no more efficient in haploid than in diploid life stages of an angiosperm and a moss. *Molecular Biology and Evolution* 30:1929–1939.
- Thompson, D. A., M. M. Desai, and A. W. Murray. 2006. Ploidy controls the success of mutators and nature of mutations during budding yeast evolution. *Current Biology* 16:1581–1590.
- Thornber, C. S. 2006. Functional properties of the isomorphic biphasic algal life cycle. *Integrative and Comparative Biology* 46: 605–614.
- Valero, M., S. Richerd, V. Perrot, and C. Destombe. 1992. Evolution of alternation of haploid and diploid phases in life cycles. *Trends in Ecology and Evolution* 7:25–29.
- Von Dassow, P., H. Ogata, I. Probert, P. Wincker, C. Da Silva, S. Audic, J. M. Claverie, et al. 2009. Transcriptome analysis of functional differentiation between haploid and diploid cells of *Emiliania huxleyi*, a globally significant photosynthetic calcifying cell. *Genome Biology* 10:R114.
- Wallace, B. 1975. Hard and soft selection revisited. *Evolution* 29: 465–473.
- Zeyl, C., T. Vanderford, and M. Carter. 2003. An evolutionary advantage of haploidy in large yeast populations. *Science* 299:555–558.

Associate Editor: Jeff Leips  
Editor: Susan Kalisz