Supplemental file S1: Analytical and statistical models to estimate the parameters of interest (c_{nucl}, c_{mit} and pH)

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1. **Analytical model to derive the coefficients when considering constant, only additive and dominance effects (c_{nucl}) or additive, dominance and epistatic effects ($c_{nuclEpist}$)**

   1.1. Constant fitness effect and constant dominance level of mutations across fitness loci

We consider that fitness is determined by a set of N loci with two segregating alleles, a wild type, A, and a deleterious one, a. To illustrate the rationale of the model we first consider that all mutations have the same effects on fitness but these effects can differ between phases of the life cycle. For any locus k, fitness is as follows:

In haploids:

A_k 1

a_k $1 - \sigma$

In diploids:

A_kA_k 1

A_ka_k $1 - hs$

a_ka_k $1 - s$

We introduce the indicator variables X_k^i that equals 1 when the a_k allele is present in a haploid genome i and 0 otherwise. The total number of deleterious alleles carried by an individual is thus $n_i = \sum_{k=1}^{N} X_k^i$ for a haploid individual, and $n_{ij} = \sum_{k=1}^{N}(X_k^i + X_k^j) = n_i + n_j$ for a diploid individual. We also assume that fitness is multiplicative across loci so that for haploid individual i:

$$w_i = w_0 \,(1 - \sigma)^{n_i} \approx w_0 \exp(-\sigma n_i) \quad (1)$$

where w_0 represents the baseline fitness of a hypothetical haploid genotype with no deleterious mutations. The approximate expression is valid if we assume small fitness effects ($\sigma \ll 1$, and $hs \ll 1$ and $s \ll 1$, see below). Similarly, for diploid individual ij:

$$W_{ij} = W_0 \exp\left(-hs \sum_{k=1}^{N}(X_k^i + X_k^j) - s(1 - 2h)\sum_{k=1}^{N} X_k^i X_k^j\right) \quad (2)$$

The terms in the exponential can be rewritten as:

$$-\frac{s}{2}\sum_{k=1}^{N}(X_k^i + X_k^j) + s\left(\frac{1 - 2h}{2}\right)\sum_{k=1}^{N}\left(X_k^i(1 - X_k^j) + X_k^j(1 - X_k^i)\right) \quad (3)$$

We can note that $X_k^i(1 - X_k^j) + X_k^j(1 - X_k^i)$ is 0 if the two haploid parents share the same allele and 1 otherwise, so $d_{ij} = \frac{1}{N}\sum_{k=1}^{N}\left(X_k^i(1 - X_k^j) + X_k^j(1 - X_k^i)\right)$ is the proportion of selected loci that are heterozygous in the diploid offspring (i.e. the observed pairwise genetic distance between haploid parents i and j at the N fitness loci) between the two haploid parents.

So:

$$W_{ij} = W_0 \exp\left(-\frac{s}{2}(n_i + n_j) + s\left(\frac{1-2h}{2}\right)Nd_{ij}\right) \quad (4)$$

We also assume the following relationship between fitness effects in haploids and diploids: $s = c\,\sigma$, so that (4) can also be written as:

$$W_{ij} = W_0 \exp\left(-\frac{c\sigma}{2}(n_i + n_j) + \frac{c\sigma}{2}(1-2h)Nd_{ij}\right) \quad (5)$$

Similarly, we can account for mitochondrial effects and noting σ', n_i', and σ' the corresponding parameters for mitochondrial mutations.

Assuming again multiplicative and small effects, we have:

$$w_i = w_0\exp(-\sigma n_i - \sigma'n_i') \quad (6)$$

and

$$W_{ij} = W_0 \exp\left(-\frac{c\sigma}{2}(n_i + n_j) + c\sigma\left(\frac{1}{2} - h\right)Nd_{ij} - c'\sigma'n_i'\right) \quad (7)$$

where parental i is the mitochondrial donor.

Noting, $A_i = -\sigma n_i$ and $A_i' = -\sigma'n_i'$ and taking the logarithm, (6) can then be rewritten as:

$$\ln(w_i) = \ln(w_0) + A_i + A_i' \quad (8)$$

and (7) as:

$$\ln(W_{ij}) = \ln(W_0) + c\frac{A_i+A_j}{2} - Hd_{ij} + c'A_i' \quad (9),$$

With $H = c\sigma(\frac{1}{2} - h)N$. Because we do not know which alleles are deleterious, d_{ij}, the genetic distance at the N selected nuclear loci cannot be computed directly. However, we can note that d_{ij} depends on the kinship, f_{ij}, between the two haploid parents and on the genetic diversity at selected loci, as the expectation of d_{ij} over all possible pairs of haploid parents with a given kinship f_{ij} is:

$$E[d_{ij}] = (1 - f_{ij})\frac{1}{N}\sum_{k=1}^{N}2x_k(1 - x_k) \quad (10)$$

where x_k is the allelic frequencies at the kth locus. Instead of d_{ij} we can thus use D_{ij}, the genetic distance computed across the whole genome, whose expectation also verifies equation (10) with summation over N_T, the total number of deleterious or neutral loci in the genome. The two distances are thus expected to be proportional to a factor $p = \frac{\pi_{deleterious}}{\pi_T}$, with p equals the ratio of the average heterozygosity at the N selected allele ($\pi_{deleterious} =$

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$\frac{1}{N}\sum_{k=1}^{N} 2x_k(1-x_k))$ over the average heterozygosity over the whole genome ($\pi_T = \frac{1}{N_T}\sum_{k=1}^{N_T} 2x_k(1-x_k)$). Hence, equation (9) can be rewritten as:

$$\ln(W_{ij}) = \ln(W_0) + c\frac{A_i + A_j}{2} - HpD_{ij} + c'A_i' \quad (11)$$

Note that $\ln(w_0)$ and $\ln(W_0)$ can include both genetic effects (e.g. a "type" factor with two levels (haploid vs. diploid) to test for intrinsic fitness differences between haploids and diploids) and environmental effects (e.g. block, treatment etc.). The coefficients c, c', and pH can be directly estimated from the data using this model.

1.2. Varying fitness effects and varying dominance levels of mutations across fitness loci

Now we can extend this model by assuming that each mutation has its own specific effect. For locus k, fitness is as follows:

In haploids:

$A_k \qquad 1$

$a_k \qquad 1 - \sigma_k$

In diploids:

$A_kA_k \qquad 1$

$A_ka_k \qquad 1 - h_ks_k$

$a_ka_k \qquad 1 - s_k$

For a haploid individual i:

$$w_i = w_0 \exp\left(-\sum_{k=1}^{N} \sigma_k X_k^i\right) \quad (11)$$

And for a diploid individual ij:

$$W_{ij} = W_0 \exp\left(-\sum_{k=1}^{N} h_ks_k\left(X_k^i + X_k^j\right) - \sum_{k=1}^{N} s_k(1 - 2h_k)X_k^i X_k^j\right) \quad (12)$$

As in (3) the terms in the exponential can be rewritten as:

$$-\sum_{k=1}^{N} s_k\left(\frac{X_k^i + X_k^j}{2}\right) + \sum_{k=1}^{N} s_k\left(\frac{1 - 2h_k}{2}\right)\left(X_k^i(1 - X_k^j) + X_k^j(1 - X_k^i)\right) \quad (13)$$

For each locus k, we can define two random variables Y and Z so that: $y_k = s_k\left(\frac{1-2h_k}{2}\right)$ and $z_k = \left(X_k^i(1 - X_k^j) + X_k^j(1 - X_k^i)\right)$. As in the constant model above, we note the pairwise

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genetic distance between parents: $E[Z] = d_{ij} = \frac{1}{N}\sum_{k=1}^{N}\left(X_k^i(1-X_k^j) + X_k^j(1-X_k^i)\right)$ and

$E[Y] = \frac{1}{N}\sum_{k=1}^{N} s_k\left(\frac{1-2h_k}{2}\right)$. If the number of loci is large, we have:

$$\sum_{k=1}^{N} s_k\left(\frac{1-2h_k}{2}\right)\left(X_k^i(1-X_k^j) + X_k^j(1-X_k^i)\right) = NE[YZ] = NCov[Y,Z] + NE[Y]E[Z].$$

We assume that variation among loci in selection coefficients or in dominance is sufficiently small, so that $Cov[Y,Z] = 0$. Thus, the second part of (13) is:

$$\sum_{k=1}^{N} s_k\left(\frac{1-2h_k}{2}\right)\left(X_k^i(1-X_k^j) + X_k^j(1-X_k^i)\right) = d_{ij}\sum_{k=1}^{N} s_k\left(\frac{1-2h_k}{2}\right) \quad (14)$$

We set:

$$\sigma_{nucl} = \frac{1}{N}\sum_{k=1}^{N}\sigma_k$$

$$s_{nucl} = \frac{1}{N}\sum_{k=1}^{N} s_k$$

$$H = \sum_{k=1}^{N} s_k\left(\frac{1-2h_k}{2}\right)$$

We also need to assume a relationship between fitness effects in homokaryons and heterokaryons. For each locus k, we have:

$$s_k = c_k\sigma_k$$

$c_{nucl} = \frac{1}{N}\sum_{k=1}^{N} c_k = \frac{s_{nucl}}{\sigma_{nucl}}$, if we assume the covariance between c_k and σ_k is zero.

Again, we assume that n_i, the number of mutations in each haploid individual is large so that:

$$\sum_{k=1}^{N} \sigma_k X_k^i = n_i\sigma_{nucl}$$

Combining these expressions, we can write fitness in (11) and (12) as:

$$w_i = w_0 \exp(-n_i\sigma_{nucl}) \quad (15)$$

$$W_{ij} = W_0 \exp\left(-\frac{c_{nucl}\sigma_{nucl}}{2}(n_i + n_j) + d_{ij}H\right) \quad (16)$$

Similarly, we can account for mitochondrial effects assuming N' mitochondrial loc and set:

$$\sigma_{mit} = \frac{1}{N'}\sum_{k=1}^{N'}\sigma_{k'}$$

$$s_{mit} = \frac{1}{N'}\sum_{k=1}^{N'} s_{k'}$$

$$s_{k'} = c_{k'}\sigma_{k'}$$

$c_{mit} = \frac{1}{N'}\sum_{k=1}^{N'} c_{k'} = \frac{s_{mit}}{\sigma_{mit}}$, if we assume the covariance between $c_{k'}$ and $\sigma_{k'}$ is zero.

Assuming multiplicative effects, we have:

$$w_i = w_0 \exp(-(\sigma_{nucl}n_i + \sigma_{mit}n_i')) \quad (17)$$

where n_i' is the number of mitochondrial mutant alleles and σ_{mit} the average fitness effect of mutant alleles across N' mitochondrial loci.

Mating between two haploid genotypes with n_i anf n_j nuclear mutant alleles and where genotype i provides a mitochondrion with n_i' mitochondrial mutant alleles produces a diploid genotype of fitness:

$$W_{ij} = W_0 \exp\left(-c_{nucl}\sigma_{nucl}\left(\frac{n_i + n_j}{2}\right) - c_{mit}\sigma_{mit}n_i' + d_{ij}H\right) \quad (18),$$

where $c_{nucl}\sigma_{nucl}$ represents the average diploid fitness effect of nuclear mutant alleles across the N selected loci and $c_{mit}\sigma_{mit}$ represents the average haploid fitness effect of mitochondrial mutant alleles across the N' selected loci, d_{ij} represents the genetic distance at the N selected loci between haploid parents i and j and W_0 represents the baseline fitness of a hypothetical diploid genotype with no deleterious mutations. Noting, $A_i = -\sigma n_i$ and $A_i' = -\sigma' n_i'$ and taking the logarithm, (17) can then be rewritten as:

$$\ln(w_i) = \ln(w_0) + A_i + A_i' \quad (19),$$

and (18) can be rewritten as:

$$\ln(W_{ij}) = \ln(W_0) + c_{nucl}\frac{A_i+A_j}{2} + c_{mit}A_i' + d_{ij}H = \ln(W_0) + c_{nucl}\frac{A_i+A_j}{2} + c_{mit}A_i' + D_{ij}pH$$

$$(20),$$

where D_{ij} is the genetic distance computed across the whole genome and $p = \frac{\pi_{deleterious}}{\pi_T}$ (see Eq. (11) above for details). Again, $\ln(w_0)$ and $\ln(W_0)$ can include both genetic effects (e.g. a "type" factor with two levels (haploid vs. diploid) to test for intrinsic fitness differences between haploids and diploids) and environmental effects (e.g. block, treatment etc.). The coefficients c, c', and pH can be directly estimated from the data using this model.

1.3. Varying fitness effects, varying dominance levels of mutations and varying epistatic effects across fitness loci

In the previous model epistatic interactions are not considered. Epistatic parameters cannot be estimated with fitness data only for haploids and diploids. Additional crosses (such as F2) would be necessary (for example see Lynch 1991). However, we can still write the model to

evaluate how epistasis might affect our previous predictions. Here we consider pairwise epistatic effects and neglect higher order epistatic interactions. In haploids, only additive x additive epistatic interactions are possible. We also assume that that they are the sole epistatic interactions in diploids (*i.e.* we neglect additive x dominance and dominance x dominance epistatic interactions). Two-locus fitness are thus written:

For haploids:

$A_k A_l$ 1

$A_k a_l$ $1 - \sigma_k$

$a_k A_l$ $1 - \sigma_l$

$a_k a_l$ $(1 - \sigma_k)(1 - \sigma_l) + \varepsilon_{kl}$

For diploids:

$A_k A_k\, A_l A_l$ 1

$A_k a_k\, A_l A_l$ $1 - h_k s_k$

$a_k a_k\, A_l A_l$ $1 - s_k$

$A_k A_k\, A_l a_l$ $1 - h_l s_l$

$A_k a_k\, A_l a_l$ $(1 - h_k s_k)\,(1 - h_l s_l) + e_{kl}$

$a_k a_k\, A_l a_l$ $(1 - s_k)\,(1 - h_l s_l) + 2e_{kl}$

$A_k A_k\, a_l a_l$ $1 - s_l$

$A_k a_k\, a_l a_l$ $(1 - h_k s_k)(1 - s_l) + 2e_{kl}$

$a_k a_k\, a_l a_l$ $(1 - s_k)\,(1 - s_l) + 4e_{kl}$

Note that ε_{kl} and e_{kl} can be positive or negative.

Multilocus fitness are now be written:

For haploid individual i:

$$w_i = w_0 \exp\left(-\sum_{k=1}^{N} \sigma_k X_k^i - \sum_{k=1}^{N}\sum_{l>k} \varepsilon_{kl} X_k^i X_l^i \right) \quad (21)$$

For diploid individual ij:

$$
\begin{aligned}
W_{ij} = W_0 \exp\Bigg(&-\sum_{k=1}^{N} h_k s_k \left(X_k^i + X_k^j \right) + \sum_{k=1}^{N} s_k (1 - 2h_k) X_k^i X_k^j \\
&- \sum_{k=1}^{N}\sum_{l>k} e_{kl} \left(X_k^i X_l^i + X_k^i X_l^j + X_k^j X_l^i + X_k^j X_l^j \right) \Bigg) \quad (22)
\end{aligned}
$$

We note:

$$\varepsilon = \frac{2}{N(N-1)} \sum_{k=1}^{N}\sum_{l>k} \varepsilon_{kl}$$

$$e = \frac{2}{N(N-1)} \sum_{k=1}^{N} \sum_{l>k} e_{kl}$$

and we assume the following relationship between effects in haploids and diploids:

$$e = c_{nuclEpist} \varepsilon$$

Finally, we can express the sum involving indicator variable as follows:

$$\sum_{k=1}^{N} \sum_{l>k} X_k^i X_l^i = \frac{n_i(n_i - 1)}{2}$$

$$\sum_{k=1}^{N} \sum_{l>k} X_k^j X_l^j = \frac{n_j(n_j - 1)}{2}$$

$$\sum_{k=1}^{N} X_k^i X_k^j = \frac{n_i + n_j}{2} + \frac{N}{2} d_{ij}$$

$$\sum_{k=1}^{N} \sum_{l>k} \left(X_k^j X_l^i + X_k^j X_l^j \right) = \sum_{k=1}^{N} \sum_{l=1}^{N} X_k^j X_l^i - \sum_{k=1}^{N} X_k^i X_k^j$$

$$= n_i n_j - \frac{n_i + n_j}{2} - \frac{N}{2} d_{ij} = \frac{1}{2} \left(n_i(n_j - 1) + n_j(n_i - 1) - N d_{ij} \right)$$

Combining all these expressions, we can write fitness as:

$$w_i = w_0 \exp \left(-n_i \sigma - \frac{\varepsilon}{2} n_i(n_i - 1) \right) \quad (23)$$

$$W_{ij} = W_0 \exp \left(-\frac{c_{nucl} \sigma}{2} (n_i + n_j) + d_{ij} \left(H - n \frac{c_{nuclEpist} \varepsilon}{2} \right) \right.$$

$$\left. - \frac{c_{nuclEpist} \varepsilon}{2} \left(n_i(n_i - 1) + n_j(n_j - 1) + n_i(n_j - 1) + n_j(n_i - 1) \right) \right) \quad (24)$$

Note that epistatic interactions also appear with the genetic distance term. This is due to the fact that in diploids, in addition to cis-interactions (which are already present in haploids) there are also trans-interactions (between mutations from the two haploid parents).

From a statistical point of view, we can write:

$$\ln(w_i) = \ln(w_0) - A_i - E_i \quad (25),$$

$$\ln(W_{ij}) = \ln(W_0) - c_{nucl} \frac{A_i + A_j}{2} + d_{ij} \left(H - n \frac{c_{nuclEpist} \varepsilon}{2} \right) - c_{nuclEpist} \left(E_i + E_j + \right.$$

$$\left. \frac{1}{4} \left(\sqrt{(8E_i + \varepsilon)(8E_j + \varepsilon)} - \varepsilon \right) \right) \quad (26),$$

where E_i and E_j correspond to epistatic effects. If n_i and n_j are large, then $\varepsilon \ll E_i, E_j$ and can be neglected. So (25) can be approximated by:

$$\ln\left(W_{ij}\right) \approx \ln(W_0) - c_{nucl}\frac{A_i + A_j}{2} + pD_{ij}\left(H - n\frac{c_{nuclEpist}\varepsilon}{2}\right) - c_{nuclEpist}\left(E_i + E_j + 2\sqrt{E_i E_j}\right)$$

(27),

where D_{ij} is the genetic distance computed across the whole genome and $p = \frac{\pi_{deleterious}}{\pi_T}$ (see Eq. (11) above for details). The $2c_{nuclEpist}\sqrt{E_i E_j}$ and $-n\frac{c_{nuclEpist}\varepsilon}{2}$ term correspond to trans-interactions. If ε and e are null on average, as predicted by some models (Martin *et al.* 2007), (19) and (20) are valid and are not affected by epistatic interactions. If ε and e is negative (antagonistic epistasis), c_{nucl} is under-estimated whereas H is over-estimated. For positive ε and e (synergistic epistasis), the reverse is expected but depends on the exact values of c_{nucl} and $c_{nuclEpist}$. Synergistic epistasis among deleterious mutations have already been detected and seems more common than negative epistasis in eukaryotes (Sanjuán and Elena 2006) but rather low in "simple" organisms such as fungi and nematodes (Peters and Keightley 2000; Sanjuán and Elena 2006).

2. **Simulations to investigate the effect of the variation of selection coefficients, of dominance levels or of c_{nucl} among loci**

We investigate the robustness of our main results regarding the estimation of *pH* and c_{nucl} using simulations. We consider a species where the haploid and diploid phases have equal lengths. Based on Eq. (1) in Scott and Rescan (2017), the equilibrium frequency of the deleterious allele at each locus, *k*, is:

$$q_k = \frac{\mu exp^{-\sigma_k}}{1 - exp^{-\frac{\sigma_k}{2}(1 + c_k h_k)}}$$

(27),

where μ represents the mutation rate, σ_k is the haploid selection coefficient at locus *k*, h_k is the level of dominance of locus *k* and c_k is the ratio of fitness effect in diploids over the fitness effect in haploids.

We simulate an experiment using 30 haploid parents with 500 loci under selection with four different types of genetic architectures. (i) We assume that σ_k, h_k and c_k are constant across loci with means respectively equal to 0.01, 0.25 and 0.5 (mutation rate is fixed at 10^{-4}). (ii) We assume that each σ_k follows a gamma distribution with mean = 0.01 and shape=2 (other parameters as in i). (iii) We assume that each h_k follows a beta distribution with mean = 0.25 and shape1=2 (other parameters as in i). (iv) We assume that c_k ($c_k = \frac{s_k}{\sigma_k}$) follows a beta distribution with mean = 0.5 and shape1=2 (other parameters as in i).

For each haploid parent and each locus k, we sample an indicator variable X_k (0: wild type allele, 1: deleterious allele) using a Bernoulli distribution with probability q_k. We assume multiplicative effects of mutations such that:

$$w_i = w_0 \prod_{k=1}^{N}(1 - \sigma_k)^{X_k},$$

with $log(w_0) \sim Gaussian(0, 0.001)$ for the environmental variation around the breeding value.

We use a diallel (i.e. full factorial) design and compute the fitness of each of the 900 diploid offspring with haploid parents i and j as:

$$W_{ij} = W_0 \prod_{k=1}^{N}(1 - c_k \sigma_k)^{X_k^i X_k^j} (1 - h_k c_k \sigma_k)^{X_k^i(1-X_k^j)+X_k^j(1-X_k^i)},$$

with $log(W_0) \sim Gaussian(0, 0.001)$ for the environmental variation. We use 10 fitness replicate measurements for each haploid or diploid genotype.

We estimated mid-parent heterosis as the difference between the average growth rate of a diploid genotype and the mean of the average growth rates of its two autozygous diploid parents. We computed the predicted H as: $H = \sum_{k=1}^{N} c_k \sigma_k \left(\frac{1-2h_k}{2}\right)$. According to Eq. (20), H represent the slope of the linear increase in mid-parent heterosis with pairwise genetic distance. For each of the 30 haploid parents, we also computed the ratio between its average fitness as an autozygous diploid over its average fitness as a haploid. The mean of the distribution of this ratio should be equal to 0.5 (i.e. the mean c_{nucl} used for the simulations). For both c_{nucl} and the slope of genetic distance (which is equal to H according to Eq. (20)), we compare the estimation of our model with the values expected based on our simulations.

The estimations based on our model were generally robust to variation among loci in selection coefficient, in dominance level or in the ratio of fitness effects in diploids vs. haploids (Figure S1 and S2). Variation in selection coefficient had the highest impact on our model prediction (Figure S1B and S2B). Indeed, very mildly deleterious mutations segregate at high frequencies compared to mildly deleterious mutations and are more likely to be homozygous in diploid offspring. Hence, the variation in selection coefficient among loci creates a negative covariance between $s_k \left(\frac{1-2h_k}{2}\right)$ and $\left(X_k^i(1-X_k^j) + X_k^j(1-X_k^i)\right)$, as our model assumed that this covariance was zero, it tends to overestimate the increase in mid-parent heterosis with genetic distance (Figure S1B).
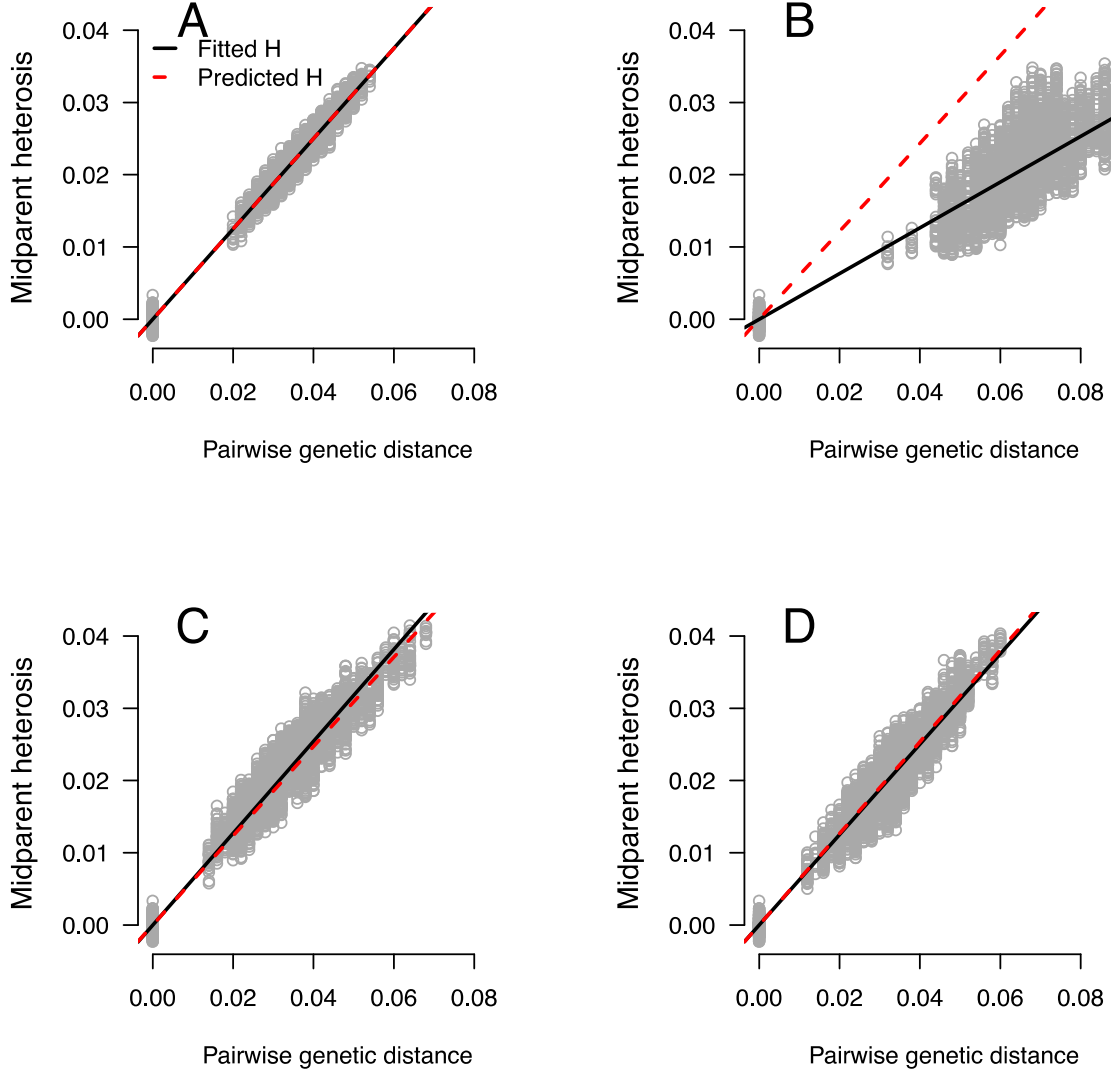
Figure S1 Comparison of the predicted and fitted increase in mid-parent heterosis with pairwise genetic distance (predicted and fitted *H)* for different genetic architectures. Simulations of a diallel cross using 30 haploid parents (900 diploid offspring) with 500 loci under selection with four different types of genetic architectures: (A) assuming that σ_k, h_k and c_k are constant across loci with means respectively equal to 0.01, 0.25 and 0.5 (mutation rate is fixed at 10^{-4}), (B) assuming that each σ_k is sampled from a gamma distribution with mean = 0.01 and shape=2 (other parameters as in A), (C) assuming that each h_k is sampled from a gamma distribution with mean = 0.25 and shape=2 (other parameters as in A) and (iv) assuming that c_k ($c_k = \frac{s_k}{\sigma_k}$) follows a gamma distribution with mean = 0.5 and shape=2 (other parameters as in A). The discrepancy between the fitted H and the prediction based on our model stems from the segregation of mildly deleterious mutations at relatively high frequencies that decrease de fitness of diploid offspring.
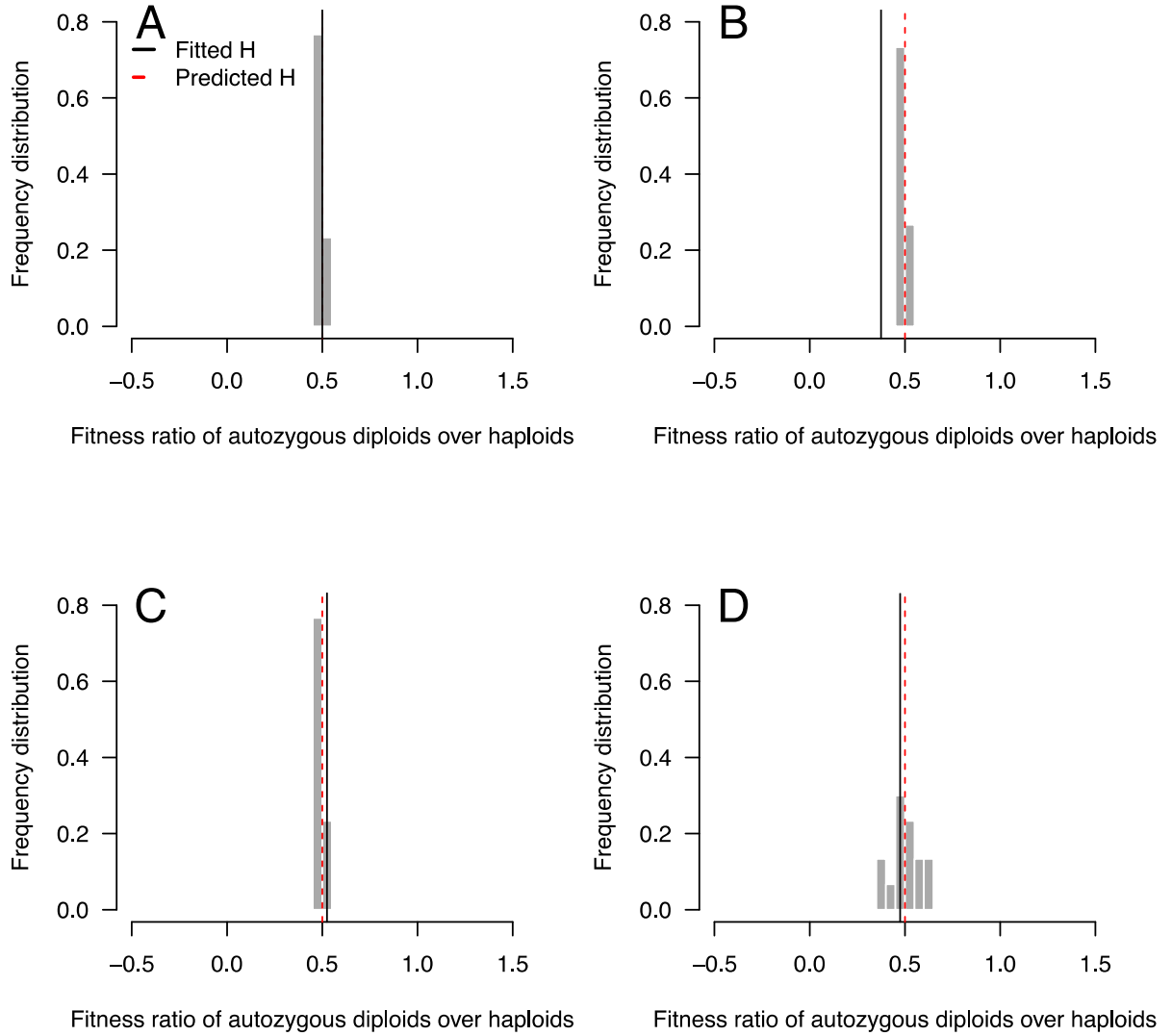
Figure S2 Comparison of the fitted and expected c_{nucl} for different genetic architectures. Simulations of a diallel cross using 30 haploid parents (900 diploid offspring) with 500 loci under selection with four different types of genetic architectures: (A) assuming that σ_k, h_k and c_k are constant across loci with means respectively equal to 0.01, 0.25 and 0.5 (mutation rate is fixed at 10^{-4}), (B) assuming that each σ_k is sampled from a gamma distribution with mean = 0.01 and shape=2 (other parameters as in A), (C) assuming that each h_k is sampled from a gamma distribution with mean = 0.25 and shape=2 (other parameters as in A) and (iv) assuming that c_k ($c_k = \frac{s_k}{\sigma_k}$) follows a gamma distribution with mean = 0.5 and shape=2 (other parameters as in A). The discrepancy between the fitted H and the prediction based on our model stems from the segregation of mildly deleterious mutations at relatively high frequencies that decrease de fitness of diploid offspring. A small number of values fell outside

of the displayed interval due to the effect of environmental variation and are omitted from the graph for clarity.

3. Quantitative genetic model for the empirical estimation of c_{nucl}, c_{mit} and pH

3.1. Statistical model

For fungi, we consider homokaryons to be equivalent to haploids and heterokaryons to be equivalent to diploids (see main text). We index genetic effects with $Nucl$ if they are nuclear and Mit if they are mitochondrial. Our general approach is to decompose nuclear and mitochondrial genetic effects into effects due to loci that are shared between homokaryons and heterokaryons (hereafter with a $HomHet$ superscript, e.g. $A_{HomNucli}^{HomHet}$) and effects due to loci specific to homokaryons (hereafter with a $HomOnly$ superscript, e.g. $A_{HomMiti}^{HomOnly}$) or heterokaryons (hereafter with a $HetOnly$ superscript, e.g. $A'_{HomHetNucli}$). We do not consider mitochondrial-nucleus interactions. For homokaryon fitness, we define:

$$z_i = \ln(w_i) = z_0 + A_{HomMiti} + A_{HomNucli} + \varepsilon,$$

where z_i is the logarithm of the fitness of homokaryon i, z_0 is the average homokaryon fitness, $A_{HomMiti}$ is the homokaryon mitochondrial genetic value, $A_{HomNucli}$ is the homokaryon nuclear genetic value and ε is the residual error. We can define:

$$A_{HomMiti} = A_{HomMiti}^{HomHet} + A_{HomMiti}^{HomOnly},$$

where $A_{HomMiti}^{HomHet}$ is the part of homokaryon mitochondrial genetic value due to loci that also have a fitness effect in heterokaryons, $A_{HomMiti}^{HomOnly}$, is the part of homokaryon mitochondrial genetic value due to loci that do not have any fitness effect in heterokaryons. Similarly, we have:

$$A_{HomNucli} = A_{HomNucli}^{HomHet} + A_{HomNucli}^{HomOnly},$$

where $A_{HomNucli}^{HomHet}$ is the part of homokaryon nuclear genetic value due to loci that also have a fitness effect in heterokaryons, $A_{HomNucli}^{HomOnly}$, is the part of homokaryon nuclear genetic value due to loci that do not have any fitness effect in heterokaryons.

Similarly for heterokaryons, we define:

$$Z_{ij} = \ln(W_{ij}) = Z_0 + A_{HetMiti} + A_{HetNuclij} + \varepsilon$$

where Z_{ij} is the logarithm of the fitness of heterokaryons formed with parental homokaryons i and j, Z_0 is the average heterokaryon fitness, $A_{HetMiti}$ is the heterokaryon mitochondrial

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genetic value (only the acceptor i is providing the mitochondria), $A_{HetNuclij}$ is the heterokaryon nuclear genetic value and ε is the residual error.

We can decompose mitochondrial effects as,

$$A_{HetMiti} = A_{AccMiti}^{HomHet} + A_{AccMiti}^{HetOnly},$$

where $A_{AccMiti}^{HomHet}$ is the part of heterokaryon mitochondrial genetic value due to loci that also have a fitness effect in homokaryons, $A_{AccMiti}^{HetOnly}$, is the part of heterokaryon mitochondrial genetic value due to loci that do not have any fitness effect in homokaryons. Let c_{mit} be the ratio of the fitness effects of mutations in heterokaryons over the fitness effects of the same mutations in homokaryons (see Eq. 18 above), such that $A_{AccMiti}^{HomHet} = c_{mit} A_{HomMiti}^{HomHet}$.

We can also define:

$$A_{HetNuclij} = \frac{A_{AccNucli} + A_{DonNuclj}}{2} + I_{AccNucli \times DonNuclj},$$

where $A_{AccNucli}$ and $A_{DonNuclj}$ are the acceptor and donor nuclear genetic values respectively and $I_{AccNucli \times DonNuclj}$ represents the interaction between acceptor and donor nuclei (see Simchen and Jinks 1964 for a similar decomposition of heterokaryon genetic value).

Let's decompose the acceptor and donor nuclear genetic values as follows:

$$A_{AccNucli} = A_{AccNucli}^{HomHet} + A_{AccNucli}^{HetOnly} \text{ and } A_{DonNuclj} = A_{DonNuclj}^{HomHet} + A_{DonNuclj}^{HetOnly},$$

where $A_{AccNucli}^{HomHet}$ and $A_{DonNuclj}^{HomHet}$ represent the part of acceptor and donor genetic values due to loci that also have fitness effects in homokaryons, whereas $A_{AccNucli}^{HetOnly}$ and $A_{DonNuclj}^{HetOnly}$ represent the part of acceptor and donor genetic values due to loci that do not have any fitness effect in heterokaryons. Let c_{nucl} be the ratio of the fitness effects of mutations in heterokaryons over the fitness effects of the same mutations in homokaryons (see Eq. 8 above), such that $A_{AccNucli}^{HomHet} = c_{nucl} A_{HomNucli}^{HomHet}$ and $A_{DonNuclj}^{HomHet} = c_{nucl} A_{HomNuclj}^{HomHet}$.

For the acceptor x donor interaction can be decomposed as follows:

$$I_{AccNucli \times DonNuclj} = pHD_{ij} + I'_{AccNucli \times DonNuclj},$$

where D_{ij} is the genome-wide genetic distance between homokaryon i and j, $p = \frac{\pi_{deleterious}}{\pi_T}$ (see Eq. (11) above for details) and $I'_{AccNucli \times DonNuclj}$ is the residual interaction after accounting for genetic distance (e.g. that accounts for potential epistatic effects between the genome i and j).

We can rewrite homokaryon fitness as:

$$z_i = \ln(w_i) = z_0 + A_{HomMiti}^{HomHet} + A_{HomMiti}^{HomOnly} + A_{HomNucli}^{HomHet} + A_{HomNucli}^{HomOnly} + \varepsilon \qquad (28)$$

and heterokaryon fitness as:

$$Z_{ij} = Z_0 + c_{mit}A_{HomMiti}^{HomHet} + A_{AccMiti}^{HetOnly} + c_{nucl}\frac{A_{HomNucli}^{HomHet}+A_{HomNuclj}^{HomHet}}{2} + \frac{A_{AccNucli}^{HetOnly}+A_{DonNuclj}^{HetOnly}}{2} +$$

$$pHD_{ij} + I'_{AccNucli\times DonNuclj} + \varepsilon \tag{29}$$

3.2. Covariance between a heterokaryon and its donor homokaryon

We want to fit a linear model expressing the fitness of a heterokaryon as a function of the fitness of its donor homokaryon parent:

$$Z_{ij} = Z_0 + slope_{heterokaryon-donor\ homokaryon}\ z_{donj} + \varepsilon,$$

where z_{donj} refers to the phenotype of the homokaryons used as donor for heterokaryon synthesis, and $slope_{heterokaryon-donor\ homokaryon}$ represents the slope of the regression of heterokaryon phenotype on donor homokaryon parent phenotype (Lynch and Walsh 1998, p538). If the resemblance between an homokaryon donor parent and its heterokaryon offspring is not environmentally determined:

$$slope_{heterokaryon-donor\ homokaryon} = \frac{Cov(Z, z_{don})}{Var(z_{don})}$$

We assume that we have enough measurement replicates, so that we can ignore environmental error and have:

$$Z_{ij} = Z_0 + c_{mit}A_{HomMiti}^{HomHet} + A_{AccMiti}^{HetOnly} + c_{nucl}\frac{A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet}}{2}$$

$$+ \frac{A_{AccNucli}^{HetOnly} + A_{DonNuclj}^{HetOnly}}{2} + pHD_{ij} + I'_{AccNucli\times DonNuclj}$$

And: $z_{donj} = z_0 + A_{HomMitj}^{HomHet} + A_{HomMitj}^{HomOnly} + A_{HomNuclj}^{HomHet} + A_{HomNuclj}^{HomOnly}$.

The covariance $Cov(Z, z_{don})$ is only due to nuclear genes with fitness effects in both homokaryons and heterokaryons, so that:

$$Cov(Z, z_{don}) = Cov\left(c_{nucl}\frac{A_{HomNucl}^{HomHet}}{2}, \quad A_{HomNucl}^{HomHet}\right) = \frac{c_{nucl}}{2}Var(A_{HomNucl}^{HomHet})$$

Hence, we have:

$$slope_{heterokaryon-donor\ homokaryon} = \frac{\frac{c_{nucl}}{2}Var(A_{HomNucl}^{HomHet})}{Var(z_{don})} \tag{30}$$

The variance, $Var(A_{HomNucl}^{HomHet})$ represents the part of the variance among homokaryon genetic values determined by nuclear loci that also have an effect in heterokaryons, whereas $Var(z_{don})$ represents the genetic variance among homokaryon donors that include both nuclear and mitochondrial genetic effects (variance due to environmental error is factored out,

as we average values over many measurement replicates). When there is no mitochondrial and no homokaryon-specific nuclear effects, $Var(z_{don}) = Var(A_{HomNucl}^{HomHet})$, and the slope of the regression equals $\frac{c_{nucl}}{2}$.

3.3. Covariance between a heterokaryon and its acceptor homokaryon

We want to fit a linear model expressing the fitness of a heterokaryon as a function of the fitness of its acceptor homokaryon parent:

$$Z_{ij} = Z_0 + slope_{heterokaryon-acceptor\ homokaryon}\ z_{acci} + \varepsilon,$$

where z_{acci} refers to the phenotype of the homokaryons used as acceptor for heterokaryon synthesis, and $slope_{heterokaryon-acceptor\ homokaryon}$ represents the slope of the regression of heterokaryon phenotype on donor homokaryon parent phenotype (Lynch and Walsh 1998, p538). If the resemblance between an homokaryon acceptor parent and its heterokaryon offspring is not environmentally determined:

$$slope_{heterokaryon-acceptor\ homokaryon} = \frac{Cov(Z, z_{acc})}{Var(z_{acc})}$$

We have: $z_{acci} = z_0 + A_{HomMiti}^{HomHet} + A_{HomMiti}^{HomOnly} + A_{HomNucli}^{HomHet} + A_{HomNucli}^{HomOnly}$.

The covariance $Cov(Z, z_{acc})$ is due to mitochondrial and nuclear genes with fitness effects in both homokaryons and heterokaryons, so that:

$$Cov(Z, z_{acc}) = Cov\left(c_{mit}A_{HomMit}^{HomHet} + c_{nucl}\frac{A_{HomNucl}^{HomHet}}{2},\quad A_{HomMiti}^{HomHet} + A_{HomNucl}^{HomHet}\right)$$

Hence, we have:

$$slope_{heterokaryon-acceptor\ homokaryon} = \frac{c_{mit}Var(A_{HomMit}^{HomHet}) + \frac{c_{nucl}}{2}Var(A_{HomNucl}^{HomHet})}{Var(z_{acc})} \qquad (31)$$

The variance, $Var(A_{HomMit}^{HomHet})$ and $Var(A_{HomNucl}^{HomHet})$ respectively represent the part of the variance among homokaryon genetic values determined by mitochondrial and nuclear loci that also have an effect in heterokaryons, whereas $Var(z_{acc})$ represents the genetic variance among acceptor homokaryons that include both nuclear and mitochondrial genetic effects (variance due to environmental error is factored out, as we average values over many measurement replicates). When there is no mitochondrial and no homokaryon-specific nuclear effects, the slope of the regression is the same as that of the regression on donor homokaryons and equals $\frac{c_{nucl}}{2}$.

3.4. Covariance between a heterokaryon and its homokaryon mid-parent

We want to fit a linear model expressing the fitness of a heterokaryons as a function of the fitness of its homokaryon mid-parent

$$Z_{ij} = Z_0 + slope \frac{z_{acci} + z_{donj}}{2} + \varepsilon,$$

where z_{acci} and z_{donj} refers to the phenotype of the homokaryons used as acceptor and donor for heterokaryons synthesis, and $slope$ represents the slope of the regression of heterokaryon phenotype on mid-homokaryon parent phenotype (Lynch and Walsh 1998, p538). In the absence of maternal effects and if the resemblance between homokaryon parents and their heterokaryon offspring is not environmentally determined:

$$slope = \frac{Cov\left(Z, \frac{z_{acc} + z_{don}}{2}\right)}{Var\left(\frac{z_{acc} + z_{don}}{2}\right)}$$

And $Z_{ij} = Z_0 + c_{mit} A_{HomMiti}^{HomHet} + A_{AccMiti}^{HetOnly} + c_{nucl} \frac{A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet}}{2} + \frac{A_{AccNucli}^{HetOnly} + A_{DonNuclj}^{HetOnly}}{2} +$

$pHD_{ij} + I'_{AccNucli \times DonNuclj}$

$$\frac{z_{acci} + z_{donj}}{2}$$

$$= \frac{z_0 + A_{HomMiti}^{HomHet} + A_{HomMiti}^{HomOnly} + A_{HomNucli}^{HomHet} + A_{HomNucli}^{HomOnly} + z_0 + A_{HomMitj}^{HomHet} + A_{HomMitj}^{HomOnly} + A_{HomNuclj}^{HomHet} + A_{HomNuclj}^{HomOnly}}{2}$$

Genetic effects that are homokaryon- or heterokaryon-specific are independent. Hence,

$$Cov\left(A_{AccMiti}^{HetOnly} + \frac{A_{AccNucli}^{HetOnly} + A_{DonNuclj}^{HetOnly}}{2}, \frac{z_{acc} + z_{don}}{2}\right) = 0$$

and $Cov\left(Z, \frac{A_{HomMiti}^{HomOnly} + A_{HomNucli}^{HomOnly} + A_{HomMitj}^{HomOnly} + A_{HomNuclj}^{HomOnly}}{2}\right) = 0$

We assume that both the residual interaction between acceptor and donor nuclei ($I'_{AccNucl \times DonNucl}$) and the masking effect of deleterious mutations in heterozygotes (pHD) are independent of the other effects. Hence,

$Cov\left(pHD, \frac{z_0 + A_{HomMiti}^{HomHet} + A_{HomMiti}^{HomOnly} + A_{HomNucli}^{HomHet} + A_{HomNucli}^{HomOnly} + z_0 + A_{HomMitj}^{HomHet} + A_{HomMitj}^{HomOnly} + A_{HomNuclj}^{HomHet} + A_{HomNuclj}^{HomOnly}}{2}\right) = 0$ and

$Cov\left(I'_{AccNucl \times DonNucl}, \frac{z_0 + A_{HomMiti}^{HomHet} + A_{HomMiti}^{HomOnly} + A_{HomNucli}^{HomHet} + A_{HomNucli}^{HomOnly} + z_0 + A_{HomMitj}^{HomHet} + A_{HomMitj}^{HomOnly} + A_{HomNuclj}^{HomHet} + A_{HomNuclj}^{HomOnly}}{2}\right) = 0$

We also assume that acceptor and donor homokaryons are chosen randomly so that their phenotype does not covary $Cov(z_{acc}, z_{don}) = 0$

Hence,

$slope$

$$= \frac{Cov\left(c_{mit}A_{HomMiti}^{HomHet} + c_{nucl}\frac{A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet}}{2}, \frac{A_{HomMiti}^{HomHet} + A_{HomNucli}^{HomHet} + A_{HomMitj}^{HomHet} + A_{HomNuclj}^{HomHet}}{2}\right)}{\frac{1}{4}\left(Var(z_{acc}) + Var(z_{don})\right)}$$

$$= \frac{Cov\left(c_{mit}A_{HomMiti}^{HomHet}, \frac{A_{HomMiti}^{HomHet}}{2}\right) + Cov\left(c_{nucl}\frac{A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet}}{2}, \frac{A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet}}{2}\right)}{\frac{1}{2}Var(z)}$$

$$= \frac{\frac{c_{mit}}{2}Cov(A_{HomMiti}^{HomHet}, A_{HomMiti}^{HomHet}) + c_{nucl}Cov\left(\frac{A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet}}{2}, \frac{A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet}}{2}\right)}{\frac{1}{2}Var(z)}$$

And we have:

$$slope = \frac{\frac{c_{mit}}{2}Var(A_{HomMiti}^{HomHet}) + c_{nucl}Var(\frac{A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet}}{2})}{\frac{1}{2}Var(z)}$$

$$= \frac{\frac{c_{mit}}{2}Var(A_{HomMiti}^{HomHet}) + \frac{c_{nucl}}{4}Var(A_{HomNucli}^{HomHet} + A_{HomNuclj}^{HomHet})}{\frac{1}{2}Var(z)}$$

$$= \frac{\frac{c_{mit}}{2}Var(A_{HomMit}^{HomHet}) + \frac{c_{nucl}}{2}Var(A_{HomNucl}^{HomHet})}{\frac{1}{2}Var(z)}$$

$$slope = \frac{c_{mit}Var(A_{HomMit}^{HomHet}) + c_{nucl}Var(A_{HomNucl}^{HomHet})}{Var(z)} \tag{32}$$

The variance, $Var(A_{HomMit}^{HomHet})$ and $Var(A_{HomNucl}^{HomHet})$ respectively represent the part of the variance among homokaryon genetic values determined by mitochondrial and nuclear loci that also have an effect in heterokaryons, whereas $Var(z)$ represents the genetic variance among homokaryons.

4. Description of the bivariate mixed model used for the estimation of c_{nucl}, c_{mit} and pH

To comply with our statistical model, MGR was log-transformed prior to the analyses. The genetic and environmental effects were partitioned using linear mixed model analyses with

Gaussian error distributions. Continuous predictor variables were scaled to mean of zero and standard deviation of one prior to the analyses (Schielzeth 2010). For the most complex (i.e. full) model, we used the following bivariate linear mixed model with the same structure of fixed and random environmental effects for homokaryons and heterokaryons, but with different structures of random genetic effects for homokaryons:

$$z = Xb + Z_{hom}u_{hom} + Z_{hommit}u_{hommit} + Z_{assay}u_{assay} + Z_{plate}u_{plate} + \varepsilon \quad (33)$$

and heterokaryons:

$$z = Xb + Z_{acc}u_{acc} + Z_{don}u_{don} + Z_{acc \times don}u_{acc \times don} + Z_{hetmit}u_{hetmit} + Z_{assay}u_{assay} + Z_{plate}u_{plate} + \varepsilon \quad (34)$$

where z is a vector of logarithm MGR observations, b is a vector of fixed effects, u_{hom}, u_{acc} and u_{don} are vectors of random homokaryon, acceptor, donor nuclear genetic effects, $u_{acc \times don}$ is a vector of random interactions between acceptor and donor nuclear genetic effects, u_{hommit} and u_{hetmit} are vectors of random homokaryon and heterokaryon mitochondrial haplotype genetic effects, u_{assay} and u_{plate} are vectors of random assay and plate effects, ε is a vector of random errors, and X, Z_{hom}, Z_{acc}, Z_{don}, $Z_{acc \times don}$, Z_{hommit}, Z_{hetmit}, Z_{assay} and Z_{plates} are incidence matrices relating the observations to the fixed and random effects respectively. Fixed effects in b comprised different intrinsic fitness effects for heterokaryons and homokaryons (*strain type* factor), the genetic distance between parental homokaryons (set at zero for homokaryons, and at the genome-wide genetic distance between parental homokaryons for heterokaryons, *genetic distance* covariate), and the senescence status of the donor ("senescent" for heterokaryons descended from senescent donors, vs. "not senescent" for homokaryons and heterokaryons descended from non-senescent donors, *donor senescent* factor). Importantly, we assume that the senescence only affects the mean of donor effects (e.g. that donor effects are on average lower for senescent than for non-senescent donor strains), but that the genetic variance among donor effects is the same whether the donor strain was senescent or not. The random genetic effect $u_{acc \times don}$ captures some effects that are not considered in our simple analytic model (e.g. epistasis among deleterious mutations). The random genetic effects u_{hom}, u_{acc} and u_{don} were assumed to follow a multivariate normal distribution with zero mean vector and variance-covariance matrix:

$$V \begin{bmatrix} u_{hom} \\ u_{acc} \\ u_{don} \end{bmatrix} = \qquad \text{(CovNucl1: full covariance of nuclear genetic effects)}$$

$$
\begin{bmatrix}
\sigma^2_{hom} & \frac{c_{nucl}}{2}\sigma^2_{HomHetNucl} & \frac{c_{nucl}}{2}\sigma^2_{HomHetNucl} \\
\frac{c_{nucl}}{2}\sigma^2_{HomHetNucl} & \sigma^2_{acc} & \frac{c^2_{nucl}}{4}\sigma^2_{HomHetNucl} \\
\frac{c_{nucl}}{2}\sigma^2_{HomHetNucl} & \frac{c^2_{nucl}}{4}\sigma^2_{HomHetNucl} & \sigma^2_{don}
\end{bmatrix} \otimes A_{30},
$$

where A_{30} represents the haploid nuclear genetic relationship matrix (all-one matrix minus the matrix of haploid nuclear pairwise sequence divergence) of dimension equal to the number of isolates (Table S3), $\otimes$ represents the Kronecker product, σ^2_{hom}, σ^2_{acc} and σ^2_{don} are the variances among homokaryon, acceptor and donor nuclear genetic effects respectively, and $\frac{c_{nucl}}{2}\sigma^2_{HomHetNucl}$ is the covariance between homokaryon nuclear genetic effects and acceptor or donor nuclear genetic effects (i.e. numerator in Eq. 12). The covariance between acceptor and donor nuclear genetic effects, $\frac{c^2_{nucl}}{4}\sigma^2_{HomHetNucl}$, is analogous to a covariance between sex-specific combining abilities in a diallel cross. This covariance actually represents the numerator of the slope of the regression of heterokaryon donor genetic effects over heterokaryon acceptor genetic effects. The random genetic effect u_{hommit} and u_{hetmit} were assumed to follow a multivariate normal distribution with zero mean vector and variance-covariance matrix:

$$
V\begin{bmatrix} u_{hommit} \\ u_{hetmit} \end{bmatrix} = \begin{bmatrix} \sigma^2_{hommit} & c_{mit}\sigma^2_{homhet} \\ c_{mit}\sigma^2_{homhet} & \sigma^2_{hetmit} \end{bmatrix} \otimes A'_{11},
$$

(CovMit1: full covariance of mitochondrial genetic effects)

where A'_{11}, represents the mitochondrial genetic relationship matrix (all-one matrix minus the matrix of mitochondrial pairwise sequence divergence) of dimension equal to the number of mitochondrial haplotypes, σ^2_{hommit} and σ^2_{hetmit} are the variances of homokaryon and heterokaryons mitochondrial genetic effects respectively, and $c_{mit}\sigma^2_{homhet}$ is the covariance between homokaryon and heterokaryon mitochondrial genetic effects (i.e. part of the numerator in Eq. 13). The assay effect accounts for environmental variation among different assays and plate effect accounts for environmental variation between different plates within the same assay. Random acceptor x donor nuclear genetic effects in $u_{acc \times don}$, assay effects in u_{assay}, and plate effects in u_{plate} were each assumed to be independently and normally distributed with a mean of zero and variance of $\sigma^2_{acc \times don}$, σ^2_{assay} and σ^2_{plate} respectively ($V[u_{acc \times don}] = \sigma^2_{acc \times don}\ I_{225}$, $V[u_{assay}] = \sigma^2_{assay}\ I_{532}$, and $V[u_{plate}] = \sigma^2_{plate}\ I_{1395}$), where I is the identity matrix. A prerequisite for the estimation of c_{nucl} and c_{mit} is that the covariances between nuclear genetic effects or between mitochondrial genetic effects are not

null. To test for this, we fit additional models with reduced variance-covariance matrices for both nuclear or mitochondrial genetic effects. For nuclear genetic effects, we fit two additional types of models: (1) In "no covariance with homokaryon nuclear genetic effects" type of models, we only fit the covariance between acceptor and donor genetic effects (σ_{accdon}^2), so that there is no covariance between homokaryon and either acceptor or donor nuclear genetic effects:

$$V \begin{bmatrix} u_{hom} \\ u_{acc} \\ u_{don} \end{bmatrix} = \begin{bmatrix} \sigma_{hom}^2 & 0 & 0 \\ 0 & \sigma_{acc}^2 & \sigma_{accdon}^2 \\ 0 & \sigma_{accdon}^2 & \sigma_{don}^2 \end{bmatrix} \otimes A_{30}.$$

(CovNucl2: covariance between acceptor and donor nuclear genetic effects only)

(2) In the "no covariance of nuclear genetic effects", all covariances between homokaryon, acceptor and donor genetic effects are set to zero:

$$V \begin{bmatrix} u_{hom} \\ u_{acc} \\ u_{don} \end{bmatrix} = \begin{bmatrix} \sigma_{hom}^2 & 0 & 0 \\ 0 & \sigma_{acc}^2 & 0 \\ 0 & 0 & \sigma_{don}^2 \end{bmatrix} \otimes A_{30}.$$

(CovNucl3: no covariance of nuclear genetic effects)

For mitochondrial genetic effects, we fit one additional type of model where the covariation between homokaryon and heterokaryon mitochondrial genetic effects is set to zero:

$$V \begin{bmatrix} u_{hommit} \\ u_{hetmit} \end{bmatrix} = \begin{bmatrix} \sigma_{hommit}^2 & 0 \\ 0 & \sigma_{hetmit}^2 \end{bmatrix} \otimes A'_{11}.$$

(CovMit2: no covariance of mitochondrial genetic effects)

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