Supplementary Information for

Life history effects on neutral diversity levels of autosomes and sex chromosomes

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1. Haploid Model

Here we rigorously solve the haploid model with age-structure and endogenous reproductive variance, relate our results to previous work that considered special cases, investigate the properties of the effective population size in age-structured populations, and show that our main results also apply for general dependencies between realized reproduction at different ages. In Section 1.1 we spell out our assumptions about endogenous reproductive variance. In Section 1.2 we solve for the joint stationary distribution of the age and relative reproductive success associated with an allele, going backwards in time. Based on this distribution, we calculate the stationary per-generation coalescence rate for a sample of two alleles, to obtain Eq. 10 in the main text:

$$N_e = \frac{M \cdot G}{W}. \tag{S1}$$

In Section 1.3 we formally show that Eq. 10 holds in the limit in which the census population size goes to infinity while the population's age structure is held constant; we then derive a general and tight bound on the rate at which this solution is approached as the population size is increased. In Section 1.4, we recast our results in terms of reproductive variance, to show that the relationship derived by Hill for the case with age-structure alone (HILL 1972):

$$N_e = G \cdot M_1 / V, \tag{S2}$$

which is our Eq. 13, applies to the extended model with endogenous reproductive variance. We also show that the reproductive variance in this case is

$$V = W \cdot (M_1 / M), \tag{S3}$$

which is our Eq. 13. This concludes the derivations of our main results.

In Section 1.5 we show that in the case without endogenous reproductive variance, our Eq. 10 (Eq. S1 above) reduces to Felsenstein's formula (FELSENSTEIN 1971), and consider a simple example of how age-structure affects the effective population size. In Section 1.6 we investigate the properties of the effective population size in age-structured populations with endogenous reproductive variance. In particular, we derive an upper bound for the effective population size and derive the conditions under which it can be attained. In Section 1.7, we consider an alternative model, which allows for general dependencies between realized (rather than expected) reproductive success at different ages, and show that Hill's formula also applies to this model.

1.1 Requirements on f_a

When we introduced the haploid model with endogenous reproductive variance, we assumed that each newborn is assigned a relative reproductive success vector $\vec{r}$, where the (constant) proportion of individuals with a given vector $\vec{r}$ in age class a was denoted by $f_a(\vec{r})$ (see Table S1 for summary of notation). Here we describe the requirements on the probability mass function f_a that these assumptions entail. First, given that the probability of being born to a parent of age a is p_a, and to a specific parent of age a and with reproductive success $\vec{r}$ is $p_a \cdot \frac{r_a}{M_a}$, we require that $E_{f_a}(r_a) = \sum_{\vec{r}} f_a(\vec{r}) \cdot r_a = 1$ for any age a. Second, given that the number of individuals with a given $\vec{r}$ can only decrease with age (due to mortality), we further require that $M_a \cdot f_a(\vec{r}) \geq M_{a+1} \cdot f_{a+1}(\vec{r})$.

Third, requiring that the number of individuals of a given age a and with a given $\vec{r}$ is constant and equal to $M_a \cdot f_a(\vec{r})$ implies that this number needs to be an integer. Notably, if we would like to model the distribution of relative reproductive success using a given (continuous or discrete) distributions $\widetilde{f_a}(\vec{r})$, which satisfies the first two requirements, we would need to discretize $\widetilde{f_a}$ to obtain a probability mass function $\tilde{f}'_a$ such that $M_a \cdot \tilde{f}'_a(\vec{r})$ is always an integer. However, if we assume that the relative sizes of the age-class, i.e., the ratios M_i/M_j, are constant, and increase the total population sizes, the discretized functions $\tilde{f}'_a$ will approach $\widetilde{f_a}$, and the value of the $W_{i,j} = E_{\tilde{f}'_j}(r_i \cdot r_j) = E(r_i \cdot r_j | \text{survival to age } j)$ terms, which summarize the effect of endogenous reproductive variance on the effective population size, will approach $E_{\widetilde{f}_j}(r_i \cdot r_j)$. We implicitly assumed this limit when we considered the special case in which relative reproductive success is independent of age and of mortality rates. More generally, while the assumption that for any age a, $M_a \cdot f_a(\vec{r})$ is an integer, might appear highly restrictive, these restrictions are relaxed under the standard coalescent assumption that the population size is sufficiently large.

Notation	Definition	Remarks
p_a	Probability that a newborn descends from a parent of age a	$\sum_a p_a = 1$
q_a	Probability that a newborn descends from a parent of age $\geq a$	$q_a = \sum_{i \geq a} p_i$
G	Expected generation time	$G = \sum_a a \cdot p_a$
M_a	Number of individuals of age a (M_1 is the number of newborns per-year)	$M_{a+1} \leq M_a$
$\vec{r}$	Relative reproductive success, where component r_a is the relative reproductive success at age a	
$f_a(\vec{r})$	The proportion of individuals with relative reproductive success $\vec{r}$ among individuals of age a	
$g_a(\vec{r})$	Given an individual I of age a and a newborn n, $g_a(\vec{r})$ is the probability that I has relative reproductive success $\vec{r}$, conditioned on n being descended from I	$g_a(\vec{r}) = r_a f_a(\vec{r})$
$\epsilon(a, \vec{r})$	Joint stationary probability of age a and relative reproductive success $\vec{r}$ along a lineage, going backwards in time	$\epsilon(a, \vec{r})$ $= \frac{1}{G} \sum_{j \geq a} p_j g_j(\vec{r})$
ϵ_a	Marginal stationary distribution of age a	$\epsilon_a = \frac{q_a}{G}$
M	Effective age-class size	See Eq. S16
$W_{i,j}$	Average value of $r_i \cdot r_j$ among individuals of sex s and age a	Defined for $i \leq j$
W	Weighted average of the $W_{i,j}$	See Eq. S15
X, X_a	An individual's number of offspring, throughout its life or at age a, respectively	
V	Reproductive variance (i.e., $V = Var(X)$)	See Eq. S43
S_a	The event of surviving to age $\geq a$	

Table S1: Notation for the haploid model, with parameters of the model in red.

1.2 Stationary coalescence rate and effective population size

Here, we extend the derivations of Sagitov and Jagers (SAGITOV AND JAGERS 2005) to account for endogenous reproductive variance. Tracing an allele backward in time, the age a_t and relative reproductive success $\vec{r}_t$ of the individual I_t who carries the allele t years in the past defines a Markov chain $(a_t, \vec{r}_t)$. To define the transition probabilities of the chain, we distinguish between two cases. First, if the individual carrying the allele is not a newborn, i.e., $a_t > 1$, then at time $t+1$

that individual will be one year younger and its relative reproductive success $\vec{r}$ will remain unchanged, i.e., $(a_{t+1}, \vec{r}_{t+1}) = (a_t - 1, \vec{r}_t)$ with probability one. Second, if the individual carrying the allele is a newborn, i.e., $a_t = 1$, then a_{t+1} equals a with probability p_a. The probability mass function of $\vec{r}_{t+1}$ conditional on a_{t+1}, follows from Bayes' theorem, further conditioning on the fact that the parent, $I_{t+1} = I$, necessarily reproduced successfully

$$P(\vec{r}_I = \vec{r} | I_{t+1} = I, a_{t+1} = a)$$

$$= \frac{P(I_{t+1}=I|\vec{r}_{t+1}=\vec{r}, a_{t+1}=a) \cdot P(\vec{r}_I=\vec{r}| a_{t+1}=a)}{P(I_{t+1}=I)} = \frac{(r_a/M_a) \cdot f_a(\vec{r})}{\sum_{\vec{k}} (r_a/M_a) \cdot f_a(\vec{k})} = r_a \cdot f_a(\vec{r}). \tag{S4}$$

We denote this probability by $g_a(\vec{r}) \equiv r_a \cdot f_a(\vec{r})$, and conclude that

$$P((a_{t+1}, \vec{r}_{t+1}) = (a, \vec{r}) | a_t = 1) = p_a \cdot g_a(\vec{r}). \tag{S5}$$

g_a is a proper probability mass function since $\sum_{\vec{r}} g_a(\vec{r}) = \sum_{\vec{r}} r_a \cdot f_a(\vec{r}) = 1$. Moreover, the parent's expected value of r_a is $E_{\vec{r} \sim g_a}(r_a) = E_{\vec{r} \sim f_a}(r_a^2) = 1 + V_{\vec{r} \sim f_a}(r_a) \geq 1$. The latter inequality makes intuitive sense, as it implies that the allele is more likely to be descended from an individual that has higher than average relative reproductive success in its age class.

We rely on the transition probabilities to derive and solve a recursion for the stationary probability $\epsilon(a, \vec{r})$ of age, a and relative reproductive successes, $\vec{r}$, of the individuals carrying the allele. Namely,

$$\epsilon(a, \vec{r}) = \epsilon(a + 1, \vec{r}) + \left(\sum_{\vec{k}} \epsilon(1, \vec{k}) \right) \cdot p_a \cdot g_a(\vec{r}), \tag{S6}$$

where the first term corresponds to aging within the same individual and the second corresponds to parenting a newborn. In order to solve these recursions, we first consider the marginal stationary distribution of age, $\epsilon_a = \sum_{\vec{r}} \epsilon(a, \vec{r})$. To this end, we sum the recursions over $\vec{r}$ to obtain recursions on the marginal distribution,

$$\epsilon_a = \epsilon_{a+1} + \epsilon_1 \cdot p_a, \tag{S7}$$

where we also require that $\sum_a \epsilon_a = 1$. This recursion was solved by Sagitov and Jagers (SAGITOV AND JAGERS 2005) for the case without endogenous reproductive variance, yielding

$$\epsilon_a = q_a / G, \tag{S8}$$

where $q_a \equiv \sum_{j \geq a} p_j$. Substituting this expression into Eq. S6, the recursions simplify to

$$\epsilon(a, \vec{r}) = \epsilon(a + 1, \vec{r}) + \frac{1}{G} \cdot p_a \cdot g_a(\vec{r}), \tag{S9}$$

where we further require that $\sum_{a, \vec{r}} \epsilon(a, \vec{r}) = 1$. The solution of these recursions is

$$\epsilon(a, \vec{r}) = \frac{1}{G}\sum_{j \geq a} p_j g_j(\vec{r}). \tag{S10}$$

The marginal stationary probability mass function of $\vec{r}$ is $\sum_a \epsilon(a, \vec{r}) = \frac{1}{G}\sum_j (j \cdot p_j) \cdot g_j(\vec{r})$, which

is a proper probability mass function because $\frac{1}{G}\sum_j j \cdot p_j = 1$, and $\sum_{\vec{r}} g_a(\vec{r}) = 1$ for any age a.

We rely on the stationary distribution to derive the probability of coalescence of two alleles, along the same lines as detailed in the main text for the case without endogenous reproductive variance. For the coalescence to occur at time t in the past, one of the alleles (A) would descend from the other (B) or both would descend from the same parental allele at that time (this is contrary to the case of non-overlapping generations, in which coalescence necessarily occurs when both alleles descend from the same parental allele in the previous generation). For example, if allele A is associated with a newborn, one coalescence scenario would be for allele B to be associated with an individual of age $a > 1$, from which A descends a single time step (e.g., year) further in the past; a second coalescence scenario would be for both alleles to be associated with newborns at the same time, and descend from the same individual. Specifically, if allele B is in an individual of age a and relative reproductive success $\vec{r}$ at time t (with probability $\epsilon(a, \vec{r})$), then allele A must be in a newborn at time t-1 (with probability ϵ_1) having descended from the same individual carrying allele B (with probability $p_a \cdot \frac{r_a}{M_a}$). Summing over the individual's possible ages and reproductive success vectors, we obtain the probability

$$\sum_{a,\vec{r}} \epsilon(a, \vec{r}) \cdot \epsilon_1 \cdot p_a \cdot \frac{r_a}{M_a} = \frac{1}{G^2}\sum_a \frac{\sum_{j \geq a} p_a p_j \sum_{\vec{r}} r_a g_j(\vec{r})}{M_a} = \frac{1}{G^2}\sum_a \frac{\sum_{j \geq a} p_a p_j W_{a,j}}{M_a}, \tag{S11}$$

where for $j \geq i$,

$$W_{i,j} = \sum_{\vec{r}} r_i g_j(\vec{r}) = \sum_{\vec{r}} r_i r_j f_j(\vec{r}) = E_{\vec{r} \sim f_j}(r_i \cdot r_j) \tag{S12}$$

is the expectation of $(r_i \cdot r_j)$ conditional on surviving to age $\geq j$. Further allowing for either allele or both to be the newborn (using the inclusion-exclusion principal to subtract the probability $\epsilon_1^2 \sum_a \frac{p_a^2 W_{a,a}}{M_a}$ that both alleles were in a newborn prior to coalescence), and measuring the coalescence rate in generations (rather than years), we obtain the per-generation coalescence rate and corresponding effective population size:

$$\frac{1}{N_e} = \frac{1}{G}\sum_a \frac{p_a^2 W_{a,a} + 2\sum_{j>a} p_a p_j W_{a,j}}{M_a}. \tag{S13}$$

Eq. S13 can be rearranged to obtain Eq. 7 of the main text. To this end, we define

$$w_i = (p_i^2 W_{i,i} + 2 \sum_{j>i} p_i p_j W_{i,j})/W, \tag{S14}$$

where

$$W = \sum_i p_i^2 W_{i,i} + 2 \sum_{i<j} p_i p_j W_{i,j} \tag{S15}$$

is a weighted average of the $W_{i,j}$. Noting that $\sum_a w_a = 1$, we then define the effective age class size as a weighted harmonic average of the age class sizes,

$$\frac{1}{M} = \sum_a \frac{w_a}{M_a}. \tag{S16}$$

Substituting this expression into Eq. S13, we obtain Eq. 7 of the main text:

$$\frac{1}{N_e} = W/(M \cdot G). \tag{S17}$$

1.3 Convergence to the stationary solution

Here, we provide a formal justification for using the stationary coalescence rate and effective population size. To this end, we define the coalescence process and expected *TMRCA* rigorously, detail the condition under which our asymptotic expression for the expected *TMRCA* and thus effective population size (Eq. 10 in the main text) are exact, and derive a tight bound on the rate of convergence to the asymptotic rate of coalescence as the population size increases. Lastly, we relate our results to previous work that considered the convergence to asymptotic coalescence rates.

In Section 1.2 we modelled the state of an allele as a Markov chain. We defined the state space of the chain as the set S containing all possible pairs $s = (a, \vec{r})$, where a is the age of the allele, and $\vec{r}$ its relative reproductive success. We calculated the transition matrix, in which $P(s, t)$ is the transition probability between state s and state t, and its stationary distribution $\epsilon(s) = \epsilon(a, \vec{r})$. In doing so and in what follows, we assume the existence of a unique stationary distribution ϵ. While this requirement imposes conditions on model parameters, we expect it to be satisfied for realistic age-structures. Notably, the non-trivial requirement is for the chain to be aperiodic, which would be satisfied, for example, if there are two consecutive ages in which reproduction can occur (EMIGH AND POLLAK 1979).

To define the coalesce process of two alleles formally, we first need to define the alleles' joint states as a Markov chain. We do so in two steps. First, we consider a chain X_t^∞ in which the states

of the alleles are completely independent. This definition corresponds to a hypothetical infinite population with the specified age-structure, in which the alleles never coalesce. The state space of the chain is $S^\infty = S \times S$, and its transition matrix is $P^\infty(\vec{s}, \vec{t}) = P(s_1, t_1) \cdot P(s_2, t_2)$, with subscripts corresponding to each of the alleles. It follows that the stationary distribution associated with this chain is $\pi^\infty(s_1, s_2) = \epsilon(s_1) \cdot \epsilon(s_2)$.

Second, we consider a corresponding chain X_t^M that incorporates coalescence. This chain corresponds to the same age-structure, but with a finite effective age class size M. The state space of the chain is $S^M = S^\infty \cup \{c\}$, where c is an absorbing state, to which the chain transitions upon coalescence (we do not track the specific state of the allele after coalescence). The transition matrix of this chain for $\vec{s}, \vec{t} \in S^\infty$ is:

$$P^M(\vec{s}, \vec{t}) = P^\infty(\vec{s}, \vec{t}) \cdot (1 - C_{\vec{s}, \vec{t}}),$$

$$P^M(c, \vec{t}) = 0,$$

$$P^M(c, c) = 1, \text{ and}$$

$$P^M(\vec{s}, c) = \sum_{\vec{y} \in S \times S} P^\infty(\vec{s}, \vec{y}) \cdot C_{\vec{s}, \vec{y}}, \tag{S18}$$

where $C_{\vec{s}, \vec{t}}$ is the probability of coalescence conditioned that the two alleles transition from states $\vec{s}$ to states $\vec{t}$. Note that the stationary distribution of the chain X_t^M is trivial, i.e., it is c with probability 1 (and not π^∞).

The probabilities of coalescence $C_{\vec{s}, \vec{t}}$ can be described explicitly using the parameters of the model, but we do not require the explicit form for our purposes here. What is of interest to us, as will become clear below, is their weighted average:

$$\sum_{\vec{x}, \vec{y} \in S^\infty} \pi^\infty(\vec{x}) \cdot P^\infty(\vec{x}, \vec{y}) \cdot C_{\vec{x}, \vec{y}}. \tag{S19}$$

This average is the probability that a pair of alleles, each drawn independently from the stationary distribution ϵ, coalesce in some state y within a single time step. In Section 1.2 we referred to this probability informally as the 'stationary probability of coalescence per-year', and found it to be

$$\sum_{\vec{x}, \vec{y} \in S^\infty} \pi^\infty(\vec{x}) \cdot P^\infty(\vec{x}, \vec{y}) \cdot C_{\vec{x}, \vec{y}} = \frac{W}{M \cdot G^2}. \tag{S20}$$

Next, we define the *TMRCA* of a sample of two alleles. Using the standard definition of a hitting time, i.e., $\tau_A = \min \{t \geq 0 : X_t \in A\}$, the *TMRCA* of the sample is simply $\tau_{\{c\}}^M$, where by τ^M and

τ^∞ we refer to the hitting times of the chains X_t^M and X_t^∞, respectively. We denote the expected *TMRCA*, given an initial state of the chain $X_0^M \in S^\infty$, by

$$e_x \equiv E(\tau_{\{c\}}^M | X_0^M = x). \tag{S21}$$

Note that this definition is restricted to the case in which the two alleles are initially distinct (i.e., $X_0^M \neq c$).

We can now derive several results about the expected *TMRCA*. By conditioning on the first step, i.e., on the value of $X_1^M = y$, we find that

$$e_x = 1 + \sum_{y \in S^\infty} P^M(x, y) \cdot e_y = 1 + \sum_{y \in S^\infty} P^\infty(x, y) \cdot (1 - C_{x,y}) \cdot e_y. \tag{S22}$$

It follows that if the initial state of the chain is sampled from the stationary distribution of the chain X_t^∞ then the expected *TMRCA* satisfies

$$\sum_{x \in S^\infty} \pi^\infty(x) \cdot e_x = 1 + \sum_{x,y \in S^\infty} \boldsymbol{\pi^\infty(x) \cdot P^\infty(x,y) \cdot e_y} - \sum_{x,y \in S^\infty} \pi^\infty(x) \cdot P^\infty(x,y) \cdot C_{x,y} \cdot e_y. \tag{S23}$$

The term in bold, simplifies to

$$\sum_{x,y \in S^\infty} \pi^\infty(x) \cdot P^\infty(x,y) \cdot e_y = \sum_{y \in S^\infty} \left[\sum_{x \in S^\infty} \pi^\infty(x) \cdot P^\infty(x,y) \right] \cdot e_y = \sum_{y \in S^\infty} \pi^\infty(y) \cdot e_y, \tag{S24}$$

and therefore Eq. S23 simplifies to

$$\sum_{x,y \in S^\infty} \pi^\infty(x) \cdot P^\infty(x,y) \cdot C_{x,y} \cdot e_y = 1. \tag{S25}$$

Relying on Eq. S20, we can then rewrite Eq. S25 as

$$\sum_{y \in S^\infty} \alpha_y \cdot e_y = \frac{M \cdot G^2}{W}, \tag{S26}$$

where $\alpha(y) = \frac{\sum_{x \in S^\infty} \pi^\infty(x) \cdot P^\infty(x,y) \cdot C_{x,y}}{W/(M \cdot G^2)}$ and $\sum_{y \in S^\infty} \alpha(y) = 1$. Intuitively, $\alpha(y)$ is the stationary probability that the coalescence eventually occurs at state y. Eq. S26 implies that if ages and relative reproductive success in the initial sample are distributed according to α, the expected *TMRCA*, in units of the generation time, is exactly $(M \cdot G)/W$. Note that we have made no asymptotic assumptions, i.e., this result is exact and holds even when the census size is very small. Also note that this result should hold in the more general context of the structured coalescent.

Next, we consider the expected *TMRCA* when the initial sample is not distributed according to α (e.g., when the alleles are sampled uniformly from a population at steady state). First, from Eq. S26 we see that

$$\left| e_x - \frac{M \cdot G^2}{W} \right| = \left| \sum_{y \in S^\infty} \alpha_y \cdot (e_x - e_y) \right| \leq \sum_{y \in S^\infty} \alpha_y \cdot \left| e_x - e_y \right|. \qquad (S27)$$

To bound the terms $\left| e_x - e_y \right|$, we consider the first visit of the chain to states c or y. The time it takes to get from x to c can be partitioned to the time it takes to get to c or y, plus the time to get from there to c, and thus

$$e_x = E\left(\tau^M_{\{y,c\}} \middle| X_0^M = x \right) + P\left(X^M_{\tau^M_{\{y,c\}}} = y \middle| X_0^M = x \right) e_y \leq E\left(\tau^M_{\{y,c\}} \middle| X_0^M = x \right) + e_y. \qquad (S28)$$

To bound the term $E\left(\tau^M_{\{y,c\}} \middle| X_0^M = x \right)$, we define a coupling of the chains X_t^M and X_t^∞, i.e. we define both chains on the same probability space, such that the chains have the exact same states until coalescence occurs. Formally, we assume that $X_0^M = X_0^\infty$, and given X_t^M, X_t^∞ such that $X_t^M \in \{X_t^\infty, c\}$, we define X_{t+1}^M and X_{t+1}^∞ as follows. First, X_{t+1}^∞ is chosen with the appropriate probability conditioned on X_t^∞. Second, if $X_t^M = c$ then $X_{t+1}^M = c$; if not, then $X_{t+1}^M = c$ with probability $C_{X_t^\infty, X_{t+1}^\infty}$, and $X_{t+1}^M = X_{t+1}^\infty$ otherwise. In this coupling, if $X_t^\infty = y$ then $X_t^M \in \{y, c\}$. It follows that

$$E\left(\tau^M_{\{y,c\}} \middle| X_0^M = x \right) \leq E\left(\tau^\infty_{\{y\}} \middle| X_0^\infty = x \right). \qquad (S29)$$

Defining $C = \max_{x,y \in S^\infty} E\left(\tau^\infty_{\{y\}} \middle| X_0^\infty = x \right)$, we conclude that for any initial sample $x \in S^\infty$, the expected *TMRCA* in units of the generation time G, e_x/G, satisfies

$$\left| \frac{e_x}{G} - \frac{M \cdot G}{W} \right| \leq \frac{C}{G}. \qquad (S30)$$

Since C is defined on the chain X_t^∞, it does not depend on the specific value of M. In other words, if we fix the age-structure (i.e., the breeding distribution p, the survival rates, and the distribution of relative reproductive success) and let the census size tend to infinity, the difference between the exact expected *TMRCA* and the asymptotic expectation, $M \cdot G/W$, remains bounded by C/G. Intuitively, the value of C corresponds to the mixing time of the chain X^∞, which is $O(1)$ and thus becomes negligible relative to the asymptotic expectation when M is sufficiently large. In other words, Eq. S30 provides a bound on the difference between the asymptotic effective population size and its value for any given effective age class size M.

Previous works utilizing a similar framework relied on Möhle's lemma (MÖHLE 1998) to demonstrate weak convergence to Kingsman's coalescence process (NORDBORG AND KRONE 2002; SAGITOV AND JAGERS 2005). For example, considering a sample of size n from the present population, and denoting the number of unique ancestors of the sample t generations in the past by Z_t, the convergence to our Eq. 9 is stated as

$$Z_{\left\lfloor t/\left(\frac{G \cdot M}{W}\right)\right\rfloor} \to R_t, \tag{S31}$$

where $(R_t)_{t \geq 0}$ is the standard Kingman coalescent for a sample of size n (KINGMAN 1982), and the limit holds for any series of age-structured populations for which $G \cdot M/W \to \infty$. Although weak convergence does not generally imply convergence of moments, Möhle's lemma can be easily extended to show that convergence holds for the expected $TMRCA$ of a sample of two alleles, i.e.,

$$\frac{E(TMRCA)}{G \cdot M/W} \to 1. \tag{S32}$$

While our result (Eq. S30) does not prove weak convergence (SAGITOV AND JAGERS 2005) and is limited to a sample of two alleles, it provides proof for convergence of the first moment (i.e., it justifies Eq. 10 in the main text) and establishes tighter asymptotic rates of convergence compared to previous work (i.e., it proves that $\left| E(TMRCA) - \frac{G \cdot M}{W} \right| \leq C/G$). These results suggest that the asymptotic approximation is applicable even to very small populations.

1.4 Reproductive variance

To recast our results for N_e in terms of the reproductive variance V, we first consider the case with non-overlapping generations in a haploid population of constant size, i.e., with Wright-Fisher sampling. We denote the number of offspring of the ith individual by k_i and the census size by N. The expected number of offspring is 1, i.e., $\frac{1}{N}\sum_i k_i = 1$, and we denote the variance in number of offspring, which we also refer to as the reproductive variance, by $V = \frac{1}{N}\sum_i (k_i - 1)^2$. In the standard neutral model, without endogenous reproductive variance, $V = 1$. Since the probability that two distinct gametes descend from the same ancestor in the previous generation is $\sum_i \frac{k_i}{N} \cdot \frac{k_i-1}{N-1} = \frac{V}{N-1}$, we find that the effective population size is

$$N_e = \frac{N-1}{V} \cong \frac{N}{V}, \tag{S33}$$

which is the expression derived by Wright (WRIGHT 1939/1986) and presented in Eq. 12 of the main text.

To extend Eq. S33 to the case with overlapping generations, we consider the first two moments of an individual's number of offspring, X, throughout its lifetime. First, we note that an individual's number of offspring can be expressed as a sum over the number at each age, i.e., $X = \sum_a X_a$, where X_a is the number of offspring at age a; $X_a = 0$ if the individual does not survive to that age. In these terms, the first two moments are

$$E(X) = \sum_a E(X_a) \text{ and } E(X^2) = \sum_a E(X_a^2) + 2 \sum_{i<j} E(X_i \cdot X_j). \tag{S34}$$

Denoting the event of surviving to age $\geq a$ by S_a, we note that

$$E(X_a^i) = Pr(S_a) \cdot E(X_a^i | S_a) = \frac{M_a}{M_1} \cdot E(X_a^i | S_a), \tag{S35}$$

The latter term, $E(X_a^i | S_a)$, can be simplified further by conditioning on $\vec{r}$. Since the probability mass function of $\vec{r}$ conditional on S_a is f_a,

$$E(X_a^i | S_a) = E_{\vec{r} \sim f_a} E(X_a^i | S_a, \vec{r}). \tag{S36}$$

Moreover, the distribution of X_a conditional on S_a and $\vec{r}$ is simply $(X_a | \vec{r}, S_a) \sim Bin(M_1, p_a \cdot r_a/M_a)$, and therefore

$$E(X_a | S_a) = E_{\vec{r} \sim f_a} \left(\frac{M_1 r_a p_a}{M_a} \right) = \frac{M_1 p_a}{M_a}$$

and

$$E(X_a^2 | S_a) = E_{\vec{r} \sim f_a} \left(M_1 \frac{r_a p_a}{M_a} + 2 \binom{M_1}{2} \left(\frac{r_a p_a}{M_a} \right)^2 \right) = \frac{M_1 p_a}{M_a} + 2 \binom{M_1}{2} \left(\frac{p_a}{M_a} \right)^2 W_{a,a}. \tag{S37}$$

Substituting these expressions into Eq. S35, we find that

$$E(X_a) = p_a \text{ and } E(X_a^2) = p_a + \frac{M_1 - 1}{M_a} p_a^2 \cdot W_{a,a}. \tag{S38}$$

To calculate the remaining terms in Eq. S34, $E(X_i \cdot X_j)$ for $j > i$, we note that conditioning on S_j, and on $\vec{r} | S_j$,

$$E(X_i \cdot X_j) = Pr(S_j) \cdot E(X_i \cdot X_j | S_j) = \frac{M_j}{M_1} \cdot E_{\vec{r} \sim f_j} E(X_i \cdot X_j | S_j, \vec{r}). \tag{S39}$$

The latter term is easily calculated, since conditional on S_j and $\vec{r}$, X_i and X_j are independent binomial variables, with $(X_i | \vec{r}, S_j) \sim Bin(M_1, p_i \cdot r_i/M_i)$ and $(X_j | \vec{r}, S_j) \sim Bin(M_1, p_j \cdot r_j/M_j)$, yielding

$$E(X_i \cdot X_j) = \frac{M_j}{M_1} \cdot E_{\vec{r} \sim f_j} \left(\frac{M_1^2 p_i p_j r_i r_j}{M_i M_j} \right) = \frac{M_1 p_i p_j W_{i,j}}{M_i}. \tag{S40}$$

Substituting the expressions from Eqs. S38 and S40 into Eq. S34 we find that

$$E(X) = 1 \text{ and } E(X^2) = 1 + M_1 \sum_i \frac{p_i^2 \cdot W_{i,i} + 2 \sum_{j>i} p_i p_j W_{i,j}}{M_i} - \sum_i \frac{p_i^2 \cdot W_{i,i}}{M_i}. \tag{S41}$$

Assuming that the total population size is sufficiently large for the ratios M_i/M_j and terms $W_{i,j}$ to be approximated as fixed, and for the higher order term $\sum_i \frac{p_i^2 \cdot W_{i,i}}{M_i}$ to be negligible, we find that

$$E(X) = 1 \text{ and } E(X^2) \cong 1 + \frac{M_1}{M} W, \tag{S42}$$

and therefore the reproductive variance is

$$V = E(X^2) - E^2(X) = \frac{M_1}{M} W, \tag{S43}$$

which is Eq. 14 of the main text. These assumptions correspond to the standard practice of neglecting higher order terms in $1/N$ in models with non-overlapping generations. From Eqs. S17 and S43 we find that the effective population size is

$$N_e = (G \cdot M_1)/V, \tag{S44}$$

which is the same form as in the case without age-structure (Eq. S33), and the general form presented in Eq. 13 of the main text.

1.5 Age-structure alone

Felsenstein used a different approach to solve the haploid model without endogenous reproductive variance, relying on the definition of the effective population size as the inbreeding effective number (FELSENSTEIN 1971). To see that his results agree with ours (as well as with those of Sagitov and Jagers (SAGITOV AND JAGERS 2005)), consider the case without endogenous reproductive variance, where Eq. S17 reduces to

$$N_e = MG = \frac{G}{\sum_i \frac{p_i^2 + 2 \sum_{j>i} p_i p_j}{M_i}} = \frac{G}{\sum_i \frac{p_i}{M_i}(q_i + q_{i+1})}, \tag{S45}$$

where $q_i = \sum_{j \geq i} p_i$. Noting that $p_i(q_i + q_{i+1}) = (q_i - q_{i+1})(q_i + q_{i+1}) = q_i^2 - q_{i+1}^2$, we find that

$$N_e = \frac{G}{\sum \frac{p_i}{M_i}(q_i + q_{i+1})} = \frac{GM_1}{\sum \frac{M_1}{M_i}(q_i^2 - q_{i+1}^2)} = \frac{GM_1}{1 + \sum_i q_{i+1}^2 (\frac{M_1}{M_{i+1}} - \frac{M_1}{M_i})}, \tag{S46}$$

where Felsenstein's functional form (p. 585 in (FELSENSTEIN 1971)) is on the rightmost side.

To better understand the effect of age-structure on the effective population size, consider a simple example in which there is no endogenous reproductive variance, and no age-dependence in reproductive success. In other words, the only difference among individuals' numbers of offspring arise from the stochasticity of mortality and reproduction. In this case, the probability of having a parent of age a is proportional to the size of the age class, i.e., $p_a = M_a/N$ where $N = \sum_a M_a$ is the census size. Following our derivations, the effective population size (Eq. 5 in the main text) then reduces to $N_e = \frac{G}{(2G-1)}N$, and if the generation time $G \gg 1$ then $N_e \approx \frac{1}{2}N$. In other words, the age structure reduces the effective population size to half of the census size.

1.6 Upper bound on the effective population size

Here, we provide an upper bound for the effective population size of age-structured populations. With non-overlapping generations, the maximal effective population size equals the census population size, and it is attained when all individuals are equally likely to reproduce. In this case, endogenous reproductive variance reduces the effective population size below the census size (Eq. 12). In contrast, with age-structure, the maximal effective population size is attained when short-lived individuals are given a higher chance of reproducing while they live. In this case, we show that the effective population size can exceed the census size, but it is bound by the number of offspring per generation, $G \cdot M_1$. We also consider the conditions on M_a and p_a under which this upper bound can be attained, and describe the distributions of endogenous reproductive variances for which it is attained.

We begin by showing that the reproductive variance $V \geq 1$. Given that we have shown that in age-structured populations $N_e = G \cdot M_1/V$ (Eq. 13), showing that $V \geq 1$ establishes that $G \cdot M_1$ is an upper bound on N_e. To this end, we consider an individual's number of offspring, X, conditional on its relative reproductive success $\vec{r}$ and longevity d. Employing the notation of Section 1.4, $X = \sum_{i=1}^{d} X_i$, where the number of offspring at age i, $X_i \sim Bin(M_1, \frac{p_i r_i}{M_i})$, and the X_is are independent of one another. It follows that

$$E(X|\vec{r}, d) = M_1 \sum_{i=1}^{d} \frac{p_i r_i}{M_i} \text{ and } Var(X|\vec{r}, d) = M_1 \sum_{i=1}^{d} \frac{p_i r_i}{M_i} (1 - \frac{p_i r_i}{M_i}) \cong E(X|\vec{r}, d), \text{ (S47)}$$

where the approximation for the variance becomes exact in the limit in which M_i/M_j are held constant and the census population size goes to infinity. In other words, when the population size is sufficiently large, $X|(\vec{r}, d)$ is well approximated by a Poisson variable. From Eq. S48 and the law of total variance we have

$$V = E\,Var(X|\vec{r}, d) + Var\,E(X|\vec{r}, d) \cong E\,E(X|\vec{r}, d) + Var\,E(X|\vec{r}, d) = E(X) + Var\,E(X|\vec{r}, d)$$
$$= 1 + Var\,E(X|\vec{r}, d) \geq 1. \tag{S48}$$

Intuitively, Eq. S48 states that the in age-structured populations the distribution of the number of offspring is overdispersed due to stochasticity in longevity and endogenous reproductive variance. This implies that, in contrast to the case of non-overlapping generations, the number of offspring in age-structured populations is generally not well approximated by a Poisson variable. Eqs. 12 and S48 imply that

$$N_e \leq G \cdot M_1, \tag{S49}$$

i.e., the effective population size is bound by the number of newborns per generation. This bound generalizes the bound $N_e \leq N$ in the case of non-overlapping generations.

Next, we consider an age-structured population with given values of M_a and p_a, and ask which distributions of relative reproductive success, $f_a(\vec{r})$, maximize N_e, and what are the conditions on M_a and p_a for this maximum to equal the bound $G \cdot M_1$. Eq. S48 implies that maximizing N_e is equivalent to minimizing $Var\,E(X|\vec{r}, d)$, and that the bound $G \cdot M_1$ is attained when $E(X|\vec{r}, d) = 1$ for any combination of $(\vec{r}, d)$ that occurs with non-zero probability. A distribution of $\vec{r}$ that minimizes $Var\,E(X|\vec{r}, d)$ can be explicitly constructed by the following algorithm:

1. Set $n = 1$. For each $d \geq 1$, initiate the $M_d - M_{d+1}$ vectors $\vec{r}$ of length d, corresponding to the $M_d - M_{d+1}$ individuals with longevity d, with zeros.

2. Choose the maximal $k \geq n$ at which the expression $\frac{M_1(q_n - q_{k+1})}{M_n - M_{k+1}}$ attains its minimum value v (see Table S1 for the definition of q). For intuition, consider the case when $n = 1$: since there are $M_1 - M_{k+1}$ individuals with longevity $1 \leq d \leq k$, and $M_1(q_1 - q_{k+1})$ offspring that descend from parents in this range of ages, v is an upper bound on the expected number of offspring that an individual with longevity in this range can have. We will assign vectors $\vec{r}$ such that v is attained.

3. For $d = n, \dots, k$: Assign values $r_n, \dots, r_d$ to the individuals of longevity d, such that $\sum_{i=n}^{d} M_1 p_i \frac{r_i}{M_i} = v$, and under the constraint that r_a over the ath age class should average to one. If $n > 1$, $r_1, \dots, r_{n-1}$ remain zero. Such an assignment always exists, but is not necessarily unique (Fig. S1).

4. If k is smaller than the maximal longevity in the population, set $n = k + 1$ and return to step 2.

The bound $G \cdot M_1$ is attainable if and only if (iff) the algorithm requires exactly one step, which occurs iff

$$M_a \geq q_a \cdot M_1 \text{ for all } a \geq 1. \tag{S50}$$

An example for an age-structured population that satisfies this condition, and for distributions of $\vec{r}$ given by the algorithm, are shown in Figs. S1A and S1B. The condition in Eq. S50 implies that

$$N_e \leq G \cdot M_1 = \sum_a q_a \cdot M_1 \leq \sum_a M_a = N \tag{S51}$$

(note that $\sum_a q_a = G$ always holds), and thus that the effective population size cannot exceed the census size. In populations that do not satisfy the condition in Eq. S50, however, the effective population size is always smaller than $G \cdot M_1$ but can be larger than the census size (Fig. S1C).
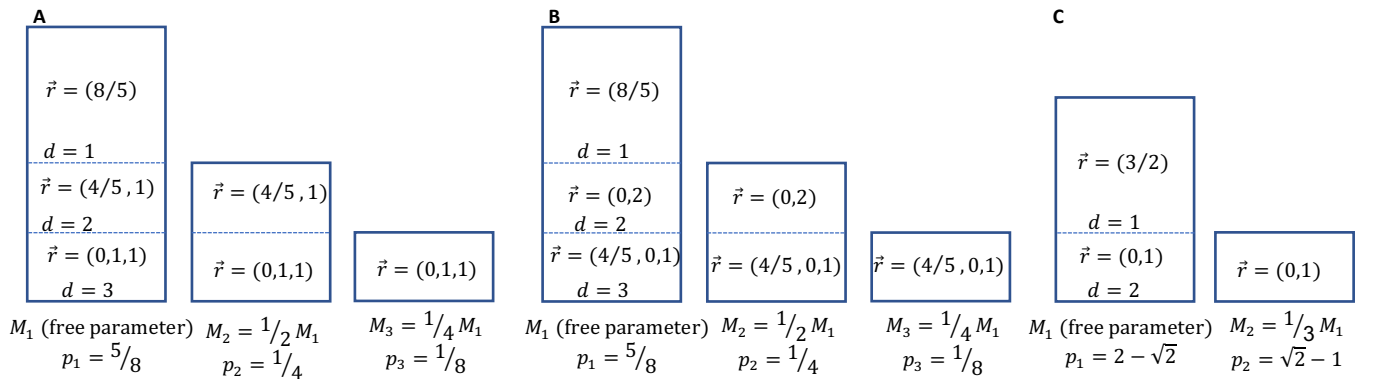

Figure S1: Maximal effective population sizes for specific age-structures. (A and B) An age structured population that satisfies the condition in Eq. S50 and thus has a maximal effective size equal to $G \cdot M_1$. In this example, $N_e = G \cdot M_1 = \frac{3}{2} \cdot M_1 < N = \frac{7}{4} \cdot M_1$. (A) and (B) show different distributions of $\vec{r}$ that derive from the algorithm and thus attain the maximal effective population size, illustrating that the construction is not unique. (C) An age-structure that does not satisfy the condition in Eq. S50. In this example the maximal effective size, $N_e = \frac{4+3\sqrt{2}}{6} \cdot M_1 \cong 1.37 \cdot M_1$, is strictly smaller than $G \cdot M_1 = \sqrt{2} M_1$, but larger than the census size, $\frac{4}{3} \cdot M_1$.

1.7 Realized reproductive success

The model we considered so far allows for dependencies between endogenous but not realized reproductive success in different ages. Here we consider an alternative model that allows for such dependencies (also see (EVANS AND CHARLESWORTH 2013)). Our model builds on the work of Sagitov and Jagers (SAGITOV AND JAGERS 2005), who parametrize their model in terms of the distribution of the realized (rather than potential) number of offspring. We generalize their model to allow for any dependency between individuals' numbers of offspring in different ages. Importantly, we show that our formula for the effective population size (Eq. 13) holds under this model.

We assume that each newborn is assigned a vector $\vec{h} = (h_1, \dots h_{l(\vec{h})})$ of non-negative integers, such that it will survive to age $l(\vec{h})$, have h_i offspring at age i, and have $S(\vec{h}) = \sum h_i$ offspring in total. The model's parameters consist of a set H of M_1 such vectors, where $\sum_{\vec{h} \in H} S(\vec{h}) = M_1$ to ensure that the population size remains constant; this parametrization allows for general dependencies between individuals' numbers of offspring at different ages. At each time step, the M_1 vectors in H are assigned to the M_1 newborns at random. The model is fully characterized by the set H. Notably, the age-class sizes are

$$M_a = \sum_{\vec{h} \in H : l(\vec{h}) \geq a} 1 \tag{S52}$$

and the probability that a newborn descends from a parent of age a is

$$p_a = \sum_{\vec{h} \in H : l(\vec{h}) \geq a} h_a / M_1. \tag{S53}$$

The generation time is defined as $G = \sum i \cdot p_i$. We can also define an individual's relative reproductive success at a given age a as the ratio of its realized success and the average realized success in that age-class, i.e.,

$$r_{\vec{h},a} = \frac{h_a}{\sum_{\vec{g} \in H : l(\vec{g}) \geq a} g_a / M_a}; \tag{S54}$$

this definition is useful for comparing our main model with this one.

This model can be solved along the same lines we described in Sections 1.2 and 1.4. Here we provide only the main results, as the derivations are almost identical. First, the stationary distribution of a (age) and $\vec{h}$ is

$$\epsilon\left(a, \vec{h}\right) = \frac{\sum_{\vec{h} \in H: l(\vec{h}) \geq a} \sum_{i=a}^{l(\vec{h})} h_i}{M_1 \cdot G}. \tag{S55}$$

We rely on this distribution to solve for the stationary yearly rate of coalescence and corresponding effective population size. To this end, we define the effective age class size as $M \equiv \left(\sum w_a / M_a\right)^{-1}$, with weights

$$w_a = \left(\sum_{\vec{h} \in H: l(\vec{h}) \geq a} p_a r_{\vec{h},a} \left(h_a - 1\right) / M_1 + 2 \sum_{\vec{h} \in H: l(\vec{h}) \geq a} p_a r_{\vec{h},a} \left(\sum_{i>a} h_i\right) / M_1\right) / W, \tag{S56}$$

where W is defined such that these weights add up to 1. In these terms, the effective population size is well approximated by the same form as Eq. (10):

$$N_e \cong M \cdot G / W,$$

where the conditions for the approximation are the same as in Section 1.4. These results establish that N_e takes the same form as it does for the model we described in the main text, although the definitions of M and W differ between the models.

We can also recast the results for this model in terms of reproductive variance V. Calculating the reproductive variance in this model is straightforward:

$$V = \frac{\sum_{\vec{h} \in H} \left(S(\vec{h}) - 1\right)^2}{M_1}. \tag{S57}$$

A simple rearrangement of terms in Eq. S57 then established that

$$N_e = G \cdot M_1 / V,$$

which is Hill's formula and our Eq. 13. Thus, our main results apply under general dependencies between *realized* reproductive success in different ages.

Note, however, that in this model, the effective population size can exceed $G \cdot M_1$. The difference between models arises because in our main model, the distribution of the number of offspring is overdispersed compared to a Poisson distribution, whereas this model allows for the distribution to be under-dispersed. As an extreme example, consider a constant-sized population with non-overlapping generations, in which each individual has exactly one offspring; in this case, $V = 0$ and $N_e = \infty$ (coalescence never occurs).

2. Diploid Model

2.1 Overview

Here we rigorously define and solve the diploid model with two sexes and endogenous reproductive variance, and derive formulas for the effective population sizes of X and autosomes. While the diploid model is more elaborate, the model and results follow along the same lines as we described for the haploid model. In Section 2.2 we detail the assumptions of the diploid model and introduce the notation required for the derivations that follow. In Section 2.3 we solve for the joint stationary distribution of the age and relative reproductive success of autosomal and X-linked alleles. We build on the joint stationary distribution to solving for the stationary per-generation coalescence rates and corresponding effective population sizes on X and autosomes. Since some of the explicit equations we derive are not presented in the main text, we briefly review them here.

Notably, to extend the haploid formula for the effective population size, $N_e = MG/W$ (Eq. 10), to the diploid case, we require explicit expressions for the effective age-class size M, generation time G, and W, corresponding to the X and autosomes. First, we define these measures for each sex in the same way that we did in the haploid model (i.e., as in Eqs. S15 and S16). We then define G and W for X and autosomes, as simple weighted averages over their values in males and females:

$$G_X = \frac{2}{3}G_F + \frac{1}{3}G_M \text{ and } G_A = \frac{1}{2}(G_M + G_F) \tag{S58}$$

and

$$W_X = \frac{2}{3}W_F + \frac{1}{3}W_M \text{ and } W_A = \frac{1}{2}(W_M + W_F) \tag{S59}$$

(Table 2 in the main text), where the weights reflect the relative number of generations that X and autosomal linked loci spend in males and females (see Table S2 for notation). The effective age class sizes on X and autosomes are defined as weighted harmonic averages. In the case without endogenous reproductive variance, they are defined as

$$\frac{1}{M_X} = \frac{1/3}{M_M} + \frac{2/3}{M_F} \text{ and } \frac{1}{M_A} = \frac{1/2}{M_M} + \frac{1/2}{M_F}. \tag{S60}$$

In the case with endogenous reproductive variance, the weights further account for the effects of endogenous variances on the relative probability of coalescence in males and females,

$$\frac{1}{M_X} = \frac{1/3(W_M/W_X)}{M_M} + \frac{2/3(W_F/W_X)}{M_F} \text{ and } \frac{1}{M_A} = \frac{1/2(W_M/W_X)}{M_M} + \frac{1/2(W_F/W_X)}{M_F} \tag{S61}$$

(Table 2 in the main text). Using these definitions, the effective population size for the X and autosomes take the form

$$N_e^A = \frac{2G_A M_A}{W_A} \text{ and } N_e^X = \frac{3}{4} \cdot \frac{2G_X M_X}{W_X}, \tag{S62}$$

where the factor 2, which is absent in the haploid case (Eq. 10), is not due to diploidy (which is already accounted for by defining N_e in diploids as ½ the inverse coalescence), but rather accounts for the effective number of age classes with two sexes (i.e., $2G$ instead of G classes in the haploid case; see SI Section 2.3). To translate these effective sizes into coalescence rates, we also account for ploidy, yielding per generation rates of $1/2N_e^A = W_A/4G_A M_A$ on autosomes and $1/(3/2)N_e^X = W_X/3G_X M_X$ on the X. Based on Eq. S62, the mutation rates on X and autosomes, and the standard forms for heterozygosity levels, we obtain the following expression for the X:A diversity ratio:

$$\frac{E(\pi_X)}{E(\pi_A)} = \frac{3}{4} \cdot \frac{f(\mu_M/\mu_F) \cdot f(G_M/G_F)}{f\left(\frac{W_M/W_F}{M_M/M_F}\right)}. \tag{S63}$$

In Section 2.4, we recast the results for the effective population size (Eq. S62) and the X:A diversity ratio (Eq. S63) in terms of male and female reproductive variances. First, we show that the reproductive variances in males and females, V_M and V_F, are given by

$$V_s = \frac{M_1}{\gamma_s} \frac{W_s}{M_s} - \frac{1-\gamma_s}{\gamma_s^2}, \tag{S64}$$

where the index s corresponds to M or F, and γ_M and γ_F are the proportions of males and females among newborns, respectively. Thus, this equation does not assume a sex ratio of 1. Rewriting Eq. S63 in terms of male and female reproductive variances we find that

$$N_e^X = \frac{3}{4} \cdot \frac{4G_X M_1}{\frac{2}{3}\gamma_M V_M + \frac{4}{3}\gamma_F V_F + \frac{2\gamma_F}{3\gamma_M} + \frac{4}{3}\frac{\gamma_M}{\gamma_F}} \text{ and } N_e^A = \frac{4G_A M_1}{\gamma_M V_M + \gamma_F V_F + \frac{\gamma_F}{\gamma_M} + \frac{\gamma_M}{\gamma_F}}, \tag{S65}$$

where M_1 is the number of newborns of both sexes per year, and that

$$\frac{E(\pi_X)}{E(\pi_A)} = \frac{3}{4} \cdot \frac{f(\mu_M/\mu_F) \cdot f(G_M/G_F)}{f\left(\frac{\gamma_F/\gamma_M + \gamma_M V_M}{\gamma_M/\gamma_F + \gamma_F V_F}\right)}. \tag{S66}$$

These equations reduce to Eqs. 18 and 21 in the main text. In Section 2.5, we compare Eq. 18 (or Eq. S65) to Hill and Pollak's more complex expressions for age structured populations (see Introduction and (HILL 1972; POLLAK 1980; POLLAK 1990; POLLAK 2011)). We show that in the general case in which the sex ratio at birth is not 1, relating our Eq. 18 and the results of Hill and

Pollak requires quite an elaborate derivation. In Section 2.6, we recast our results in terms of reproductive success of alleles rather than individuals, in order to provide intuition for the differences in denominator between Hill's haploid formula, $N_e = G \cdot M_1/V$, and our extensions for diploids, e.g., $N_e = 4G_A M_1/(2 + V_A)$ for autosomes, assuming equal sex ratios at birth.

Notation	Definition	Remarks
$p_{s,a}$	Probability that a parent of sex s is of age a	$\Sigma_a p_{F,a} = \Sigma_a p_{M,a} = 1$
$q_{s,a}$	Probability that a parent of sex s is of age $\geq a$	$q_{s,a} = \Sigma_{i \geq a} p_{s,i}$
G_M, G_F	Male and female generation times	$G_s = \Sigma_a a \cdot p_{s,a}$
G_X, G_A	Generation times for X and autosomes	See Eq. S58
$M_{s,a}$	Number of individuals of sex s and age a	$M_{s,a+1} \leq M_{s,a}$
M_1	Number of newborns of both sexes per-year	
γ_M, γ_F	Proportions of males and females among newborns	$\gamma_s = M_{s,1}/M_1$
$\vec{r}$	Relative reproductive success	
$f_{s,a}(\vec{r})$	Proportion of individuals with relative reproductive success $\vec{r}$ among individuals of sex s and age a	
$g_{s,a}(\vec{r})$	Given a newborn that descended from a parent of sex s and age a, $g_{s,a}(\vec{r})$ is the probability that the parent has relative reproductive success $\vec{r}$	$g_{s,a}(\vec{r}) = r_a \cdot f_{s,a}(\vec{r})$
$\epsilon^X(s,a,\vec{r})$, $\epsilon^A(s,a,\vec{r})$.	Joint stationary probability of sex s, age a, and relative reproductive success $\vec{r}$ for the X and autosomes	See Eqs. S74 and S75
$\epsilon^X_{s,a}, \epsilon^A_{s,a}$	Marginal stationary distribution of sex s and age a for the X and autosomes	
M_M, M_F	Effective male and female age-class sizes	See Eq. S86
M_X, M_A	Effective X and autosome linked age-class sizes	See Eq. S90
$W_{s,i,j}$	Expectation of $r_i \cdot r_j$ among individuals of sex s conditional on surviving to age $a \geq j$	Defined for $j \geq i$
W_M, W_F	Weighted averages of the $W_{M,i,j}$ and the $W_{F,i,j}$, respectively	See Eq. S85
W_X, W_A	Weighted averages of W_M and W_F for X and autosome linked loci	See Eq. S59
$X_{s,a}, X_s$	Random variables describing the number of offspring an individual of sex s has at age a or throughout life, respectively	
V_M, V_F	Male and female reproductive variances (i.e., $V_s = V(X_s)$)	See Eq. S108
$S_{s,a}$	The event of a newborn of sex s surviving to age $\geq a$	
$f(x)$	$f(x) \equiv (2x + 4)/(3x + 3)$	
μ_M, μ_F	Male and female expected mutation rates per generation	See Section 3
μ_X, μ_A	Expected mutation rates per generation on X and autosomes; $\mu_X = \frac{1}{3}\mu_M + \frac{2}{3}\mu_F$ and $\mu_A = \frac{1}{2}\mu_M + \frac{1}{2}\mu_F$	
X^X_m, X^A_m	The number of newborns carrying a random X or autosome linked allele m	
V^*_X, V^*_A	Reproductive variances of X and autosome linked alleles, respectively (i.e., $V^*_X \equiv V(X^X_m)$ and $V^*_A \equiv V(X^A_m)$)	See Eqs. S126 and S130

Table S2: Notation for the diploid model with two sexes, with parameters of the model in red.

2.2 Assumptions and notation

We consider a panmictic, diploid population of constant size, with two sexes, and sex- and age-dependent mortalities, fecundities and reproductive variances. We measure age in years, and assume that the number of individuals of sex s and age a, $M_{s,a}$, is constant. Specifically, the sizes of the newborn age classes, $M_{M,1}$ and $M_{F,1}$, may take any integer values, meaning that we do not assume that the sex-ratios at birth equals 1. More generally, the size of classes can vary between sexes, but for each sex they decrease with age, i. e. , $M_{s,a+1} \leq M_{s,a}$, reflecting sex- and age-specific mortalities. We further assume that age classes are partitioned according to individuals' age-dependent reproductive success. Namely, individuals are randomly assigned a vector $\vec{r}$ at birth, reflecting their expected relative reproductive success at each age (see below). We then assume that the number of individuals in the population of sex s, age a and relative reproductive success $\vec{r}$, is constant and equal to $M_{s,a} \cdot f_{s,a}(\vec{r})$, where $f_{s,a}$ is the probability mass function of $\vec{r}$ among individuals of sex s and age a. Individuals with the same value of $\vec{r}$ are chosen to survive to the next age class at random, i.e., there are no differences in viability, but $M_{s,a} \cdot f_{s,a}(\vec{r}) \geq M_{s,a+1} \cdot f_{s,a+1}(\vec{r})$ due to mortality, where rates of mortality can depend on the value of $\vec{r}$.

Sex and age dependent reproductive success is described backwards in time, in terms of the probability of an individual being chosen as a parent. Every newborn has a mother and a father, which are chosen independently. The probability that the parent of sex s is of a given age is described by a discrete distribution $A_s = (p_{s,a})_{a=1}^{\infty}$, where the expectations $G_M = E(A_M)$ and $G_F = E(A_F)$ are the generation times for males and females, respectively. The average probability per individual of age a is therefore $p_{s,a}/M_{s,a}$, which can be viewed as the fertility associated with that age and sex. The probability of being born to a specific parent of age a and relative reproductive success $\vec{r}$ is $p_{s,a} \cdot \frac{r_a}{M_{s,a}}$, where r_a is the a-th component of $\vec{r}$. The value of r_a thus reflects an individual's expected (rather than realized) relative reproductive success.

Similar to the haploid case (cf. Section 1.1), our assumptions imply several requirements on the form of the probability mass functions $f_{s,a}$. First, requiring that the probability of a parent of sex s being of age a is $p_{s,a}$, implies that for any sex s and age a, $E_{f_{s,a}}(r_a) = 1$. Second, requiring that

$M_{s,a} \cdot f_{s,a}(\vec{r}) \geq M_{s,a+1} \cdot f_{s,a+1}(\vec{r})$ implies that $f_{s,a}(\vec{r})/f_{s,a+1}(\vec{r}) \geq M_{s,a+1}/M_{s,a}$. Third, requiring that for any sex s and age a, $M_{s,a} \cdot f_{s,a}(\vec{r})$ is an integer, implies that the probability mass functions $f_{s,a}$ are discrete and can only take values $i/M_{s,a}$ for $i = 0, 1, \ldots, M_{s,a}$. While the latter requirement may appear to be highly restrictive, if we fix the ratios $M_{s,a}/M_{s',a'}$, and assume that the total population size is sufficiently large, we can relax this requirement and assume any continuous or discrete distributions $f_{s,a}$ that satisfy the first two requirements (by the same reasoning we applied to the haploid case in Section 1.2).

2.3 Solution backwards in time

Here, we extend the derivations of Pollak (POLLAK 2011) to account for endogenous reproductive variance. Tracing an allele backward in time, the sex s_t, age a_t and relative reproductive success $\vec{r}_t$ of the individual I_t carrying the allele t years in the past defines a Markov chain, $(s_t, a_t, \vec{r}_t)$. To define the transition probabilities of the chain, we distinguish between two cases. First, if the allele is not carried by a newborn, i.e., if $a_t > 1$, then at time $t + 1$ the individual carrying it was one year younger, and its sex s and relative reproductive success $\vec{r}$ remain unchanged, i.e., $(s_{t+1}, a_{t+1}, \vec{r}_{t+1}) = (s_t, a_t - 1, \vec{r}_t)$ with probability 1. Second, if the allele is carried by a newborn, i.e., if $a_t = 1$, then the sex of the parent, s_{t+1}, is equally likely to be male or female if the allele is autosomal or if it is X-linked and the newborn was a female; if the allele is X-linked and the newborn was a male then the sex of the parent will be female with probability 1. Conditional on the parent's sex, s_{t+1}, its age $a_{t+1} = a$ with probability $p_{s_{t+1},a}$. The probability mass function of $\vec{r}_{t+1}$ conditional on (s_{t+1}, a_{t+1}), follows from Bayes' theorem, further conditioning on the fact that the parent, $I_{t+1} = I$, necessarily reproduced successfully

$$P(\vec{r}_I = \vec{r}|I_{t+1} = I, a_{t+1} = a)$$

$$= \frac{P(I_{t+1}=I|\vec{r}_{t+1}=\vec{r}, a_{t+1}=a) \cdot P(\vec{r}_I=\vec{r}| a_{t+1}=a)}{P(I_{t+1}=I)} = \frac{(r_a/M_{s,a}) \cdot f_{s,a}(\vec{r})}{\sum_{\vec{k}} (r_a/M_{s,a}) \cdot f_{s,a}(\vec{k})} = r_a \cdot f_{s,a}(\vec{r}). \qquad (S67)$$

We denote this probability by $g_{s,a}(\vec{r}) \equiv r_a \cdot f_{s,a}(\vec{r})$, and conclude that when $a_t = 1$, s_{t+1} is distributed as we described above and $P((a_{t+1}, \vec{r}_{t+1}) = (a, \vec{r})|s_{t+1}) = p_{s,a} \cdot g_{s,a}(\vec{r})$.

$g_{s,a}$ is a proper probability mass function since $\sum_{\vec{r}} g_{s,a}(\vec{r}) = \sum_{\vec{r}} r_a \cdot f_{s,a}(\vec{r}) = 1$. Moreover, the parent's expected value of r_a is $E_{\vec{r} \sim g_{s,a}}(r_a) = E_{\vec{r} \sim f_{s,a}}(r_a^2) = 1 + V_{\vec{r} \sim f_{s,a}}(r_a) \geq 1$. The latter

inequality makes intuitive sense, as it implies that the allele is more likely to be descended from an individual that has higher than average relative reproductive success in its age class.

We rely on the transition probabilities to derive and solve recursions for the stationary probabilities, $\epsilon_A(s, a, \vec{r})$ and $\epsilon_X(s, a, \vec{r})$, of sex s, age a, and relative reproductive successes $\vec{r}$, of autosome and X linked alleles, respectively. For autosomal alleles

$$\epsilon^A(s, a, \vec{r}) = \epsilon^A(s, a+1, \vec{r}) + \left(\sum_{t,\vec{k}} \epsilon^A(t, 1, \vec{k})\right) \cdot \frac{1}{2} p_{s,a} \cdot g_{s,a}(\vec{r}), \tag{S68}$$

where the first term corresponds to aging by one year and the second corresponds to parenting a newborn. For X linked alleles

$$\epsilon^X(s, a, \vec{r}) = \epsilon^X(s, a+1, \vec{r}) + \left(\frac{1}{2}\sum_{\vec{k}} \epsilon^X(F, 1, \vec{k}) + \mathbb{I}_{s=F} \sum_{\vec{k}} \epsilon^X(M, 1, \vec{k})\right) \cdot p_{s,a} \cdot g_{s,a}(\vec{r}), \tag{S69}$$

where $\mathbb{I}$ denotes an indicator function (i.e., $\mathbb{I}_{s=F}$ is 1 when $s = F$ and 0 otherwise), and, similar to the autosomal case, the first term corresponds to aging by one year and the second corresponds to parenting a newborn.

In order to solve these recursions, we first consider the marginal stationary distribution of age and sex, $\epsilon_{s,a}^A = \sum_{\vec{r}} \epsilon^A(s, a, \vec{r})$ for autosomes and $\epsilon_{s,a}^X = \sum_{\vec{r}} \epsilon^X(s, a, \vec{r})$. To this end, we sum the recursions over $\vec{r}$ to obtain recursions on the marginal distributions,

$$\epsilon_{s,a}^A = \epsilon_{s,a+1}^A + \left(\epsilon_{M,1}^A + \epsilon_{F,1}^A\right) \cdot \frac{1}{2} p_{s,a} \text{ and } \epsilon_{s,a}^X = \epsilon_{s,a+1}^X + \left(\frac{1}{2}\epsilon_{F,1}^X + \mathbb{I}_{s=F}\epsilon_{M,1}^X\right) \cdot p_{s,a}, \tag{S70}$$

where we also require that $\sum_{s,a} \epsilon_{s,a}^A = \sum_{s,a} \epsilon_{s,a}^X = 1$. These recursions were solved by Pollak (POLLAK 2011) for the case without endogenous reproductive variance, yielding

$$\epsilon_{s,a}^A = q_{s,a}/2G_A, \ \epsilon_{M,a}^X = q_{M,a}/3G_X \text{ and } \epsilon_{F,a}^X = 2q_{F,a}/3G_X, \tag{S71}$$

where $q_{s,j} \equiv \sum_{j \geq a} p_{s,j}$ is the probability that a parent of sex s is at least j years old. Substituting these expressions into Eqs. S68 and S69, the recursions simplify to

$$\epsilon^A(s, a, \vec{r}) = \epsilon^A(s, a+1, \vec{r}) + \frac{1}{2G_a} p_{s,a} \cdot g_{s,a}(\vec{r}) \tag{S72}$$

for autosomes and

$$\epsilon^X(s, a, \vec{r}) = \epsilon^X(s, a+1, \vec{r}) + \frac{1+\mathbb{I}_{s=F}}{3G_X} \cdot p_{s,a} \cdot g_{s,a}(\vec{r}) \tag{S73}$$

for the X, where we further require that $\sum_{s,a,\vec{r}} \epsilon^A(s, a, \vec{r}) = \sum_{s,a,\vec{r}} \epsilon^X(s, a, \vec{r}) = 1$. The solution to these recursions is

$$\epsilon^A(s, a, \vec{r}) = \frac{1}{2G_A} \epsilon(s, a, \vec{r}) \tag{S74}$$

for autosomes and

$$\epsilon^X(s, a, \vec{r}) = \frac{1+\mathbb{I}_{s=F}}{3G_X} \epsilon(s, a, \vec{r}) \tag{S75}$$

for the X, where $\epsilon(s, a, \vec{r}) \equiv \sum_{j \geq a} p_{s,j} \cdot g_{s,j}(\vec{r})$.

The marginal stationary probability mass function of $\vec{r}$ follows,

$$\epsilon_{\vec{r}}^A = \sum_{s,a} \epsilon^A(s, a, \vec{r}) = \sum_{s,j} \frac{j \cdot p_{s,j}}{2G_A} \cdot g_{s,j}(\vec{r}) \tag{S76}$$

for autosomes, and

$$\epsilon_{\vec{r}}^X = \sum_{s,a} \epsilon^X(s, a, \vec{r}) = \sum_{s,j} \frac{(1+\mathbb{I}_{s=F}) \cdot j \cdot p_{s,j}}{3G_X} \cdot g_{s,j}(\vec{r}) \tag{S77}$$

for the X. These are proper probability mass functions since they are weighted averages of the probability mass functions $g_{s,j}$, since $\sum_{s,j} \frac{j \cdot p_{s,j}}{2G_A} = \sum_{s,j} \frac{(1+\mathbb{I}_{s=F}) \cdot j \cdot p_{s,j}}{3G_X} = 1$.

Similar to the haploid case, we rely on the stationary distribution to derive the probability of coalescence of two alleles. Consider the autosomal case first. For coalescence to occur at time t in the past, one of the alleles (A) would descend from the other (B) or both would descend from the same parental allele at that time (we provide examples for both scenarios in the haploid section). Specifically, if allele B is in an individual of sex s, age a and relative reproductive success $\vec{r}$ at time t (with probability $\epsilon^A(s, a, \vec{r})$), then allele A must be in a newborn at time $t - 1$ (with probability $\epsilon_{M,1} + \epsilon_{F,1}$), having descended from the same individual carrying allele B (with probability $\frac{1}{2} p_{s,a} \cdot \frac{r_a}{M_a}$) and from allele B specifically (with probability ½). Summing over the individual's possible sexes, ages and reproductive success vectors, we obtain the probability

$$\sum_{s,a,\vec{r}} \epsilon^A(s, a, \vec{r}) \cdot \left(\epsilon_{M,1}^A + \epsilon_{F,1}^A\right) \cdot \frac{1}{2} p_{s,a} \cdot \frac{r_a}{2M_{s,a}} = \frac{1}{8(G_A)^2} \sum_{s,a} \frac{\sum_{j \geq a} p_{s,a} p_{s,j} \sum_{\vec{r}} r_a \cdot g_{s,j}(\vec{r})}{M_{s,a}}$$

$$= \frac{1}{8(G_A)^2} \sum_{s,a} \frac{\sum_{j \geq a} p_{s,a} p_{s,j} W_{s,a,j}}{M_{s,a}}, \tag{S78}$$

where, for $j \geq i$,

$$W_{s,i,j} \equiv E_{\vec{r} \sim f_{s,j}}(r_i \cdot r_j) = E_{\vec{r} \sim g_{s,j}}(r_i) = \sum_{\vec{r}} r_i \cdot g_{s,j}(\vec{r}) \tag{S79}$$

is the expectation of $(r_i \cdot r_j)$ over individuals of sex s and age j. Further allowing for either allele or both to be the newborn, and using the inclusion-exclusion principal to subtract the probability

$$\left(\epsilon_{M,1}^A + \epsilon_{F,1}^A\right)^2 \sum_{s,a,\vec{r}} \left(\frac{1}{2}p_{s,a}\right)^2 \cdot \frac{r_a g_{s,a}(\vec{r})}{2M_{s,a}} = \frac{1}{8(G_A)^2} \sum_{s,a} \frac{p_{s,a}p_{s,a}W_{s,a,a}}{M_{s,a}} \tag{S80}$$

that both alleles were in a newborn prior to coalescence, the autosomal stationary coalescence rate per year is

$$\frac{1}{8(G_A)^2} \sum_{s,a} \frac{p_{s,a}^2 W_{s,a,a} + 2\sum_{j>a} p_{s,a}p_{s,j}W_{s,a,j}}{M_{s,a}}. \tag{S81}$$

The per generation coalescence rate (in terms of the autosomal generation time G_A) and corresponding effective population size are therefore

$$\frac{1}{2N_e^A} = \frac{1}{8 \cdot G_A} \sum_{s,a} \frac{p_{s,a}^2 W_{s,a,a} + 2\sum_{j>a} p_{s,a}p_{s,j}W_{s,a,j}}{M_{s,a}} \tag{S82}$$

For the X, the stationary coalescence rate per year is

$$2\left(\epsilon_{M,1}^X + \frac{1}{2}\epsilon_{F,a}^X\right) \sum_{a,\vec{r}} \epsilon^X(F,a,\vec{r}) \cdot p_{F,a} \cdot \frac{r_a}{2M_{F,a}} + 2 \cdot \frac{1}{2}\epsilon_{F,a}^X \sum_{a,\vec{r}} \epsilon^X(M,a,\vec{r}) \cdot p_{M,a} \cdot \frac{r_a}{M_{M,a}}$$

$$-\left(\epsilon_{M,1}^X + \frac{1}{2}\epsilon_{F,1}^X\right)^2 \sum_{a,\vec{r}} p_{F,a}^2 \cdot \frac{r_a g_{F,a}(\vec{r})}{2M_{F,a}} - \left(\frac{1}{2}\epsilon_{F,1}^X\right)^2 \sum_{a,\vec{r}} p_{M,a}^2 \cdot \frac{r_a g_{M,a}(\vec{r})}{M_{M,a}}$$

$$= \frac{1}{9(G_X)^2} \sum_s (1 + \mathbb{I}_{s=F}) \sum_a \frac{p_{s,a}^2 W_{s,a,a} + 2\sum_{j>a} p_{s,a}p_{s,j}W_{s,a,j}}{M_{s,a}}, \tag{S83}$$

and the corresponding per generation coalescence rate, which defines the effective population size for the X, N_e^X, is

$$\frac{1}{2N_e^X} = \frac{1}{9G_X} \sum_s (1 + \mathbb{I}_{s=F}) \sum_a \frac{p_{s,a}^2 W_{s,a,a} + 2\sum_{j>a} p_{s,a}p_{s,j}W_{s,a,j}}{M_{s,a}} \tag{S84}$$

(defined in terms of the X-linked generation time G_X).

As outlined in Section 2.1, the effective population sizes, N_e^X and N_e^A, can be rewritten in terms of the effective age class sizes, to obtain expressions that are analogous to Eq. 10 in the haploid case. To this end, the terms G, W and M in Eq. 10 need to be defined for the X and autosomes. First, we define these terms separately for males and females, by applying the haploid definitions. Specifically, we define

$$W_s = \sum_i p_{s,i}^2 W_{s,i,i} + 2\sum_{i<j} p_{s,i}p_{s,j}W_{s,i,j} \tag{S85}$$

as a weighted average of the $W_{s,i,j}$, and define

$$\frac{1}{M_s} = \sum_a \frac{w_{s,a}}{M_{s,a}} \tag{S86}$$

as a weighted harmonic average of the age classes sizes of sex s, with weights

$$w_{s,i} = (p_{s,i}^2 W_{s,i,i} + 2\sum_{j>i} p_{s,i}p_{s,j}W_{s,i,j})/W_s, \tag{S87}$$

where $\sum_a w_{s,a} = 1$. To extend the definitions of G, W and M to the X and autosomes, we define them as weighted averages over males and females. Specifically, G and W are defined as simple weighted averages,

$$G_A = \frac{1}{2}(G_M + G_F) \text{ and } G_X = \frac{2}{3}G_F + \frac{1}{3}G_M \tag{S88}$$

and

$$W_A = \frac{1}{2}(W_M + W_F) \text{ and } W_X = \frac{2}{3}W_F + \frac{1}{3}W_M. \tag{S89}$$

The effective age class size M for X and autosomes is defined as a weighted harmonic average,

$$\frac{1}{M_A} = \frac{1/2(W_M/W_A)}{M_M} + \frac{1/2(W_F/W_A)}{M_F} \text{ and } \frac{1}{M_X} = \frac{1/3(W_M/W_X)}{M_M} + \frac{2/3(W_F/W_X)}{M_F}. \tag{S90}$$

Expressing Eqs. S82 and S84 in these terms, we find that

$$N_e^A = \frac{2M_A G_A}{W_A} \text{ and } N_e^X = \frac{3}{4} \cdot \frac{2M_X G_X}{W_X}, \tag{S91}$$

which is Eq. 15 in the main text. The factor 2 in the numerators is absent in the analogous haploid expression, $N_e = M \cdot G/W$ (Eq. 10 and S17), and is not explained by diploidy, which is already accounted for by the defining N_e as *half* the inverse of the coalescence rates in the diploid case. To see that this is the case, consider how we might 'adjust' the haploid expression to describe autosomal alleles in diploids. Namely, we might expect to have $2N_e = (2M) \cdot G/W$, where the factors of 2 follow from having the effective population and age-class sizes for alleles rather than individuals. Instead, the factor 2 accounts for the doubling the effective number of age classes, i.e., *2G* classes in the diploid model with two sexes instead of G classes in the haploid model, where intuitively, this doubles the expected coalescence time because for a pair of alleles to coalescence they must be in an individual of a given age *and sex*.

Assuming the standard expressions for neutral heterozygosity, $E(\pi_A) = 4N_e^A \mu_A$ and $E(\pi_X) = 4N_e^X \mu_X$ (see Section 3), and rearranging the expressions in Eq. S91, we find that

$$\frac{E(\pi_X)}{E(\pi_A)} = \frac{3}{4} \cdot \frac{f(\mu_M/\mu_F) \cdot f(G_M/G_F)}{f\left(\frac{W_M/W_F}{M_M/M_F}\right)}. \tag{S92}$$

When the mutation rate, age structure, and endogenous reproductive variance are identical in both sexes Eq. S92 reduces to the naïve neutral expectation of ¾. When these factors differ among sexes, Eq. S92 provides a simple expression for the effect of each factor.

2.4 Reproductive variance

To recast our results for the effective population sizes in terms of reproductive variances in males, V_M, and females, V_F, we follow the same steps as described for the haploid case (Section 1.4). First, we consider the case with non-overlapping generations in a diploid population of constant size, with N_M males and N_F females. We denote the total population size by $N \equiv N_M + N_F$, the proportions of males and females by $\gamma_s \equiv \frac{N_s}{N}$, and the number of offspring of the ith individual of sex s by k_i^s. To maintain a constant population size, we require that the number of offspring arising from parents of each sex equals N, and therefore the sex-specific expectations are $E(k_i^s) = \frac{1}{N_s}\sum_i k_i^s = \frac{N}{N_s}$. We denote the sex-specific variances by $V_s \equiv V(k_i^s)$.

We are interested in the probability that two distinct alleles descend from the same allele in the previous generation, as this probability is, by definition, $1/2N_e^A$ for autosomes and $1/2N_e^X$ for the X. For autosomes, the probability that the two alleles descend from individuals of sex s is ¼, the probability that they descend from the same individual of that sex is $\sum_{i=1}^{N_s} \frac{k_i^s}{N} \cdot \frac{k_i^s-1}{N-1}$, and the probability that they descend from the same allele is $1/2$, and therefore

$$\frac{1}{2N_e^A} = \frac{1}{8}\sum_s \sum_{i=1}^{N_s} \frac{k_i^s}{N} \cdot \frac{k_i^s-1}{N-1}. \tag{S93}$$

Substituting $\sum_{i=1}^{N_s} \frac{k_i^s}{N} \cdot \frac{k_i^s-1}{N-1} = \frac{\gamma_s}{N-1}\left(E\left(k_i^{s\,2}\right) - E(k_i^s)\right) = \frac{1}{N-1}\left(\gamma_s V_s + \frac{1}{\gamma_s} - 1\right)$ into Eq. S93, we find that

$$N_e^A = \frac{4(N-1)}{\gamma_M V_M + \gamma_F V_F + \gamma_F/\gamma_M + \gamma_M/\gamma_F} \cong \frac{4N}{\gamma_M V_M + \gamma_F V_F + \gamma_F/\gamma_M + \gamma_M/\gamma_F} \tag{S94}$$

(cf. (WRIGHT 1939/1986)).

For the X chromosome, the probability that two alleles descend from individuals of sex s depends on γ_M and γ_F. However, as we go further backwards in time, this probability approaches 1/9 for both being male and 4/9 for both being female, regardless of γ_M and γ_F. The probability that both

alleles descend from the same individual of that sex is $\sum_{i=1}^{N_s} \frac{k_i^S}{N} \cdot \frac{k_i^S-1}{N-1}$, and the probability that they descend from the same allele is ½ for females and 1 for males, and therefore

$$\frac{1}{2N_e^X} = \frac{1}{9}\sum_{i=1}^{N_M} \frac{k_i^M}{N} \cdot \frac{k_i^M-1}{N-1} + \frac{1}{2}\cdot\frac{4}{9}\sum_{i=1}^{N_F} \frac{k_i^F}{N} \cdot \frac{k_i^F-1}{N-1}, \tag{S95}$$

and thus

$$N_e^X = \frac{3}{4} \cdot \frac{4(N-1)}{\frac{2}{3}\gamma_M V_M + \frac{4}{3}\gamma_F V_F + \frac{2}{3}\frac{\gamma_F}{\gamma_M} + \frac{4}{3}\frac{\gamma_M}{\gamma_F}} \cong \frac{3}{4} \cdot \frac{4N}{\frac{2}{3}\gamma_M V_M + \frac{4}{3}\gamma_F V_F + \frac{2}{3}\frac{\gamma_F}{\gamma_M} + \frac{4}{3}\frac{\gamma_M}{\gamma_F}}. \tag{S96}$$

Assuming a sex ratio of 1 (i.e., $\gamma_M = \gamma_F = 1/2$), Eqs. S94 and S96 reduce to

$$N_e^A = \frac{4N}{2+\frac{1}{2}V_M+\frac{1}{2}V_F} \text{ and } N_e^X = \frac{3}{4} \cdot \frac{4N}{2+\frac{1}{3}V_M+\frac{2}{3}V_F}. \tag{S97}$$

To extend these results to the case with overlapping generations, we consider the first two moments of an individual's number of offspring, X_s, throughout its lifetime. First, we note that an individual's number of offspring can be expressed as a sum over the number at each age, i.e., $X_s = \sum_a X_{s,a}$, where $X_{s,a}$ denotes the number of offspring at age a; and $X_{s,a} = 0$ if the individual does not survive to age a. In these terms, the first two moments are

$$E(X_s) = \sum_a E(X_{s,a}) \text{ and } E(X_s^2) = \sum_a E(X_{s,a}^2) + 2\sum_{j>i} E(X_{s,i} \cdot X_{s,j}). \tag{S98}$$

Denoting the event of surviving to age $\geq a$ by $S_{s,a}$, we note that

$$E(X_{s,a}^i) = Pr(S_{s,a}) \cdot E(X_{s,a}^i|S_{s,a}) = \frac{M_{s,a}}{M_{s,1}} \cdot E(X_{s,a}^i|S_{s,a}). \tag{S99}$$

The latter term, $E(X_{s,a}^i|S_{s,a})$, can be simplified further by conditioning on $\vec{r}$. Since the probability mass function of $\vec{r}$ conditional on $S_{s,a}$ is $f_{s,a}$,

$$E(X_{s,a}^i|S_{s,a}) = E_{\vec{r}\sim f_{s,a}}E(X_{s,a}^i|S_{s,a},\vec{r}). \tag{S100}$$

Moreover, the distribution of $X_{s,a}$ conditional on $S_{s,a}$ and $\vec{r}$ is

$$(X_{s,a}|\vec{r},S_{s,a}) \sim Bin(M_1, p_{s,a} \cdot r_a/M_{s,a}), \tag{S101}$$

where $M_1 = M_{M,1} + M_{F,1}$ is the number of newborns of both sexes per-year, and therefore

$$E(X_{s,a}|S_{s,a}) = E_{\vec{r}\sim f_{s,a}}\left(\frac{M_1 r_a p_{s,a}}{M_{s,a}}\right) = \frac{M_1 p_{s,a}}{M_{s,a}} \tag{S102}$$

and

$$E(X_{s,a}^2|S_{s,a}) = E_{\vec{r}\sim f_{s,a}}\left(M_1\frac{r_a p_{s,a}}{M_{s,a}} + 2\binom{M_1}{2}\left(\frac{r_a p_{s,a}}{M_{s,a}}\right)^2\right) = \frac{M_1 p_{s,a}}{M_{s,a}} + 2\binom{M_1}{2}\left(\frac{p_{s,a}}{M_{s,a}}\right)^2 W_{s,a,a}.$$

Substituting these expressions into Eq. S99, we find that

$$E(X_{s,a}) = \frac{p_{s,a}}{\gamma_s} \text{ and } E(X_{s,a}^2) = \frac{p_{s,a}}{\gamma_s} + \frac{M_1-1}{M_{s,a}} \frac{p_{s,a}^2}{\gamma_s} \cdot W_{s,a,a}, \tag{S103}$$

where γ_M and γ_F are the proportions of males and females at birth (i.e., $\gamma_s = M_{s,1}/M_1$). To calculate the remaining terms in Eq. S98, $E(X_{s,i} \cdot X_{s,j})$ for $j > i$, we note that conditioning on $S_{s,j}$, and on $\vec{r}|S_{s,j}$,

$$E(X_{s,i} \cdot X_{s,j}) = P(S_{s,j}) \cdot E(X_{s,i} \cdot X_{s,j}|S_{s,j}) = \frac{M_{s,j}}{M_{s,1}} \cdot E_{\vec{r} \sim f_{s,j}} E(X_{s,i} \cdot X_{s,j}|S_{s,j}, \vec{r}). \tag{S104}$$

The latter term is easy to calculate: conditional on $S_{s,j}$ and $\vec{r}$, $X_{s,i}$ and $X_{s,j}$ are independent binomial variables: $(X_{s,i}|\vec{r}, S_{s,j}) \sim Bin(M_1, p_{s,i} \cdot r_i/M_{s,i})$ and $(X_{s,j}|\vec{r}, S_{s,j}) \sim Bin(M_1, p_{s,j} \cdot r_j/M_{s,j})$, and therefore

$$E(X_{s,i} \cdot X_{s,j}) = \frac{M_{s,j}}{M_{s,1}} \cdot E_{\vec{r} \sim f_{s,j}} \left(\frac{M_1^2 p_{s,i} p_{s,j} r_i r_j}{M_{s,i} M_{s,j}} \right) = \frac{M_1 p_{s,i} p_{s,j} W_{s,i,j}}{\gamma_s M_{s,i}}. \tag{S105}$$

Substituting the expressions from Eqs. S103 and S105 into Eq. S98 we obtain

$$E(X_s) = \frac{1}{\gamma_s} \text{ and } E(X_s^2) = \frac{1}{\gamma_s} + \frac{M_1}{\gamma_s} \sum_i \frac{p_{s,i}^2 \cdot W_{s,i,i} + 2\sum_{j>i} p_{s,i} p_{s,j} W_{s,i,j}}{M_{s,i}} - \sum_a \frac{p_{s,a}^2 \cdot W_{s,a,a}}{\gamma_s M_{s,a}}. \tag{S106}$$

Assuming that the total population size is sufficiently large for the ratios $M_{s,i}/M_{t,j}$ and terms $W_{s,i,j}$ to be approximated as fixed, and for the higher order terms $\sum_a \frac{p_{s,a}^2 \cdot W_{s,a,a}}{\gamma_s M_{s,a}}$ to be negligible, we find that

$$E(X_s) = \frac{1}{\gamma_s} \text{ and } E(X_s^2) \cong \frac{1}{\gamma_s} + \frac{M_1}{\gamma_s} \frac{W_s}{M_s}. \tag{S107}$$

The reproductive variances of sex s, are therefore

$$V_s = E(X_s^2) - E^2(X_s) \cong \frac{M_1}{\gamma_s} \frac{W_s}{M_s} - \frac{1-\gamma_s}{\gamma_s^2}. \tag{S108}$$

From Eqs. S91 and S108, we obtain that

$$N_e^A = \frac{4G_A M_1}{\gamma_M V_M + \gamma_F V_F + \gamma_F/\gamma_M + \gamma_M/\gamma_F} \text{ and } N_e^X = \frac{3}{4} \cdot \frac{4G_X M_1}{\frac{2}{3}\gamma_M V_M + \frac{4}{3}\gamma_F V_F + \frac{2}{3}\frac{\gamma_F}{\gamma_M} + \frac{4}{3}\frac{\gamma_M}{\gamma_F}}, \tag{S109}$$

where $G_A M_1$ and $G_X M_1$ are the total numbers of newborns per-generation, for autosomes and the X, respectively. Eq. S109, which is equivalent to Eq. 18 in the main text, generalizes Eqs. S94 and S96 to the case with age-structure.

Assuming that $E(\pi_A) = 4N_e^A \mu_A$ and $E(\pi_X) = 4N_e^X \mu_X$ (see Section 3), we find that

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$$\frac{E(\pi_X)}{E(\pi_A)} = \frac{3}{4} \cdot \frac{f(\mu_M/\mu_F) \cdot f(G_M/G_F)}{f\left(\frac{\gamma_F/\gamma_M + \gamma_M V_M}{\gamma_M/\gamma_F + \gamma_F V_F}\right)}, \tag{S110}$$

which is Eq. 21 in the main text. When the sex ratio at birth is 1 (i.e. that $\gamma_M = \gamma_F = 1/2$), Eqs. S109 and S110 reduce to

$$N_e^A = \frac{4G_A M_1}{2 + \frac{1}{2}V_M + \frac{1}{2}V_F}, \quad N_e^X = \frac{3}{4} \cdot \frac{4G_X M_1}{2 + \frac{1}{3}V_M + \frac{2}{3}V_F}, \text{ and } \frac{E(\pi_X)}{E(\pi_A)} = \frac{3}{4} \cdot \frac{f(\mu_M/\mu_F) \cdot f(G_M/G_F)}{f\left(\frac{2+V_M}{2+V_F}\right)}. \tag{S111}$$

2.5 Hill and Pollak's results for age-structured populations

As we reviewed in the Introduction, Hill derived an expression for the effective population size of autosomes in age structured populations (Eq. 2) and Pollak derived a similar expression for the X (HILL 1972; POLLAK 1980; POLLAK 1990; POLLAK 2011). Here we relate these expressions with our Eq. 18 (and S109), showing that in the general case this relationship is non-trivial.

The relationship between our results and those of Hill and Pollak is straightforward in the special case in which the sex ratio at birth is 1 (i.e., $\gamma_M = \gamma_F = 1/2$). Hill and Pollak's equations are cast in term of the variances and covariances of the number of male and female offspring of a parent of sex s, $X_{s,M}$ and $X_{s,F}$, respectively. When $\gamma_M = \gamma_F = 1/2$, substituting

$$V_s = Var(X_s) = Var(X_{s,M}) + 2Cov(X_{s,M}, X_{s,F}) + Var(X_{s,F}). \tag{S112}$$

into Eq. 18 (or S109) yields Hill and Pollak's expressions. In the general case (when $\gamma_s \neq 1/2$), however, this substitution falls short.

Relating our results with those of Hill and Pollak in the general case requires us to express the variances and covariances $Var(X_{s,t})$ and $Cov(X_{s,M}, X_{s,F})$ in terms of the birth proportions γ_s and variances V_s (for $s, t = M, F$). To this end, we note that conditioned on X_s, the total number of offspring of either sex, $X_{s,M}$ and $X_{s,F}$, can be approximated by

$$X_{s,t}|X_s \sim Bin(X_s, \gamma_t). \tag{S113}$$

This approximation neglects dependencies of the order of $1/M_1^2$ between the sexes of different offspring, which arise because we hold the total number of newborns of each sex per year fixed;

but it is consistent with standard coalescent approximations, in neglecting contributions that are smaller than on an order of $1/N_e$. From Eqs. S113 and S107, we find that

$$E(X_{s,t}) = EE(X_{s,t}|X_s) = E(\gamma_t X_s) = \gamma_t/\gamma_s. \tag{S114}$$

Further using the law of total variance, we find that

$$Var(X_{s,t}) = E\,Var(X_{s,t}|X_s) + Var\,E(X_{s,t}|X_s) = E(\gamma_M \gamma_F X_s) + Var(\gamma_t X_s)$$
$$= 1 - \gamma_s + \gamma_t^2 V_s. \tag{S115}$$

And using the law of total covariance, we find that

$$Cov(X_{s,M}, X_{s,F}) = E\,Cov(X_{s,M}, X_{s,F}|X_s) + Cov\left(E(X_{s,M}|X_s), E(X_{s,F}|X_s)\right). \tag{S116}$$

Given that $X_{s,M} + X_{s,F} = X_s$, we can express the first term in Eq. S116 as

$$Cov(X_{s,M}, X_{s,F}|X_s) = E(X_{s,M} \cdot (X_s - X_{s,F})|X_s) - E(X_{s,M}|X_s) \cdot E(X_{s,F}|X_s)$$
$$= E(X_s \cdot X_{s,M} - X_{s,M}^2|X_s) - \gamma_M \gamma_F X_s^2$$
$$= \gamma_M X_s^2 - \gamma_M \gamma_F X_s - \gamma_M^2 X_s^2 - \gamma_M \gamma_F X_s^2 = -\gamma_M \gamma_F X_s. \tag{S117}$$

Intuitively, Eq. S117 shows that once we condition on the total number of offspring, the numbers of daughters and sons are negatively correlated. Lastly, substituting Eq. S117 into Eq. S116 and relying on Eqs. S113 and S107, we find that

$$Cov(X_{s,M}, X_{s,F}) = -\gamma_M \gamma_F/\gamma_s + Cov(\gamma_M X_s, \gamma_F X_s) = \gamma_M \gamma_F (V_s - 1/\gamma_s). \tag{S118}$$

In summary, we find that

$$Var(X_{s,t}) = 1 - \gamma_s + \gamma_t^2 V_s \text{ and } Cov(X_{s,M}, X_{s,F}) = \gamma_M \gamma_F (V_s - 1/\gamma_s). \tag{S119}$$

With these non-trivial identities at hand, we can relate our results with those of Hill and Pollak (HILL 1972; POLLAK 1980; POLLAK 1990; POLLAK 2011). Substituting these identities into Hill's equation (HILL 1972) yields our expression for $1/N_e^A$ in Eq. 18 (and S109):

$$\frac{1}{N_e^A} = \frac{2 + \sigma_{MM}^2 + 2(\gamma_M/\gamma_F)Cov(mm,mf) + (\gamma_M/\gamma_F)^2\sigma_{MF}^2}{16M_1 \cdot \gamma_M \cdot G_A} + \frac{2 + \sigma_{FF}^2 + 2(\gamma_F/\gamma_M)Cov(fm,ff) + (\gamma_F/\gamma_M)^2\sigma_{FM}^2}{16M_1 \cdot \gamma_F \cdot G_A}$$
$$= \frac{4\gamma_M^2 V_M + 3\gamma_F + \gamma_M^2/\gamma_F}{16\gamma_M M_1 G_A} + \frac{4\gamma_F^2 V_F + 3\gamma_M + \gamma_F^2/\gamma_M}{16\gamma_F M_1 G_A} = \frac{\gamma_M V_M + \gamma_F V_F + \gamma_F/\gamma_M + \gamma_M/\gamma_F}{4M_1 G_A}. \tag{S120}$$

A similar exercise starting from Pollak's expression (POLLAK 2011) yields our expression for the X. Our Eq. 18 (and S109) is considerably simpler than Hill's and Pollak's results, as it circumvents the need to consider variances in the number of offspring of each sex separately, or the covariance between the number of sons and daughters.

2.6 Allelic reproductive variance

Here we derive expressions for the effective population size of the X and autosomes in terms of reproductive success of alleles rather than of individuals. We show that substituting the allelic reproductive variance into the haploid expression for N_e (Eqs. 13 and S44) yields the correct expression for autosomal alleles, whereas for the X this formulation applies only when the sex ratio at birth equals 1 (i.e., $\gamma_M = \gamma_F = 1/2$). These results provide intuition for the differences between our expression for N_e in the haploid case (Eq. 13) and our expressions for X and autosomes (Eq. 18).

We begin with some motivation. We define the reproductive success of an allele as an individual's number of offspring that carry that allele, and denote the reproductive variance associated with X and autosome linked alleles by V_X^* and V_A^*, respectively. In these terms, we might hope that our expression for N_e in the haploid case (Eq. 13) would apply to the X and autosomes, i.e., that

$$\mathbf{2} \cdot N_e^X = G_X\left(\frac{\mathbf{3}}{\mathbf{2}} \cdot M_1\right)/V_X^* \text{ and } \mathbf{2} \cdot N_e^A = G_A(\mathbf{2} \cdot M_1)/V_A^*, \tag{S121}$$

where the (bold) factors of 2 on the left-hand side follow from considering the effective size for alleles rather than individuals, and the (bold) factors of 3/2 for the X and 2 for autosomes on the right-hand side follow from considering the number of newborn alleles rather than individuals. Below, we show that assuming a sex ratio of 1 at birth, then

$$V_X^* = \frac{1}{4}\left(2 + \frac{1}{3}V_M + \frac{2}{3}V_F\right) \text{ and } V_A^* = \frac{1}{4}\left(2 + \frac{1}{2}V_M + \frac{1}{2}V_F\right), \tag{S122}$$

where the weights reflect the proportion of generations spent in males and females, and the additive factor 2 results from ploidy. Substituting these expressions into Eq. S121 we indeed obtain the correct effective population sizes, i.e.,

$$N_e^X = \frac{3}{4} \cdot \frac{4 G_X M_1}{2 + \frac{1}{3}V_M + \frac{2}{3}V_F} \text{ and } N_e^A = \frac{4 G_A M_1}{2 + \frac{1}{2}V_M + \frac{1}{2}V_F}. \tag{S123}$$

However, as we further show, this 'shortcut' yields the wrong answer for the X when the sex ratio at birth deviates from 1.

First, we calculate the allelic variances. Consider an allele m carried by an individual I_m of sex s_m. We define the allele's realized reproductive success as the number of I_m's offspring who carry a copy of m, and denote it by X_m^A when m is autosomal and by X_m^X when it is X-linked. We denote

I_m's total number of offspring (whether they carry m or not) by X_I. First consider an autosomal allele. Since each offspring of I_m carries a copy of m with probability ½, the conditional distribution $X_m^A|X_I \sim Bin(X_I, 1/2)$. From the law of total variance,

$$E(X_m^A) = \frac{1}{2}E(X_I) \text{ and } V(X_m^A) = \frac{1}{4}[E(X_I) + V(X_I)]. \tag{S124}$$

Further conditioning on the sex of the individual carrying the allele, s_I, we note that $E(X_I|s_I) = 1/\gamma_{s_I}$ (Eq. S107) and $V(X_I|s_I) = V_{s_I}$, where the individual I_m is male with probability γ_M and female with probability γ_F. Applying the law of total variance again, we find that

$$E(X_I) = 2 \text{ and } V(X_I) = \gamma_M V_M + \gamma_F V_F + \frac{(\gamma_M - \gamma_F)^2}{\gamma_M \gamma_F}. \tag{S125}$$

Substituting these expressions into Eq. S124, we find that

$$E(X_m^A) = 1 \text{ and } V_A^* \equiv V(X_m^A) = \frac{1}{4}[\gamma_M V_M + \gamma_F V_F + \frac{\gamma_M}{\gamma_F} + \frac{\gamma_F}{\gamma_M}]. \tag{S126}$$

When the sex ratio at birth is 1, and thus $\gamma_M = \gamma_F = 1/2$, Eq. S126 reduces to the autosomal part of Eq. S122. From Eqs. S109 and S126, we find that

$$N_e^A = \frac{G_A \cdot M_1}{V_A^*} \tag{S127}$$

for any sex-ratio. Given that the effective population sizes are defined by requiring coalescence rates of $1/N_e$ in haploids and $1/(2 \cdot N_e^A)$ in diploids, Eq. S127 is, in fact, analogous to Eq. S44.

Next, consider an X-linked allele. If the individual carrying the allele, I_m, is male, then only his female offspring will inherit the allele, and thus, $X_m^X|(s_I = M, X_I) \sim Bin(X_I, \gamma_F)$. Since $E(X_I|s_I = M) = 1/\gamma_M$ (Eq. S107) and $V(X_I|s_I) = V_{s_I}$, the law of total variance implies that

$$E(X_m^X|s_I = M) = \gamma_F/\gamma_M \text{ and } V(X_m^X|s_I = M) = \gamma_F^2 V_M + \gamma_F. \tag{S128}$$

The case in which I_m is a female is similar to the autosomal case, and thus, $X_m^X|(s_I = F, X_I) \sim Bin(X_I, 1/2)$,

$$E(X_m^X|s_I = F) = \frac{1}{2\gamma_F} \text{ and } V(X_m^X|s_I = F) = \frac{1}{4}V_F + \frac{1}{4\gamma_F}. \tag{S129}$$

Given that there are $M_{M,1}$ X-linked alleles in newborn males and $2M_{F,1}$ in newborn females, the probability that an X-linked allele in a newborn is in a male is $\gamma_M/(1 + \gamma_F)$ and the probability it is in a female is $2\gamma_F/(1 + \gamma_F)$. Applying the law of total variance therefore implies that

$$E(X_m^X) = 1 \text{ and } V_X^* = Var(X_m^X) = \frac{\gamma_M \gamma_F^2}{1 + \gamma_F}V_M + \frac{\gamma_F}{2(1 + \gamma_F)}V_F + \frac{1 + 2\gamma_M \gamma_F}{2(1 + \gamma_F)} + \frac{(1 - 2\gamma_F)^2}{2\gamma_M \gamma_F}. \tag{S130}$$

When the sex ratio at birth is 1, and thus $\gamma_M = \gamma_F = 1/2$, Eq. S130 reduces to the X related expression of Eq. S122. From Eqs. S109 and S130, we find that

$$N_e^X = \frac{G_X \cdot M_1}{V_X^*},\qquad\qquad\qquad(S131)$$

only holds when $\gamma_M = \gamma_F = 1/2$. Thus, the haploid result (Eqs. 13 and S44) applies to X-linked alleles only when the sex ratio at birth equals 1.

To explain why this result fails in the general case, consider the reproductive success of an X-linked allele in consecutive generations. As we have shown above, an allele's expected reproductive success is γ_F/γ_M in males and $1/(2\gamma_F)$ in females (averaged over sexes the expectation is 1). Now consider the expected reproductive success in the next generation: if the allele was in a male in the previous generation it will necessarily be in a female, and the expected reproductive success of the offspring allele would be $1/(2\gamma_F)$; if the allele was in a female in the previous generation, the expected reproductive success is obtained by averaging over the sex of the offspring, and is $\frac{1}{2} + \gamma_F$. Thus, unless $\gamma_M = \gamma_F = 1/2$, the reproductive success of an X-linked allele will be negatively correlated between parents and offspring. This violates the assumption of the haploid model that the reproductive success of individuals and their offspring are independent.

3. Mutational process

Here we describe the assumptions on the mutational model and derive formulas for the expected levels of heterozygosity. To incorporate what has recently been revealed about the dependencies of mutation rates on sex and age (e.g., (KONG *et al.* 2012; SEGUREL *et al.* 2014; WONG *et al.* 2016; GAO *et al.* 2019)), we allow for mutation rate in the diploid model to depend on sex and age. Namely, we assume that the number of de novo mutations that a parent of sex s and age a bequeaths to its newborn is a random variable with expectation $\mu_{s,a}$ per base pair. Since mutation rates can vary with sex and age, the mutation rates per generation in males and females depend on the distributions of their breeding ages (i.e. A_M and A_F, which were defined in Section 2). We denote the expected mutation rate per generation in males by $\mu_M = E_{A_M}(\mu_{M,a}) = \sum_a p_{M,a} \cdot \mu_{M,a}$ and the expected rate in females by $\mu_F = E_{A_F}(\mu_{F,a})$. The average rates on the autosomes and the X are given by $\mu_A = \frac{1}{2}(\mu_M + \mu_F)$ and $\mu_X = \frac{2}{3}\mu_F + \frac{1}{3}\mu_M$ (Table 2). For the haploid model, we assume the expected number of mutations μ_a to be dependent of age and define the per generation rate as $\mu = E_A(\mu_a)$. In the special case in which the parameters $\mu_{s,a}$ (or the μ_a in the haploid case) depend linearly on age, these expectations will depend only on the expected generation times G_M and G_F, i.e., they are insensitive to higher moments of the distributions of breeding ages in males and females. As we show below, higher moments of the distributions of mutation rates per generation do not affect our results, which is how we avoid any further assumptions about these distributions.

The standard expressions for heterozygosity (e.g., $E(\pi_A) = 4N_e^A \mu_A$) are usually derived assuming that the genealogical and mutational processes are independent (HUDSON 1990). This assumption is violated in our case, because both the time to the most recent common ancestor and the number of accumulated mutations depend on the ages of the individuals along the lineage. To derive the expected autosomal heterozygosity $E(\pi_A)$ under these conditions, we track alleles A and B backwards in time. Let X_i denote the number of mutations occurring on the lineage leading from allele A in the ith generation and T denote the number of generations until the alleles coalesce. The number of mutations on the lineage leading to allele A is then $\sum_{i=1}^{T} X_i$. Although X_i and T are dependent variables, Wald's equation (BLACKWELL 1946) implies that $E\left(\sum_{i=1}^{T} X_i\right) = E(T) \cdot E(X_i)$ (to see that Wald's equation holds, note that the indicator function $\mathbb{I}_{T \geq n}$ is independent of X_n, since

the first depends on the sexes and ages in the first $n - 1$ generations, and the second on the nth generation). We have already shown that $E(T) = 2N_e^A$. Since $E(X_i|s_i, a_i) = \mu_{s,a}$ (where s_i and a_i are the sex and age in the ith generation), it follows that $E(X_i) = E(\mu_{s,a}) = \mu_A$. We conclude that the lineage leading to allele A has on average $E(\sum_{i=1}^{T} X_i) = 2N_e^A \cdot \mu_A$ mutations and therefore $E(\pi_A) = 4N_e^A \mu_A$. A similar argument shows that for the haploid model $E(\pi) = 2N_e\mu$.

This argument requires modification for the X-chromosome, because the sexes s_i and s_{i+1} in consecutive generations along the lineage are dependent variables, leading to a dependence between X_{i+1} and s_i, in violation of the conditions for Wald's equation. Instead, we define T as the number of females on the lineage until the coalescence occurs, and define X_i as the number of mutations between the ith and $i + 1$ females on the lineage. Under this definition, Wald's equation holds and $E(\pi_X) = 2E(\sum_{i=1}^{T} X_i) = 2E(X_i)E(T)$. It is then easy to show that $E(X_i) = \frac{3}{2}\mu_X$ and $E(T) = (4/3)N_e^X$, implying that $E(\pi_X) = 4N_e^X \mu_X$.

4. Life history and population size that change over time

Thus far we considered models with constant population size and life history parameters. Here we extend our results to models in which population size and life history traits change over time. Specifically, we consider models with piecewise-constant age-structures, endogenous reproductive variances and population sizes. We rely on our results showing that with constant population sizes, the coalescence process with age structure is well approximated by Kingsman's coalescence process with non-overlapping generations, with the appropriate parameters (i.e., effective population sizes and time units). This allows us to approximate the coalescence rates per year in each time interval with constant parameters. We then derive simple recursions for expected heterozygosities on the X and autosomes at any point in time (Section 4.2), rely on these recursions to solve the example discussed in the main text (Eq. 24 and Fig 2), and specify how existing coalescence simulators can be used in order to account for life history effects (Section 4.3). The approximations we detail can be also be applied to models with multiple populations and piecewise-constant migration rates.

4.1 Model

We measure time in years, backwards from the present, $t = 0$, and assume we are given n time intervals, where the i-th interval is $[T_{i-1}, T_i)$, and $0 = T_0 < T_1 < \cdots < T_n = \infty$. The effective population sizes, generation times, and mutation rates, for the X and autosomes are defined as before, and are assumed to be constant in each time interval, where we denote their values in the i-th interval with an addition index i.

It may sometimes be useful to specify the model in terms of different, equivalent sets of parameters. For example, in Amster et al. (AMSTER *et al.* 2019), we rely on estimates of the autosomal effective population size, $N_e^{A,i}$, for a given set of time intervals, $i = 1, \ldots, n$, which were inferred for human populations, assuming a constant autosomal generation time of $G_A = 30$ years. We then express the effective population sizes and generation times on the X in these intervals in terms of the sex ratios of generation times, $(G_M/G_F)_i$, and reproductive variances, $[(\gamma_M V_M + \gamma_F/\gamma_M)/(\gamma_F V_F + \gamma_M/\gamma_F)]_i$, for $i = 1, \ldots, n$, as

$$N_e^{X,i} = \frac{3}{4} \cdot \frac{f((G_M/G_F)_i)}{f([(\gamma_M V_M + \gamma_F/\gamma_M)/(\gamma_F V_F + \gamma_M/\gamma_F)]_i)} \cdot N_e^{A,i}, \tag{S132}$$

(relying on Eq. 20) and

$$G_X^i = G_A \cdot f((G_M/G_F)_i) = \frac{2}{3} G_A[1 + 1/(1 + (G_M/G_F)_i)], \tag{S133}$$

where $f(x) = \frac{2x+4}{3x+3}$ is the same function used in the main text (Eqs. 20 and 21). We also rely on a model that describes human maternal and paternal mutation rates as a function of their respective generation times (JÓNSSON *et al.* 2017), and therefore specify the mutation rates per generation on the X and autosomes in time interval i as

$$\mu_A^i = \mu_A(G_A, (G_M/G_F)_i) \text{ and } \mu_X^i = \mu_X(G_A, (G_M/G_F)_i). \tag{S134}$$

4.2 A recursion for heterozygosity on X and autosomes

Provided the effective population size, generation times, and mutation rates in each time interval for the X and autosomes, we can write down a simple recursion for the expected heterozygosities at present, π_X and π_A. We first consider the autosomal case, and denote the expected heterozygosity at time t by $\pi_A(t)$. The n-th time interval, $[T_{n-1}, \infty)$, is infinitely long with constant effective population size and mutation rate, and therefore

$$\pi_A(T_{n-1}) = 4N_e^{A,n}\mu_A^n. \tag{S135}$$

Next, we assume that we know that we know $\pi_A(T_i)$ and solve for $\pi_A(T_{i-i})$. To this end, we denote the event of two alleles sampled at time T_{i-i} coalescing in the i-th time interval (i.e., until time T_i) by E, and its complement, i.e., that they do not coalesce, by E^C. Under the infinite sites assumption, the heterozygosity at time T_{i-i} is then

$$\pi_A(T_{i-i}) = \mathrm{P}(E) \cdot \pi_A(T_{i-i}|E) + \mathrm{P}(E^C) \cdot \pi_A(T_{i-i}|E^C)$$
$$= \mathrm{P}(E) \cdot \left(2 \cdot \mathrm{E}(t_{MRCA}|E) \cdot \mu_A^i/G_A^i\right) + \left(1 - \mathrm{P}(E^C)\right)\left(\pi_A(T_i) + 2(T_i - T_{i-i}) \cdot \mu_A^i/G_A^i\right), \tag{S136}$$

where P denotes probability, and t_{MRCA} denotes the time to the most recent common ancestor of the aforementioned sample. Approximating the time to coalescence in the i-th interval with an exponential distribution with rate $1/2G_A^i N_e^{A,i}$ (where G_A^i is included for the process to be describe in years rather than generations), we find that

$$\mathrm{P}(E) = 1 - \exp\left(-\frac{T_i - T_{i-1}}{2G_A^i N_e^{A,i}}\right), \tag{S137}$$

and

$$E(t_{MRCA}|E) = 2G_A^i N_e^{A,i} - (T_i - T_{i-1})\frac{1-\mathrm{P}(E)}{\mathrm{P}(E)}. \tag{S138}$$

Substituting these expressions into Eq. S136, we find that

$$\pi_A(T_{i-1}) = \left(1 - \exp\left(-\frac{T_i - T_{i-i}}{2G_A^i N_e^{A,i}}\right)\right) \cdot 4N_e^{A,i}\mu_A^i + \exp\left(-\frac{T_i - T_{i-i}}{2G_A^i N_e^{A,i}}\right) \cdot \pi_A(T_{i+1}). \tag{S139}$$

By the same token, we find that for the X:

$$\pi_X(T_{n-1}) = 4N_e^{X,n}\mu_X^n, \tag{S140}$$

and

$$\pi_X(T_{i-1}) = \left(1 - \exp\left(-\frac{T_i - T_{i-i}}{2G_X^i N_e^{X,i}}\right)\right) \cdot 4N_e^{X,i}\mu_X^i + \exp\left(-\frac{T_i - T_{i-i}}{2G_X^i N_e^{X,i}}\right) \cdot \pi_X(T_{i+1}). \tag{S141}$$

Eqs. S135 and S139-S141 can be solved recursively for π_A and π_X (i.e., for $\pi_A(T_0)$ and $\pi_X(T_0)$), respectively. The same recursions can be used to solve for $\pi_A(t)$ and $\pi_X(t)$ at any time t, where for t in the i-th interval, we solve the same recursion until time T_i, and for the last step, we replace T_{i-1} by t in Eqs. S139 and S141.

4.3 Simulations

The coalescence process on the X and autosomes accounting for life history effects can be simulated using standard tools. For example, to use *ms* (HUDSON 2002), one can use per-generation coalescence rates (e.g., $1/2N_e^{A,i}$ and $1/2N_e^{X,i}$ for intervals $i = 1, \dots, n$, in the aforementioned model), and convert the duration of time intervals into units of generations, with the appropriate generation time (e.g., $(T_i - T_{i-i})/G_A^i$ and $(T_i - T_{i-i})/G_X^i$ for intervals $i = 1, \dots, n$, in the aforementioned model).

Simulating the mutational process requires a custom tool, as the standard ones assume fixed mutation rates, whereas we assume rates can change. It is, however, straightforward to implement such a tool, e.g., taking trees generated by ms (i.e., with the -T flag) as input, and incorporating piecewise constant mutation rates. We provide such a tool in https://github.com/sellalab/XA_poly.

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