Consequences of life history for inbreeding depression and mating system evolution in plants

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Many plants are perennial, but most studies of inbreeding depression and mating system evolution focus on annuals. This paper extends a population genetic model of inbreeding depression due to recessive deleterious mutations to perennials. The model incorporates life history and mating system variation, and multiplicative selection across many genetic loci. In the absence of substantial mitotic mutation, perennials have higher mean fitness and lower, or even negative, inbreeding depression than annuals with the same mating system. As in annuals, self fertilization exposes deleterious recessive mutations to selection, increasing mean fitness and decreasing inbreeding depression. Including mitotic mutation decreases mean fitness while increasing inbreeding depression. Perenniality introduces a kind of selective sieve, such that strongly recessive mutations contribute disproportionately to mean fitness and inbreeding depression. In the presence of high mitotic mutation, this selective sieve may provide a mechanistic basis for high inbreeding depression observed in some long lived perennials. Without substantial mitotic mutation, it is difficult to reconcile genetically based models of inbreeding depression with the empirical generalization that perennials outcross while related annuals self fertilize.

Keywords: mating system; inbreeding depression; plant; life history; dominance; theory

1. INTRODUCTION

Many annual plants are self fertilizing, whereas perennials outcross (Stebbins 1950, pp. 176–181; Böhle *et al.* 1996; Barrett & Harder 1996; Bena *et al.* 1998). Several explanations for this association have been advanced. The reproductive assurance hypothesis argues that annual plants self fertilize to assure fitness, whereas perennials are not constrained by the need for immediate reproductive success (Stebbins 1950, pp. 176–181). Hypotheses derived from phenotypic analyses note that adult inbreeding depression is compounded over the perennial life history, and production of selfed seed influences future survival and reproduction of perennials but not annuals (Morgan *et al.* 1997; also Arroyo & Squeo 1990). Both of these factors favour the maintenance of outcrossing in perennials. Recent life history arguments note that self fertilization increases the optimal allocation to reproduction at the expense of survival, provided inbreeding depression is less than one-half (Zhang 2000). This suggests that self fertilization drives the evolution of annual life history. Inbreeding depression is implicit in each of these explanations, yet few studies explore life history and mating system evolution using explicit genetic models of inbreeding depression.

The most likely source of inbreeding depression (reduced fitness of self relative to outcrossed progeny) is increased homozygosity of partly recessive, deleterious alleles (Lande & Schemske 1985; Charlesworth & Charlesworth 1987). Empirical observations suggest that outcrossing perennials harbour substantial amounts of inbreeding depression (Lande *et al.* 1994; Husband & Schemske 1996). Lande *et al.* (1994) show that very small dominance coefficients generate the extremely high inbreeding depression characteristic of conifers, even in the face of continued partial self fertilization. Muirhead & Lande (1997) introduce asexuality (perenniality) into a mixed mating model, restricting their attention to nearly recessive lethal

mutations. There is substantial inbreeding depression associated with small dominance coefficients, with increasing asexuality resulting in greater inbreeding depression. These authors do not address why dominance coefficients might be small in perennials, assume equal rates of mutation during both sexual and asexual reproduction, and do not address the evolution of self fertilization.

Here I develop multilocus genetic models of inbreeding depression incorporating a simple life history. The model allows for partially recessive deleterious alleles, nearly recessive lethals, unequal rates of mitotic and meiotic mutation, and a mixture of self fertilization and outcrossing. Specific questions addressed include the following: (i) What are the consequences of perenniality for equilibrium mean fitness and inbreeding depression in random mating populations? (ii) How does perenniality affect mean fitness and inbreeding depression in mixed mating populations? (iii) How do life history and deleterious mutation influence the evolution of the mating system? Table 1 summarizes important parameters used in the presentation.

2. METHODS

(a) Life history

A model capable of describing both annual and perennial life histories is presented in figure 1 (Charnov & Schaffer 1973; Morgan *et al.* 1997). Adult plants survive one time-period (e.g. 1 year) with probability P_1 . A mixture of self fertilization (frequency S) and outcrossing ($1 - S$) results in the production of many new offspring. The ‘competing’ model of self fertilization is used, with reproduction through self fertilization reducing ovules but not pollen available to participate in outcrossing (Lloyd 1979). Only $1 - P_1$ of the new individuals are recruited to reproductive maturity after a single time-period, reflecting density dependent regulation during recruitment. In the absence of genetically based fitness differences, the expectation of life of

Table 1. Parameters and their meaning.

symbol	meaning
life history and mating	
P_1	adult survival
S	rate of self fertilization
mutation and selection	
U, U_a	meiotic and mitotic mutation rates, per diploid genome
h	dominance coefficient
s	selection coefficient

an individual in this model is $L = 1/(1 - P_1)$ time-periods; annuals have $P_1 = 0$ and $L = 1$.

(b) *Equilibrium populations*

Mutation and selection at many loci can be incorporated into the life histories of figure 1. The order of events is selection followed by (mitotic and meiotic) mutation and mating. Suppose individuals with i heterozygous and j homozygous mutations are at frequency x_{ij} . Individuals survive with probability $P_1 w_{ij}$, and the average survival in the population is $P_1 \bar{w}$, where $\bar{w} = \sum_{ij} x_{ij} w_{ij}$ is the population mean fitness. Let the frequency vector $\mathbf{x}$ describe the population before selection, and $\mathbf{x}' = \mathbf{w}\mathbf{x}/\bar{w}$ the frequency after selection. The operator $\mathbf{M}(\mathbf{x}')$ returns the frequency vector following meiotic mutation and mixed mating, and embodies equations developed elsewhere (Kondrashov 1985; Charlesworth *et al.* 1990, 1991). Meiotic mutations are introduced following a Poisson distribution with mean U . The operator $\mathbf{N}(\mathbf{x}')$ returns the frequency vector following mitotic mutation. Mitotic mutations also follow a Poisson distribution, at rate U_a , and $\mathbf{N}$ is constructed so that the frequency vector after mitotic mutation, $\mathbf{x}''$, is $x''_{ij} = \sum_{k=0}^i x'_{kj} U_a^{i-k} e^{-U_a} / (i-k)!$. The transition between time-periods is then

$$\mathbf{x}'' = (1 - P_1 \bar{w}) \mathbf{M}(\mathbf{x}') + P_1 \bar{w} \mathbf{N}(\mathbf{x}'). \quad (2.1)$$

Analysis of the multilocus model involves numerical solution of equation (2.1). This model accommodates identity disequilibrium generated through selection and partial self fertilization (Lande *et al.* 1994). Individuals consist of many cells, not all of which experience identical mutational regimes. The entries in $\mathbf{x}$ in equation (2.1) are therefore interpreted as the population-level frequency of cells contributing to gamete production (e.g. apical meristems) in each generation (cf. Klekowski 1988; Otto & Orive 1995; Otto & Hastings 1998).

The fitness model $\mathbf{w}$ is of deleterious mutation. Partially recessive deleterious alleles represent the most likely source of inbreeding depression (Charlesworth & Charlesworth 1987). At a single locus, heterozygotes have fitness $1 - hs$ and homozygotes $1 - s$ relative to genotypes without deleterious mutation. A multiplicative fitness model,

$$w_{ij} = (1 - hs)^i (1 - s)^j \quad (2.2)$$

is used to combine fitness effects across loci, and applies to both juveniles and adults.

(c) *Parameter values and fitness measures*

Principal parameters requiring specification are the per locus and genomic mutation rates, and the selection and dominance coefficients. Estimates of genomic mutation rates from annual

Figure 1. A simple model describing annual ($P_1 = 0$) and perennial ($P_1 > 0$) life histories with self fertilization (S) and outcrossing ($1 - S$).

plants suggest plausible values of between 0.1 and 2 per genome (Johnston & Schoen 1995; Schultz *et al.* 1999; Shaw *et al.* 2000); precise estimates are a matter of considerable controversy (e.g. Fry *et al.* 1999; Lynch *et al.* 1999; Bataillon 2000; Keightley & Bataillon 2000). In perennials, both soma and germ line contribute to mutation (Klekowski 1988). Available estimates suggest that mutation at specific loci occurs between one and 10 times more frequently during a single meiotic division than during premeiotic divisions in barley and maize (Lindgren 1975). Mitotic mutation rates between zero and unity relative to meiotic rates were therefore investigated. The focus of investigation here is mildly deleterious, partially recessive mutations ($h = 0.2$, $s = 0.1$) and lethal strongly recessive mutations ($h = 0.02$, $s = 1.0$).

Lifetime measures of fitness and inbreeding depression are reported here. During a single time-period the fitness of a genotype with i heterozygous and j homozygous mutations, in the absence of mitotic mutation, is $P_1 \bar{w} \times (w_{ij}/\bar{w}) = P_1 w_{ij}$. Fitness summed over successive time periods is a geometric series, $P_1 w_{ij} + (P_1 w_{ij})^2 + \dots$, which is proportional to

$$(1 - P_1 w_{ij})^{-1}. \quad (2.3)$$

Lifetime fitness in the presence of mitotic mutation is calculated in a similar fashion. Lifetime inbreeding depression was defined as unity minus the average lifetime fitness of selfed progeny relative to average lifetime fitness of outcrossed progeny.

3. RESULTS

(a) *Random mating populations*

Figure 2 shows how expected longevity, L , influences mean fitness, $\bar{w}$, and inbreeding depression, δ , under multilocus mutation to deleterious partly recessive alleles ($U = 1.0$, $h = 0.2$, $s = 0.1$). In the absence of mitotic mutation ($U_a = 0$) mean fitness increases and inbreeding depression decreases with longevity. This can be understood in terms of the balance between mutation and selection. Mutation occurs once per generation (i.e. during meiosis), whereas selection occurs in each time-period. Thus, as longevity increases, the contribution of mutation decreases relative to that of selection. Stronger selection decreases the average number of deleterious mutations, increasing mean fitness and decreasing inbreeding depression.

Inbreeding depression becomes negative with sufficient longevity and the absence of mitotic mutation. Negative inbreeding depression occurs when selfed fitness exceeds

Figure 2. Influence of longevity and mitotic mutation rate (U_a) on (a) mean fitness and (b) inbreeding depression under multilocus deleterious mutation ($U = 1.0$, $h = 0.2$, $s = 0.1$).

outcrossed fitness. The effect can be understood by consideration of the different effects of self fertilization on the mean and variance of fitness. Progeny derived from self fertilization have decreased mean but increased variance in fitness, with fitness defined by equation (2.2). In the absence of mitotic mutation, fitness over a perennial's life history is $(1 - P_1 w_{ij})^{-1}$ (see equation (2.3)). The relationship between w_{ij} and $(1 - P_1 w_{ij})^{-1}$ is accelerating, the more so as $P_1 \rightarrow 1$. By Jensen's inequality (i.e. for a function f with positive second derivative, $(f(a) + f(b))/2 \geq f((a+b)/2)$), greater variation in the distribution of w_{ij} increases the mean of $(1 - P_1 w_{ij})^{-1}$. The increase is more marked as $P_1 \rightarrow 1$. From the numerical calculations, the effect of the variance on fitness outweighs the effect of the mean when expected longevity exceeds about 50 ($P_1 > 0.98$; figure 2).

Increasing mitotic mutation U_a decreases mean fitness (figure 2). This is because mitotic mutation increases the rate of mutation per episode of selection. In random mating populations, both mitotic and meiotic mutation introduce deleterious alleles as heterozygotes, and selection acts primarily on heterozygous mutations. From Haldane's cost of selection (Haldane 1957), it follows that the mean fitness is constant across life history when mitotic and meiotic mutation rates are equal ($U_a = U$). This is not the case in self-fertilizing populations (see figures 3 and 4) or under synergistic selection (M. T. Morgan, unpublished data), where selection does not eliminate mutations independently of one another.

Figure 3. Relationship between mean fitness and rate of self fertilization under multilocus deleterious meiotic (U) and mitotic (U_a) mutation. (a) Mildly deleterious ($h = 0.2$, $s = 0.1$) mutation at $U = 1.0$. (b) Lethal ($h = 0.02$, $s = 1.0$) mutation at $U = 0.1$. (c) Lethal ($h = 0.02$, $s = 1.0$) mutation at $U = 1.0$.

At fixed expected longevity, inbreeding depression increases with mitotic mutation (figure 2). This reflects the increased total mutation rate, increasing the average number of heterozygous mutations in the random mating population. For a given mitotic mutation rate, increasing longevity may decrease (e.g. $U_a = 0.1 U$) or increase ($U_a = U$) inbreeding depression. The explanation for this reflects the changing balance between mean and variance of selfed progeny fitness. At higher mitotic mutation rates, the decrease in mean selfed fitness caused by increasing equilibrium numbers of deleterious mutations is not offset by the indirect effects of increased variance.

Figure 4. Relationship between inbreeding depression and rate of self fertilization under multilocus deleterious meiotic (U) and mitotic (U_a) mutation. (a) Mildly deleterious ($h=0.2$, $s=0.1$) mutation at $U=1$. (b) Lethal ($h=0.02$, $s=1.0$) mutation at $U=0.1$. (c) Lethal ($h=0.02$, $s=1.0$) mutation at $U=1.0$.

Table 2 illustrates how mode of gene action influences mean fitness in random mating populations. For an annual, mean fitness is independent of dominance coefficient (Haldane 1957; Kimura & Maruyama 1966). Mean fitness increases with dominance coefficient in perennials, even in random mating populations. The effect is very slight (no consequence to three decimal places) at low mutation ($U=0.1$), but more pronounced at higher mutation rates ($U=1$). An explanation for this effect again involves Jensen's inequality. Greater dominance increases the variance in fitness implied by equation (2.2). By the arguments above, the greater

variance increases lifetime mean fitness given in equation (2.3).

Inbreeding depression is inversely proportional to dominance coefficient in random mating populations (table 2; Lande & Schemske 1985), but decreases with longevity (figure 2, table 2). Longevity has greatest effect on inbreeding depression at small or intermediate dominance (e.g. $h \leq 0.05$ at $U=0.1$, $h \leq 0.2$ at $U=1.0$). Substantial inbreeding depression (e.g. $\delta > 0.5$) occurs in short lived species and with mutations of low dominance coefficient.

(b) *Mixed mating populations*

Figure 3 displays the relationship between population mean fitness and selfing rate for various life history and mutational parameters. Figure 3a describes the consequences of genomic mutation to mildly deleterious, partially recessive alleles ($U=1.0$, $h=0.2$, $s=0.1$). In annuals, increasing self fertilization increases population mean fitness because selection acts to efficiently eliminate homozygous rather than heterozygous mutations (Haldane 1957; Lande & Schemske 1985; Charlesworth *et al.* 1990). Perennials with low rates of mitotic mutation have high mean fitness, as in outcrossing populations. This is because the opportunities for mutation (i.e. each generation) are decreased relative to opportunities for selection (i.e. each time-period). Increasing mitotic mutation rate decreases population mean fitness at all selfing rates; mean fitness in perennials is comparable with that in annuals when mitotic and meiotic mutation rates are equal. The equivalence at high selfing rates is surprising, because mitotic mutations accumulate unfettered by selection for several time-periods before the first reproductive (selfing) event exposes the mutation to selection as a heterozygote.

Figure 3b,c describes the relationship between mean fitness and selfing rate for lethal recessives ($h=0.02$, $s=1.0$) at intermediate ($U=0.1$) and high ($U=1.0$) rates of deleterious mutation. The consequences of perennality, self fertilization, and mitotic mutation for lethal recessives are qualitatively similar to those for partially deleterious mutations. In perennials, greater mitotic mutation and greater outcrossing reduce population mean fitness. At low mitotic and meiotic mutation rates, perennality effectively reduces the consequences of mutation for population mean fitness (figure 3b). Unusual behaviour occurs at high rates of mutation to lethal recessive alleles (figure 3c; Lande *et al.* 1994; Muirhead & Lande 1997). Increasing self fertilization initially decreases mean fitness for all parameters investigated, particularly at greater rates of mitotic mutation. This contrasts with the purging effect seen in models of partially deleterious mutation in annuals (figure 3a; Lande & Schemske 1985; Charlesworth *et al.* 1990, 1991; Byers & Waller 1999).

Figure 4 displays the relationship between inbreeding depression and selfing rate for the combination of mutational and life history parameters investigated in figure 3. In annuals, increasing self fertilization decreases inbreeding depression gradually for deleterious partially recessive alleles (figure 4a; Charlesworth *et al.* 1990, 1991), dramatically for lethal recessives at moderate rates of mutation (figure 4b; Lande & Schemske 1985), and at a threshold for high rates of lethal recessive mutation

Table 2. Mean fitness, $\bar{w}$ and inbreeding depression, δ , determined by dominance coefficient, h , in annuals (lifespan $L=1$) and perennials ($L>1$) under multiple locus deleterious mutation in a random mating population.

(Selection coefficient $s=0.1$. Mean fitness values for $U=0.1$ identical to three decimal places.)

expected longevity, $L = 1/(1 - P_1)$							
h	1	2	5	10	20	50	100
mean fitness, $\bar{w}$							
$U = 0.1, U_a = 0$							
0.01	0.905	0.949	0.979	0.989	0.995	0.998	0.999
0.30	0.905	0.949	0.979	0.989	0.995	0.998	0.999
$U = 1.0, U_a = 0$							
0.10	0.368	0.467	0.600	0.698	0.791	0.920	0.976
0.20	0.368	0.469	0.611	0.720	0.837	0.954	0.980
0.30	0.368	0.472	0.621	0.743	0.872	0.960	0.982
inbreeding depression, δ							
$U = 0.1, U_a = 0$							
0.01	0.914	0.829	0.739	0.670	0.557	0.343	0.196
0.02	0.699	0.614	0.529	0.448	0.336	0.178	0.090
0.05	0.362	0.321	0.264	0.205	0.136	0.058	0.020
0.10	0.181	0.162	0.128	0.092	0.054	0.015	-0.004
0.20	0.072	0.064	0.047	0.029	0.011	-0.008	-0.016
0.30	0.033	0.028	0.017	0.006	-0.004	-0.015	-0.020
$U = 1.0, U_a = 0$							
0.10	0.865	0.823	0.769	0.728	0.681	0.499	0.107
0.20	0.528	0.494	0.449	0.405	0.316	0.017	-0.133
0.30	0.283	0.264	0.229	0.183	0.068	-0.124	-0.203

(figure 4c; Lande *et al.* 1994; Muirhead & Lande 1997). Inbreeding depression decreases with perennality *per se* (e.g. $L=20$, $U_a=0.01U$) and increases with greater mitotic mutation ($L=20$, $U_a=0.1U$, $U_a=U$). High mitotic mutation ($U_a=U$) elevates inbreeding depression in perennials above that in annuals. This is in contrast to the effects of mitotic mutation on mean fitness, where mitotic mutation is approximately equivalent to meiotic mutation for most parameter values.

(c) **Expected longevity**

Table 3 shows the relationship between expected longevity based on demographic parameters, $L = 1/(1 - P_1)$, and realized longevity under lethal recessive ($h=0.02$, $s=1.0$, $U=0.1$) and partially deleterious ($h=0.2$, $s=0.1$, $U=1.0$) mutational models. Realized longevity is the average lifespan of individuals, weighted by their reproductive contribution at each age; it is shorter than expected longevity due to fitness differences between individuals (table 3). For random mating annuals ($L=0$), realized longevity is the mean fitness of the population, i.e. $\exp -U$ (Kimura & Maruyama 1966). Greater expected longevity increases realized longevity, but for most parameters the relationship is surprisingly weak. Mitotic mutation further moderates the relationship between expected and realized longevity, so that substantial realized longevity occurs only at low rates of mitotic mutation. Greater self fertilization partly restores the relationship between expected and realized longevity at high mitotic mutation rates, but the contribution is only slight. For instance, the realized longevity for random

mating perennials with expected longevity $L=20$ experiencing deleterious recessive mutation at $U=U_a=1.0$ is approximately 1.5 times longer than the realized longevity of annuals. The same comparison for self-fertilizing ($S=1.0$) populations results in a 2.2-fold increase in realized longevity.

4. DISCUSSION

The preceding analysis shows that, in the absence of mitotic mutation, longevity increases mean fitness while decreasing inbreeding depression. This is true in both random (figure 2) and mixed mating (figures 3 and 4) populations. The underlying reason is that perennality decreases the opportunity for heritable mutation compared to selection. Only with high rates of mitotic mutation do perennials exhibit mean fitness ($U_a \approx 0.2U$, e.g. figure 2) and inbreeding depression ($U_a \approx U$, figure 2) comparable to annuals.

Self fertilization occurs predominantly in annuals, while outcrossing characterizes perennials (Stebbins 1950, pp. 176–181). Previous phenotypic models suggest that inbreeding depression compounded over the perennial life history may contribute to this association (Morgan *et al.* 1997). The model presented here allows inbreeding depression to evolve in response to mutational, fitness, life history and mating system parameters. Results obtained when inbreeding depression is evolutionarily dynamic contrast with the earlier phenotypic models. For all parameter values investigated (cf. figures 2 and 4; table 2),

Table 3. Realized expectation of life under multilocus lethal ($U=0.1$, $h=0.02$, $s=1$) or deleterious ($U=1$, $h=0.2$, $s=0.1$) mutation.

(Values are calculated for selfing rates $S=0, 0.5$ and 1 ; expected longevity in the absence of mutation $L=1/(1-P_1)=1, 2, 5, 10, 20$. Mitotic mutation at rates $U_a=0.01U, 0.1U, U$, except for $L=1$ where mitotic mutation must be $U_a=0$.)

expected longevity	lethal, $U=0.1$, $U_a=$			deleterious, $U=1$, $U_a=$		
	0.001	0.01	0.1	0.01	0.1	1.0
$S=0$						
$L=1$	0.90	0.90	0.90	0.37	0.37	0.37
2	1.80	1.79	1.65	0.61	0.59	0.45
5	4.49	4.34	3.28	1.17	1.00	0.52
10	8.95	8.29	4.87	1.94	1.38	0.55
20	17.7	15.2	6.45	3.42	1.75	0.57
$S=0.5$						
$L=1$	0.95	0.95	0.95	0.48	0.48	0.48
2	1.89	1.88	1.79	0.89	0.85	0.61
5	4.69	4.59	3.76	2.17	1.75	0.71
10	9.29	8.79	5.83	4.27	2.81	0.75
20	18.3	16.2	7.99	7.89	3.93	0.78
$S=1$						
$L=1$	0.95	0.95	0.95	0.60	0.60	0.60
2	1.90	1.89	1.80	1.18	1.13	0.85
5	4.72	4.63	3.88	2.85	2.40	1.12
10	9.39	8.94	6.20	5.36	3.78	1.25
20	18.6	16.6	8.73	9.66	5.25	1.33

increasing longevity decreases inbreeding depression. In the absence of substantial mitotic mutation, perennials appear more susceptible to invasion by genes modifying the rate of self fertilization than do annuals. Without additional modification, inbreeding depression due to deleterious recessive or partially recessive mutation seems unlikely to contribute to our understanding of the empirical association between self fertilization and annuality. Secondary support for this conclusion comes from table 3, where expected longevity increases more dramatically in self-fertilizing than in random-mating species. Genetic explanations for prevalence of self fertilization in perennials requires high levels of mitotic mutation (figure 4a) or elevated mutation to lethal recessives (figure 4c).

In annual plants the population mean fitness depends on the (genomic) mutation rate, but not details of gene action (i.e. $\bar{w} = \exp -U$, table 2; Haldane 1957; Kimura & Maruyama 1966). Mean fitness in perennials depends on details of gene expression such as the dominance coefficient, as illustrated for scenarios without mitotic mutation in table 2. Longevity is less effective at decreasing the fitness consequences of more recessive (e.g. $h=0.1$) compared to more dominant (e.g. $h=0.3$) mutations. Perenniality thus introduces a kind of selective sieve (cf. Haldane 1957) whereby genetic load and therefore inbreeding depression become increasingly due to recessive, rather than partially dominant, mutations. This sieve may partly explain extraordinary levels of inbreeding depression sometimes seen in forest trees, even at intermediate rates of self fertilization (see Muirhead & Lande 1997). In particular, the sieve favours accumulation of strongly recessive mutations required for the threshold effect seen in figure 4c.

A selective sieve generates substantial inbreeding depression, but only at high rates of genomic mutation to lethal alleles. High inbreeding depression observed in forest trees sometimes occurs early in the life history, e.g. in Scots pine (Karkkainen *et al.* 1996) and Douglas fir (Sorensen 1999). One possibility is that this inbreeding depression reflects expression of genes with stage-specific (i.e. seedling) gene expression. For mutations with stage-specific gene expression, perenniality increases opportunities for (mitotic and meiotic) mutation without concurrent increase in opportunities for selection. This might result in substantial inbreeding depression early in the life history. The argument for high rates of mutation relative to selection for genes acting early in the life history is, however, partly inconsistent with models for the evolution of deleterious mutations in random mating age-structured populations (Charlesworth & Hughes 1996). For a uniform mutation rate to deleterious alleles with fitness effects restricted to each age, the number of deleterious mutations and inbreeding depression increases with age. The sensitivity of selection (i.e. $\partial w / \partial n$, where n is the number of deleterious mutations affecting a particular age) usually decreases with age (Charlesworth 1994; also Orive 1995). Strong selection during early stages should purge deleterious mutations. A simple analysis of stage-specific selection under mixed mating is precluded by the association between loci induced by self fertilization. Empirical observations also indicate that inbreeding depression decreases with age in predominantly outcrossing taxa (Husband & Schemske 1996; Sorensen 1999). This suggests that at least some deleterious mutations do not have stage-specific effects.

There are several extensions to the model presented here, including alternative models of selection, incorporation of

stage-specific mutational effects, exploration of selection at the cellular level, and explicit investigation of mating system modifiers. Charlesworth (1998) argues that synergistic epistasis, rather than multiplicative fitness interactions, are required to account for inbreeding load in *Drosophila*. The evolution of mating systems has been investigated in models of annuals with synergistic selection (Charlesworth *et al.* 1991). These models generate increased mean fitness and inbreeding depression compared with multiplicative models with comparable mutation rates. The qualitative effects of synergy on inbreeding depression and mating system evolution is similar to that of multiplicative models, except at very high selfing rates where mean fitness can increase, and inbreeding depression decrease, slightly. Thus synergistic models of selection are unlikely to reconcile genetically based models of inbreeding depression with the empirical association of life history and mating system. The consequence of age-specific deleterious mutation has been investigated in random mating, age- and stage-structured, populations (Orive 1995; Charlesworth & Hughes 1996; see above). Investigation of age-specific mutations in mixed mating plant populations is complicated by patterns of vegetative growth in organisms with overlapping soma and germline. Otto & Orive (1995) and also Klekowski (1988) and Otto & Hastings (1998) model the fate of individual cells and their descendants experiencing deleterious mutation. In general, selection against deleterious mutations at the cellular level reduces the effective rate of deleterious mutation. The extent of reduction depends on the details of meristem formation and dynamics; extension to mixed mating species has not yet been conducted. Finally, inbreeding depression has proved a valuable guide to understanding the selection of self fertilization. It is nonetheless important to extend the population-level arguments developed here to explicitly model genetic modifiers of the mating system acting at the individual level.

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