The Evolution of Haploid, Diploid and Polymorphic Haploid-Diploid Life Cycles: The Role of Meiotic Mutation

David W. Hall

Section of Integrative Biology, University of Texas, Austin, Texas 78712-1064

Manuscript received April 19, 2000
Accepted for publication June 13, 2000

ABSTRACT

Here I present a simple population genetic model to investigate the evolution of polymorphic haploid-diploid life cycles. The key feature of the model is the assumption of mutation occurring during meiosis. I show that, in addition to regions favoring haploid or diploid life cycles, there are substantial regions of the parameter space under which polymorphic haploid-diploid life cycles are expected to evolve.

ALL meiotic organisms spend some proportion of their life as a haploid and as a diploid. In *diploid* organisms, mitotic divisions are essentially restricted to the diploid phase. In *haploid* organisms, mitotic divisions are restricted to the haploid phase. *Haploid-diploid* life cycles are those in which mitotic divisions occur in both the haploid and diploid phases within a population (Bell 1994). Since the life cycle is one of the most fundamental attributes of an organism, understanding the variation seen among meiotic organisms in their life cycles is an important problem in evolutionary biology. In particular, we would like to identify and determine the relative importance of the factors that affect the evolution of the life cycle.

I distinguish two types of haploid-diploid life cycle. In *biphasic* species (Figure 1a), individuals have mitotic divisions in the diploid phase, undergo meiosis, and then have mitotic divisions in the haploid phase. In *polymorphic* species (Figure 1b), individuals undergo mitotic divisions in *either* the haploid or the diploid phase. Thus, after syngamy individuals can either undergo meiosis immediately to produce haploid offspring who will undergo somatic development, or meiosis can be delayed such that somatic development occurs in the diploid phase.

In this article, I seek to understand under what conditions polymorphic haploid-diploid life cycles are expected to evolve in response to meiotic mutation. While previous work has considered the evolution of polymorphic life cycles in response to mutation, none has specifically addressed meiotic mutation, instead implicitly focusing on mitotic mutation.

Previous models: The relative advantages of diploid *vs.* haploid life cycles have been considered in several studies. Some of these have used the relative fitness of a haploid *vs.* a diploid population (Charlesworth 1991; Kondrashov and Crow 1991) to understand conditions favoring one ploidy over the other and, as such, have not considered the evolution of a haploid-diploid life cycle. Other models have explicitly allowed a haploid-diploid life cycle to be a possible evolutionary outcome (Perrot *et al.* 1991; Bengtsson 1992; Goldstein 1992; Otto and Goldstein 1992; Bell 1994; Michod and Gayley 1994; Orr and Otto 1994; Otto and Marks 1996). Models addressing polymorphic life cycles have uniformly found that a haploid-diploid cycle is unable to evolve. Instead a population is expected to evolve to a haploid or a diploid life cycle depending on the values of the parameters. The few models addressing biphasic life cycles (Jenkins 1993; Jenkins and Kirkpatrick 1994; Hughes and Otto 1999) have found that a haploid-diploid cycle can evolve, at least under certain fitness functions.

With mutation occurring primarily during meiosis, I find that there is a significant region of the parameter space in which a polymorphic haploid-diploid life cycle can evolve. This is because meiotic mutation leads to a negative frequency dependence between the advantage of diploidy and the proportion of the population that is currently diploid.

THE MODEL

Apart from the timing of mutation, the model follows that of Perrot *et al.* (1991) and Otto and Goldstein (1992). I consider an organism with synchronized mating such that fusion of haploid gametes occurs at a particular time set by external signals such as day length. Following the fusion of haploid gametes to form diploid zygotes, a cell either immediately undergoes meiosis, or meiosis is delayed until just prior to the next episode of mating. Ploidy level is thus controlled by the timing of meiosis (Perrot *et al.* 1991; Otto and Goldstein 1992). Delaying meiosis results in an individual that enters adulthood and undergoes selection as a diploid. By undergoing meiosis immediately following zygote

Author e-mail: davehall@uts.cc.utexas.edu

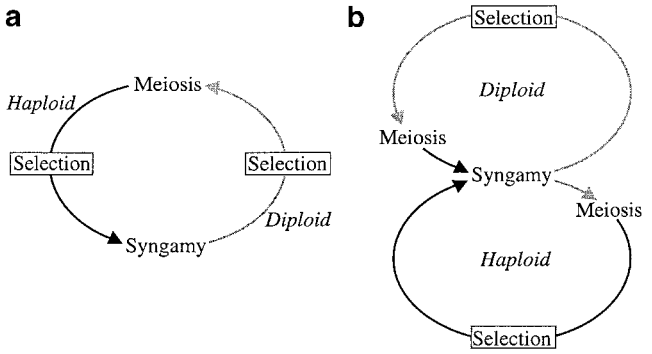

FIGURE 1.—Haploid-diploid life cycles. (a) In a biphasic haploid-diploid life cycle, mitotic development occurs in both the haploid and diploid phase. Genotypes that modify the life cycle alter the amount of time an individual spends in the diploid phase before undergoing meiosis. All individuals of a particular genotype will possess the same life cycle. (b) In a polymorphic haploid-diploid life cycle, mitotic development is limited to either the haploid or the diploid phase. Genotypes that modify the life cycle alter the probability that an individual will undergo meiosis immediately following syngamy, or delay meiosis until just before the next round of syngamy. Individuals of a particular genotype can thus differ in their life cycle, with some remaining diploid and others undergoing meiosis to produce haploids.

formation, individuals are produced that undergo selection as haploids (Figure 2).

The probability that a cell fails to undergo meiosis immediately following zygote formation and thus enters adulthood as a diploid is controlled by a modifier locus, C. The C_1C_1, C_1C_2 and C_2C_2 genotypes at this locus cause a cell to remain diploid with probability d_{11}, d_{12}, and d_{22}, respectively. The modifier heterozygote shows intermediate dominance (*i.e.*, $d_{11} < d_{12} < d_{22}$ or $d_{11} > d_{12} > d_{22}$), and differences between modifier genotypes, in terms of the probability of undergoing early meiosis, are assumed to be small such that terms of order $(d_{ij} - d_{kl})^2$ can be ignored.

Fitness of adults is determined by a viability locus that segregates a favored allele, A_0, and a deleterious allele, A_1. Selection is such that the A_0A_0 and A_0 genotypes have fitness 1; A_1A_1 and A_1 have fitness $1 - s$, and A_0A_1 has fitness $1 - hs$ ($0 \le h \le 1$, $0 \le s \le 1$). Mutation is assumed to occur during meiosis at rate μ from A_0 to A_1. Unlike previous models, mitotic mutation is ignored. The recombination rate r between the modifier and viability loci can take any value ($0 \le r \le \frac{1}{2}$). See Figure 2 for an overview of the model.

RESULTS

Setting x_1, x_2, x_3, and x_4 as the frequencies of A_0C_1, A_1C_1, A_0C_2, and A_1C_2, respectively, just prior to syngamy, the recursions for the model simplify to

$$\begin{aligned}\overline{W}x_1' = {} & x_1^2(1-\mu) + x_1x_3(1-\mu) + x_1x_2(1-\mu)(1-d_{11}hs) \\ & + x_1x_4(1-\mu)(1-r)(1-d_{12}hs) + x_2x_3(1-\mu)r(1-d_{12}hs)\end{aligned}$$

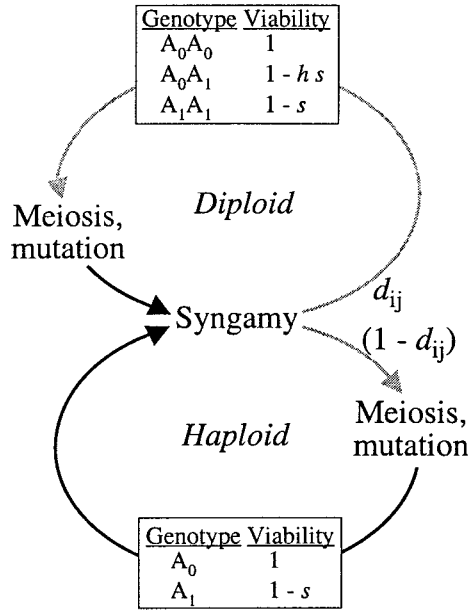

FIGURE 2.—Model outline. The polymorphic life cycle follows PERROT *et al.* (1991) and OTTO and GOLDSTEIN (1992), except for the location of mutation, which is assumed to occur during meiosis. Following syngamy, an individual of genotype C_iC_j remains diploid with probability d_{ij} or undergoes meiosis to produce haploids with probability $(1 - d_{ij})$. Diploids and haploids then undergo directional viability selection. Following selection, haploids produce gametes mitotically and diploids produce gametes meiotically that then enter the random mating pool.

$$\begin{aligned}\overline{W}x_2' = {} & x_1^2\mu(1-s(1-d_{11})) + x_1x_3\mu(1-s(1-d_{12})) \\ & + x_1x_2(1+\mu)(1-d_{11}hs-s(1-d_{11})) \\ & + x_1x_4(r(1-\mu)+\mu)(1-d_{12}hs-s(1-d_{12})) \\ & + x_2x_3((1-r)(1-\mu)+\mu)(1-d_{12}hs-s(1-d_{12})) \\ & + x_2^2(1-s) + x_2x_4(1-s)\end{aligned}$$

$$\begin{aligned}\overline{W}x_3' = {} & x_3^2(1-\mu) + x_1x_3(1-\mu) + x_3x_4(1-\mu)(1-d_{22}hs) \\ & + x_1x_4(1-\mu)r(1-d_{12}hs) + x_2x_3(1-\mu)(1-r)(1-d_{12}hs)\end{aligned}$$

$$\begin{aligned}\overline{W}x_4' = {} & x_3^2\mu(1-s(1-d_{22})) + x_1x_3\mu(1-s(1-d_{12})) \\ & + x_3x_4(1+\mu)(1-d_{22}hs-s(1-d_{22})) \\ & + x_1x_4((1-r)(1-\mu)+\mu)(1-d_{12}hs-s(1-d_{12})) \\ & + x_2x_3(r(1-\mu)+\mu)(1-d_{12}hs-s(1-d_{12})) \\ & + x_4^2(1-s) + x_2x_4(1-s),\end{aligned}$$

where $\overline{W}$ is a normalizer that ensures that the x_i's sum to one and is equal to the sum of the right-hand sides of the recursions. With no variation at the modifier locus, such that C_1 is fixed, the population exhibits a polymorphic life cycle where a proportion d_{11} of the population is diploid and $(1 - d_{11})$ is haploid as adults prior to selection. A mutation-selection equilibrium at the viability locus results such that

$$\hat{x}_1 = 1 - \hat{x}_2 \text{ and } \hat{x}_2 = \mu \frac{(1 - s(1 - d_{11}))}{s(1 - d_{11}(1 - h))} + O(\mu^2), \quad (1)$$

where $O(\mu^2)$ represents terms that are squared in the mutation rate and can thus be ignored. The equilibrium given in Equation 1 is invalid for the limiting case when $d_{11} = 1$ (a diploid life cycle) and $h = 0$ (fully recessive mutations). In this case, the mutation-selection equilibrium is $\hat{x}_2 = \sqrt{\mu/s}$ as expected (Haldane 1927). For the remainder of the article, I assume that the population is not in this limiting case and is thus at the equilibrium given in Equation 1. The equilibrium frequency of the deleterious allele is larger when viability selection is weak (s near zero) and when more individuals are diploid (d_{11} close to 1).

When a new allele is introduced at low frequency at the modifier locus into a population at the equilibrium given in Equations 1, recursions in the rare genotypes (x_3 and x_4) can be linearized, since we can ignore terms that are squared in these frequencies, to give

$$\begin{aligned} Tx_3' &= \hat{x}_1 x_3(1 - \mu) + \hat{x}_1 x_4(1 - \mu) r(1 - d_{12}hs) \\ &\quad + \hat{x}_2 x_3(1 - \mu)(1 - r)(1 - d_{12}hs) \end{aligned}$$

$$\begin{aligned} Tx_4' &= \hat{x}_1 x_3 \mu(1 - s(1 - d_{12})) \\ &\quad + \hat{x}_1 x_4((1 - r)(1 - \mu) + \mu)(1 - d_{12}hs - s(1 - d_{12})) \\ &\quad + \hat{x}_2 x_3(r(1 - \mu) + \mu)(1 - d_{12}hs - s(1 - d_{12})). \end{aligned}$$

The roots of the characteristic equation of these linear recursions give the eigenvalues. If the leading eigenvalue is >1, the introduced allele increases in frequency. If the introduced modifier did not alter ploidy levels, such that it was neutral, the leading eigenvalue would equal 1 and the other eigenvalue would be positive and <1 (from Perron-Frobenius theorem; Gantmacher 1959). Under weak selection, the leading eigenvalue is close to 1 in value. If the leading eigenvalue is >1, then the sign of the characteristic equation evaluated at 1, $C(1)$, is negative. If the leading eigenvalue is <1 then $C(1)$ is positive. Thus, the sign of $C(1)$ determines stability when selection is weak. Evaluating $C(1)$ gives the condition for the invasion of an introduced rare modifier allele (C_2) as

$$\begin{aligned} &(d_{11} - d_{12}) Q(d_{12}) < 0, \\ &\text{where } Q(d_{12}) = s(\mu r(1 - d_{12}) \\ &\qquad + \hat{x}_2(r(1 - 2h) - hs(1 - r) \\ &\qquad + d_{12}h(1 - h)s(1 - 2r))). \end{aligned} \quad (2)$$

The second term of $Q(d_{12})$, which involves $\hat{x}_2$, is the same as that obtained by Otto and Goldstein (1992). The first term of $Q(d_{12})$ is positive and thus favors the invasion of modifiers that increase diploidy. Diploidy is thus favored over a larger range than seen in Otto and Goldstein's (1992) model. As linkage tightens, the first term decreases in magnitude, and haploidy is favored, in agreement with the results of Otto and Goldstein (1992). With $r = 0$, the evolution of a diploid life cycle is precluded.

A change of basis (Uyenoyama and Bengtsson 1989; Uyenoyama 1991) was performed such that the invasion criterion could be partitioned into a term involving average fitness and a term due to associations that arise between the two loci during invasion of the C_2 allele (see appendix). The new basis is such that one axis represents the frequency of the C_2 allele (designated the p axis) and the other axis represents the standard measure of linkage disequilibrium, D, between the two loci (see Crow and Kimura 1970). With an appropriate choice of vector $\{p^*, D^*\}^T$ in the new basis and assuming weak selection (see appendix), this analysis gives the condition for the increase of C_2 when rare as

$$(d_{11} - d_{12})(\bar{V}_D - \bar{V}_H)p^* + s((1 - r)(1 - d_{12}) + d_{12}h)D^* < 0, \quad (3)$$

where $\bar{V}_H$ and $\bar{V}_D$ represent the average fitness of individuals that enter selection as haploids and diploids, respectively. D^* is the asymptotic disequilibrium that arises between the A and C loci upon the introduction of the C_2 allele. Negative D^* implies that the C_2 allele is positively associated with the A_0 allele. Since the A_0 allele is favored by selection, negative D^* facilitates the invasion of the C_2 allele as seen in Equation 3. From Equation 3, stronger selection (large s) implies D^* has a larger effect on the invasion criterion for the C_2 allele. This is because the benefit of an association between the C_2 allele and the favored viability allele increases as the strength of selection increases. The sign of D^* during invasion of the C_2 allele is proportional to $-(d_{11} - d_{12})\mu p^*$ (from Equation A2 in the appendix), which is negative for modifiers that increase haploidy, and thus the disequilibrium that arises between the two loci always favors haploidy. With $r = 0$, the D^* term dominates such that the evolution of a diploid life cycle is precluded, in agreement with previous work (Otto and Goldstein 1992, for example).

The first term of inequality (3) measures the effect of changing the ploidy level on mean fitness and, as such, ignores associations between the two loci. An expression for $(\bar{V}_D - \bar{V}_H)$ can be calculated as

$$(\bar{V}_D - \bar{V}_H) = \mu s + \hat{x}_2 s(1 - 2h). \quad (4)$$

Substituting for $\hat{x}_2$ from Equation 1 into Equation 4 gives

$$(\bar{V}_D - \bar{V}_H) = \mu \frac{(1 - 2h + 2hs - d_{11}hs)}{1 - d_{11} + d_{11}h}. \quad (5)$$

Based solely on mean fitness (Equation 5), ploidy levels are expected to evolve as shown in Figure 3. Note that there is a substantial region of the parameter space in which a polymorphic life cycle is expected to evolve.

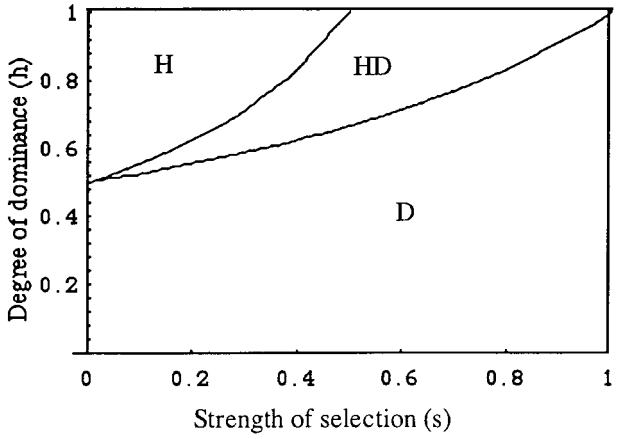

FIGURE 3.—Regions of the parameter space in which a haploid (H), diploid (D), or a polymorphic haploid-diploid (HD) life cycle is expected to evolve, in the absence of associations between the modifier locus and viability locus.

Since the association term always favors haploidy, it reduces the region of the parameter space that favors diploidy relative to the mean fitness result, especially as linkage tightens, and this can be seen in Figure 4, which shows the full result obtained from inequality (2) or (3).

DISCUSSION

The results from this model agree with previous work (PERROT *et al.* 1991; BENGTSSON 1992; OTTO and GOLDSTEIN 1992; OTTO 1994; OTTO and MARKS 1996) in that recessive mutations (small h) and looser linkage (r close to ½) both favor diploid life cycles while dominant mutations (large h) and tight linkage (r close to 0) both favor haploid life cycles. However, in a departure from previous work, polymorphic haploid-diploid life cycles are expected to evolve for a substantial region of the parameter space. In particular, a combination of loose linkage, strong selection, and mutations that are not too recessive favors a polymorphic haploid-diploid life cycle (see Figure 4).

Mean fitness of haploids *vs.* diploids: In previous models that have examined the evolution of haploid-diploid polymorphic life cycles, the frequency of deleterious alleles in haploids and in diploids entering selection is the same. As such, the only difference between haploids and diploids is in how those deleterious alleles are subjected to selection. In haploids, the deleterious allele is selected against in the haploid genotype and as such suffers a fitness cost equal to s. In diploids, the deleterious allele occurs primarily in the heterozygote and as such suffers a fitness cost equal to hs. The frequency of the heterozygote in diploids is approximately twice the frequency of the deleterious allele. Thus, in previous models, the relative fitness of diploids *vs.* haploids is

$$(\bar{V}_D - \bar{V}_H) = \hat{x}_2 s(1 - 2h). \quad (6)$$

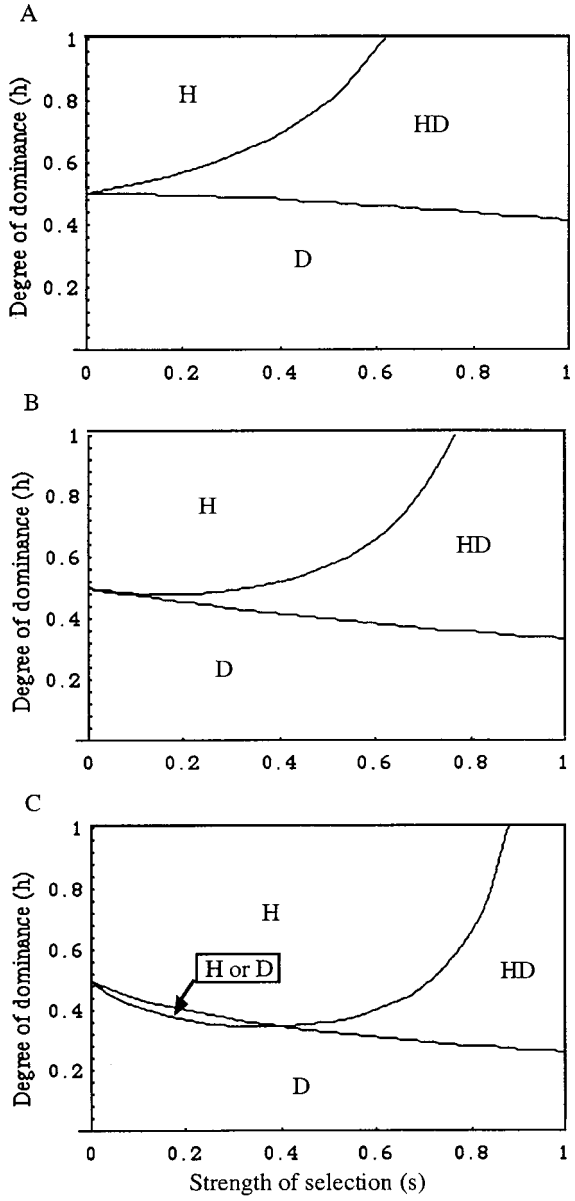

FIGURE 4.—Regions of the parameter space in which a haploid (H), diploid (D), or a polymorphic haploid-diploid (HD) life cycle is expected to evolve for three levels of linkage: (A) $r = ½$; (B) $r = ¼$; (C) $r = ⅛$. In the "H or D" region in C, an unstable equilibrium exists such that either a haploid or a diploid life cycle is expected to evolve, depending on the value of d_{11}.

Diploids thus have a mean fitness advantage over haploids when mutations are recessive ($h < ½$). Thus diploidy is advantageous with respect to mean fitness because of the masking of deleterious mutations (see PERROT *et al.* 1991; OTTO and GOLDSTEIN 1992; JENKINS and KIRKPATRICK 1994, 1995; OTTO 1994; OTTO and MARKS 1996). Note that in the additive case ($h = ½$), the mean fitness of haploids and diploids is equal.

In the model presented here, mutation occurs during meiosis. Mutation thus occurs prior to selection in haploids and after selection, prior to mating, in diploids

(Figure 2). For this reason, haploids entering selection have a higher frequency of the deleterious allele than diploids entering selection. This difference is reflected in the mean fitness of haploids *vs.* diploids as seen in Equation 4. By comparing Equations 4 and 6, it is clear that diploids can have a mean fitness advantage over haploids, even in situations where the deleterious allele is partially dominant ($h > \frac{1}{2}$), and this is seen in Figure 3. Meiotic mutation thus causes diploidy to be favored over a larger range than seen in previous models because the frequency of the deleterious allele in haploids entering selection is greater than in diploids.

The difference in the frequency of the deleterious allele in haploids *vs.* diploids entering selection is affected by the resident level of diploidy in the population. In particular, if the population consists primarily of haploids, the equilibrium frequency ($\hat{x}_2$) of the deleterious allele is small and new mutations arising during meiosis cause a large difference in the frequency of the deleterious allele in haploids *vs.* diploids. Thus diploidy is more likely to be favored in a population consisting primarily of haploids. In the region of the parameter space where polymorphic haploid-diploid life cycles are favored, diploidy has an advantage when rare, but not when common. This frequency dependence is the key attribute of the model that allows the evolution of polymorphic haploid-diploid life cycles. In previous models, the mean fitness of haploids *vs.* diploids did not exhibit frequency dependence.

Genetic associations: As seen in previous studies (Perrot *et al.* 1991; Bengtsson 1992; Otto and Goldstein 1992; Bell 1994; Otto 1994; Otto and Marks 1996), associations that arise during invasion of an allele modifying ploidy favor the evolution of haploidy. The positive association between modifiers that increase haploidy and the favored viability allele (Equation A2) arises through selection. Modifiers that increase haploidy are predominant in the haploid part of the population. After selection, the frequency of the favored viability allele in haploids is relatively high due to efficient removal of the deleterious allele by selection. Thus modifiers that increase haploidy end up with a purged genome that favors their invasion. The association between the modifier and viability loci becomes larger as linkage tightens, which favors haploidy to a greater extent (see Figure 4).

Meiotic mutation: The model presented requires the assumption of mutation linked to meiosis. Several lines of evidence suggest this is a reasonable assumption. There are data from mice that allow the mutation rate to be estimated for the perigametic interval, which is the period following the last mitotic division in the germ line and the first mitotic division in the zygote and thus includes meiosis as a major component (reviewed in Russell and Russell 1996; Russell 1999). These data indicate that the perigametic interval is highly mutagenic, at least for some loci. In particular, perhaps as many as 50% of all mutations arise during the perigametic interval in mice (Russell and Russell 1996). Since meiosis is the main event that occurs during the perigametic interval, these data suggest that meiosis is highly mutagenic. In addition, the observation that the per generation mutation rates for Drosophila, mouse, and human are similar has led to the hypothesis that a large fraction of mutations occur during meiosis, which occurs once per generation as opposed to during germ line mitotic divisions, which differ in number among these organisms (Russell 1999). Finally, some types of mutation are expected to occur more frequently during meiosis. For example, mutations that involve unequal crossing over (causing deletions and duplications), intrachromosomal crossing over (causing deletions and inversions), and nonhomologous interchromosomal crossing over (causing reciprocal translocations) are much more likely to occur during meiosis when recombinational machinery is active.

I thank M. Uyenoyama and M. Kirkpatrick for critical review during various stages of this project. I also thank A. Kondrashov for bringing my attention to the mouse perigametic mutation literature.

LITERATURE CITED

Bell, G., 1994 The comparative biology of the alternation of generations, pp. 1–26 in *The Evolution of Haploid-Diploid Life Cycles*, edited by M. Kirkpatrick. American Mathematical Society, Providence, RI.

Bengtsson, B. O., 1992 Deleterious mutations and the origin of the meiotic ploidy cycle. Genetics **131:** 741–744.

Charlesworth, B., 1991 When to be diploid. Nature **351:** 273–274.

Crow, J. F., and M. Kimura, 1970 *An Introduction to Population Genetics Theory.* Harper & Row, New York.

Gantmacher, F. R., 1959 *The Theory of Matrices.* Chelsea, New York.

Goldstein, D. B., 1992 Heterozygote advantage and the evolution of a dominant diploid phase. Genetics **132:** 1195–1198.

Haldane, J. B. S., 1927 A mathematical theory of natural and artificial selection, V, selection and mutation. Proc. Camb. Philos. Soc. **23:** 838–844.

Hughes, J. S., and S. P. Otto, 1999 Ecology and the evolution of biphasic life cycles. Am. Nat. **154:** 306–320.

Jenkins, C. D., 1993 Selection and the evolution of genetic life cycles. Genetics **133:** 401–410.

Jenkins, C. D., and M. Kirkpatrick, 1994 Deleterious mutation and ecological selection in the evolution of life cycles, pp. 53–68 in *The Evolution of Haploid-Diploid Life Cycles*, edited by M. Kirkpatrick. American Mathematical Society, Providence, RI.

Jenkins, C. D., and M. Kirkpatrick, 1995 Deleterious mutation and the evolution of genetic life cycles. Evolution **49:** 512–520.

Kondrashov, A. S., and J. F. Crow, 1991 Haploidy or diploidy: which is better? Nature **351:** 314–317.

Lancaster, P., and M. Tismenetsky, 1985 *The Theory of Matrices.* Academic Press, Orlando, FL.

Michod, R. E., and T. Gayley, 1994 Genetic error, heterozygosity and the evolution of the sexual life cycle, pp. 97–119 in *The Evolution of Haploid-Diploid Life Cycles*, edited by M. Kirkpatrick. American Mathematical Society, Providence, RI.

Orr, H. A., and S. P. Otto, 1994 Does diploidy increase the rate of adaptation? Genetics **136:** 1475–1480.

Otto, S. P., 1994 The role of deleterious and beneficial mutations in the evolution of ploidy levels, pp. 69–96 in *The Evolution of Haploid-Diploid Life Cycles*, edited by M. Kirkpatrick. American Mathematical Society, Providence, RI.

Otto, S. P., and D. B. Goldstein, 1992 Recombination and the evolution of diploidy. Genetics **131:** 745–751.

Otto, S. P., and J. C. Marks, 1996 Mating systems and the evolution-

ary transition between haploidy and diploidy. Biol. J. Linn. Soc. **57:** 197–218.

Perrot, V., S. Richerd and M. Valero, 1991 Transition from haploidy to diploidy. Nature **351:** 315–317.

Russell, L. B., 1999 Significance of the perigametic interval as a major source of spontaneous mutations that result in mosaics. Environ. Mol. Mutagen. **34:** 16–23.

Russell, L. B., and W. L. Russell, 1996 Spontaneous mutations recovered as mosaics in the mouse specific-locus test. Proc. Natl. Acad. Sci. USA **93:** 13072–13077.

Uyenoyama, M. K., 1991 On the evolution of genetic incompatibility systems: VI. A three-locus modifier model for the origin of gametophytic self-incompatibility. Genetics **128:** 453–469.

Uyenoyama, M. K., and B. O. Bengtsson, 1989 On the origin of meiotic recombination: a genetic modifier model. Genetics **123:** 873–885.

Communicating editor: M. Slatkin

APPENDIX

The linearized recursion equations can be written in matrix form as $\mathbf{v}' = \mathbf{M}\mathbf{v}$, where $\mathbf{M}$ is the 2×2 transformation matrix, $\mathbf{v}$ is the column vector $\{x_3, x_4\}^T$, and $\mathbf{v}'$ is the same vector in the next generation. Denote $\mathbf{v}_n = \{p,D\}^T$ as a vector in the new basis, where p is equal to the frequency of the introduced modifier allele C_2 ($= x_3 + x_4$) and D is the standard measure of linkage disequilibrium ($= x_1x_4 - x_2x_3$). The recursion equations in the new basis can be written in matrix form as $\mathbf{v}_n' = \mathbf{N}\mathbf{v}_n$, where $\mathbf{N}$ is the 2×2 transformation matrix in the new basis. $\mathbf{N}$ is equal to $\mathbf{AMA}^{-1}$, where $\mathbf{A}$ is the 2×2 matrix satisfying $\mathbf{v}_n = \mathbf{A}\mathbf{v}$. Note that the relationship between the old and new basis holds only for the introduction of the new modifier such that terms that are squared in the frequency of the new modifer can be ignored. Changing the basis does not affect the eigenvalues of the transformation matrix (Lancaster and Tismenetsky 1985, chapter 4, p.152) and thus the characteristic equation evaluated at 1, $C(1)$, is the same for both transformation matrices, *i.e.*, $\mathrm{Det}(\mathbf{I} - \mathbf{M}) = \mathrm{Det}(\mathbf{I} - \mathbf{N})$.

Define a vector $\mathbf{v}_g = \{p^*, D^*\}$ in the new basis such that the vector $(\mathbf{I} - \mathbf{N})\mathbf{v}_g$ has its first entry equal to the characteristic equation evaluated at 1, and its second entry equal to zero. If $\lambda = 1$ were an eigenvalue of $\mathbf{N}$, then all of the entries of $(\mathbf{I} - \mathbf{N})\mathbf{v}_g$ would be zero, and $\mathbf{v}_g$ would be a right eigenvector of $\mathbf{N}$. If $\mathbf{z}$ is a row vector of ones, then $\mathbf{z}(\mathbf{v}_g - \mathbf{v}_g') = \mathbf{z}(\mathbf{I} - \mathbf{N})\mathbf{v}_g = \mathbf{z}\{C(1), 0\}^T = C(1)$ and thus the condition for invasion under weak selection, $C(1) < 0$, is equivalent to $\mathbf{z}(\mathbf{v}_g - \mathbf{v}_g') < 0$. Thus the behavior of the system over one generation, when started at $\mathbf{v}_g$, gives the asymptotic behavior of the system in the neighborhood of the C_1 fixation. D^* is thus the asymptotic disequilibrium that builds up between the viability and modifier loci upon introduction of a new modifier allele. The matrix equation $(\mathbf{I} - \mathbf{N})\mathbf{v}_g$ can be written as

$$\begin{bmatrix} 1 - n_{11} & -n_{12} \\ -n_{21} & 1 - n_{22} \end{bmatrix} \begin{bmatrix} p^* \\ D^* \end{bmatrix} = \begin{bmatrix} C(1) \\ 0 \end{bmatrix}. \tag{A1}$$

The matrix equation (A1) gives D^* equal to $p^* n_{21}/(1 - n_{22})$. The sign and magnitude of D^* upon the introduction of the C_2 allele can be found by substituting for n_{21} and n_{22}. I find that during invasion

$$D^* = -\frac{(d_{11} - d_{12})\mu(1 - h(1 - s))p^*}{(1 - d_{12}(1 - h))(r + (1 - r)s(1 - d_{12}(1 - hs)))}$$

$$\propto -(d_{11} - d_{12})\mu p^* \tag{A2}$$

and is thus negative for modifiers that increase haploidy ($d_{12} < d_{11}$). Negative D^* implies that the new modifier (C_2) becomes associated with the favored viability allele (A_0) after its introduction into the population.

The matrix equation (A1) also gives

$$(1 - n_{11})p^* - n_{12}D^* = C(1) \tag{A3}$$

and thus for stability

$$(1 - n_{11})p^* - n_{12}D^* > 0. \tag{A4}$$

This inequality involves a mean effect term (the p^* term) and an association term (the D^* term). Since $-n_{12}$ is positive (see Equation 3 in text), negative values of D^* favor invasion, and thus modifiers that increase haploidy are favored by genetic associations that build up between the modifier and viability loci [from (A2)]. Substituting values from $\mathbf{N}$ into (A4) gives the stability condition given in Equation 3 of the text.