

BRIEF COMMUNICATIONS

Evolution, 52(2), 1998, pp. 604–610

THE MAINTENANCE OF SEX BY PARASITISM AND MUTATION ACCUMULATION UNDER EPISTATIC FITNESS FUNCTIONS

R. STEPHEN HOWARD¹ AND CURTIS M. LIVELY²

¹*Department of Biology, Middle Tennessee State University, Box X087, Murfreesboro, Tennessee 37132*

E-mail: rshoward@frank.mtsu.edu

²*Department of Biology, Indiana University, Bloomington, Indiana 47405*

Abstract.—The mutation accumulation hypothesis predicts that sex functions to reduce the population mutational load, while the Red Queen hypothesis holds that sex is adaptive as a defense against coevolving pathogens. We used computer simulations to examine the combined and separate effects of selection against deleterious mutations and host-parasite coevolution on the spread of a clone into an outcrossing sexual population. The results suggest that the two processes operating simultaneously may select for sex independent of the exact shape of the function that maps mutation number onto host fitness.

Key words.—Host-parasite coevolution, Muller's ratchet, mutational deterministic hypothesis, Red Queen hypothesis, sexual reproduction, synergistic epistasis.

Received April 22, 1997. Accepted December 19, 1997.

Of the many hypotheses suggested for the evolutionary maintenance of sex (reviews in Bell 1982; Kondrashov 1993), two seem to dominate the present literature: the mutational accumulation hypothesis, and the Red Queen hypothesis. Under the mutational accumulation model, sexual populations gain an advantage over asexual populations due to the efficiency of recombination in reducing the population mutation load. Muller (1964) was the first to suggest that asexual populations might be undermined by mutation accumulation, reasoning that stochastic processes would lead to an inexorable decline in the fitness of clones. This version of the mutation accumulation hypothesis is widely known as "Muller's ratchet." More recent studies have extended Muller's basic idea to include cases in which mutation accumulation is decoupled from stochastic processes, such that an advantage to sex can accrue even in infinite populations. This extension represents the deterministic model of mutation accumulation put forward by Kondrashov (1982, 1988). For both versions of the mutation accumulation hypothesis, any advantage to sex depends strongly on the genomic mutation rate and the relationship between mutation number and individual fitness (the fitness function). Unfortunately, estimates of mutation rate vary widely (Mukai et al. 1972; Houle et al. 1992; review in Peck and Eyre-Walker 1997), and little is known about the general shape of the fitness function in natural populations.

Under the Red Queen hypothesis, cross fertilization is advantageous because it allows for the production of genetically variable progeny, some of which escape infection by parasites that are "tracking" common host genotypes (Clarke 1976; Glesener and Tilman 1978; Jaenike 1978; Bremermann 1980; Hamilton 1980; Lloyd 1980). The theory has gained empirical support from a wide variety of approaches (e.g., Schmitt and Antonovics 1986; Burt and Bell 1987; Lively 1987, 1992; Schrag et al. 1994; Jokela and Lively 1995; Gemmill et al. 1997), but seems to require that parasites have very severe effects on host fitness, which could restrict its generality (May and Anderson 1983). In addition, parasites may select

for clonal diversity instead of sex per se, which could lead to replacement of the ancestral sexual population by a set of genetically diverse clones (Lively and Howard 1994). Both of these difficulties can be overcome, however, by either rank-order truncation selection against the most infected individuals (Hamilton et al. 1990) or stochastic accumulation of mutations in clones that are driven through periodic bottlenecks by parasites (Howard and Lively 1994; Lively and Howard 1994).

The basic idea behind the second model is that there is an interaction between Muller's ratchet and Red Queen dynamics. If parasites prevent the fixation of clones in the short term, they will drive the clone through cycles (Red Queen dynamics), which accelerates the rate of mutation accumulation and reduces the time to extinction. In the original model, we found that moderate effects of parasites combined with mutation rates of 0.5 to 1.0 per genome per generation led to the evolutionary stability of sex (Howard and Lively 1994). We assumed, however, that mutations act independently (multiplicative selection). Here we relax this assumption and examine the interaction between mutation accumulation and antagonistic coevolution under the synergistic fitness functions required by the mutational deterministic hypothesis. This is an important step since synergism among mutations is expected to reduce the effectiveness of the ratchet (Charlesworth et al. 1993; Kondrashov 1994; but see Butcher 1995). We also employ a more conservative assumption regarding the mutational load of invading asexual mutants. The results suggest that mutation accumulation and antagonistic coevolution can combine to favor the maintenance of sexual reproduction and that the outcome is robust to the exact shape of the fitness function.

METHODS

We used individual-based computer simulation models to study host-parasite coevolution and mutation accumulation under four different fitness functions: multiplicative, exponential-quadratic, linear, and threshold (Fig. 1). The host-

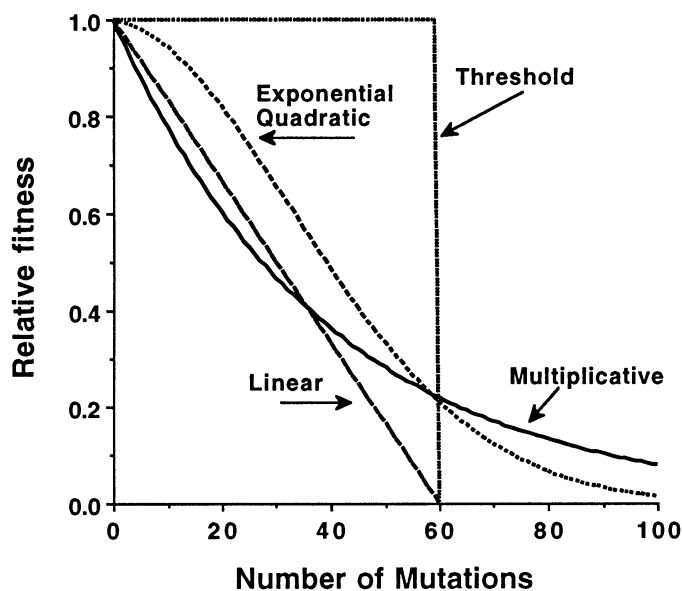


FIG. 1. Fitnesses of individuals with different numbers of mutations (n) under threshold ($w[n] = 1 - [n/k]^a$, for $a = 1000$), exponential-quadratic ($w[n] = \exp - [\alpha n + 0.5\beta n^2]$, for $\alpha = 0.002$, $\beta = 0.0008$), linear ($w[n] = 1 - [n/k]^a$, for $a = 1$), and multiplicative ($w[n] = [1 - s]^n$, for $s = 0.025$) fitness functions. For threshold and linear selection, individuals with more than $K = 60$ mutations are inviable. The values used for α and β in the exponential quadratic function are the same as those used by Charlesworth (1990).

parasite interaction was mediated by two unlinked, diallelic loci. Parasites were obligately sexual and underwent two generations for each host generation. In addition, all hosts possessed 500 unlinked loci at which harmful mutations accumulated randomly with a Poisson mean of U per genome per generation. Finally, to maintain variation in the parasite alleles involved in the host-parasite interaction (especially under high parasite virulence), mutation between allelic forms in the parasite population occurred with a probability of 0.03. This high rate of “mutation” is more meant to mimic the effects of migration among structured deems rather than mutation per se.

At the beginning of each simulation, we initialized a freely recombining sexual population at mutation-selection balance for a given mutation rate and fitness function. A single asexual host genotype was then introduced into the population. Following Charlesworth (1990), the number of mutations in this asexual individual was calculated as $i = \bar{n} - 2\sqrt{\bar{n}}$, where \bar{n} is equal to the equilibrium mean number of mutations in the sexual population. Since the variance is approximately equal to the mean, the variable i represents two standard deviations less than the mean for the sexual population, which is the minimum probable number of mutations (Charlesworth 1990). In our previous study, founders for asexual lineages were randomly sampled from the sexual population (Howard and Lively 1994); thus, the present assumption makes the persistence of sexuals more difficult and provides a more conservative test.

For each parasite generation, hosts were drawn individually and exposed to a randomly selected parasite with probability T . If the parasite matched the host exactly at both loci,

the host was marked as infected and the parasite entered into the pool of reproductives; parasites that failed to match hosts exactly at both loci died. Host reproduction was simulated by drawing individuals at random with replacement. If the selected individual was sexual, another individual was randomly selected for cross-fertilization. If uninfected, each individual produced a lifetime average of 10 embryos and achieved a total of 10 cross-fertilizations through male function. If infected, average fecundity was reduced by a factor of $1 - E$, where E is the loss of reproductive potential that results from infection. If the selected individual was asexual, 20 embryos were produced by uninfected females, and, on average, $20(1 - E)$ embryos by infected parents. In the absence of parasitism and selection against deleterious mutations, this scheme embodies the full twofold cost of sexual reproduction (Maynard Smith 1978). Embryos were then subjected to selection against deleterious mutations according to the relationship between the fitness function and the number of mutations in their genomes. Under the multiplicative fitness function, for example, the probability of survival is evaluated as $(1 - s)^n$, where s is the effect of a single deleterious mutation and n is the number of such mutations in the genome.

For each of the four fitness functions investigated (Fig. 1), we conducted five replicate runs of the simulation for each of 100 possible combinations of parasite effect (E) and probability of parasite transmission (T). At the end of each host generation, the number of sexual and asexual hosts was counted and population mutation loads were computed. These data were stored in a computer file for subsequent analysis. Individual runs were allowed to continue until either the sexual or asexual population went extinct or until both coexisted for at least 300 generations. Runs in which asexual lineages failed to persist for at least five generations were not included.

RESULTS

The general pattern that emerged from the simulations is that the evolutionary stability of sexual reproduction is strongly dependent on both mutation rate and intensity of parasitism, but seems relatively unaffected by the shape of the fitness function (Fig. 2). For the case of multiplicative selection, a genomic mutation rate (U) of 0.5 resulted in protection for sex over 30% of the total parameter space (Table 1). Here, parasite effects (E) of 0.6 generated an advantage to sex when the probability of parasite transmission (T) was at least 0.7. For the case of extreme virulence ($E = 1.0$), sex was protected for values of T larger than 0.3. Increasing the mutation rate, U , to 1.0 generated an advantage to sex in 36% of the grids, and for parasite effects as low as 0.5, provided the probability of transmission was at least 0.8. For highly virulent parasites ($E = 1.0$), an advantage to sex was generated when T was greater than 0.2. A further increase in the mutation rate to 1.5 resulted in protection for sex over 40% of the parameter space. Here, transmission probabilities of 0.7 generated an advantage to sex for virulence levels as low as $E = 0.5$. Finally, support for sex under extreme virulence ($E = 1.0$) was achieved for transmission probabilities greater than 0.2.

Under the exponential-quadratic fitness function, mutation

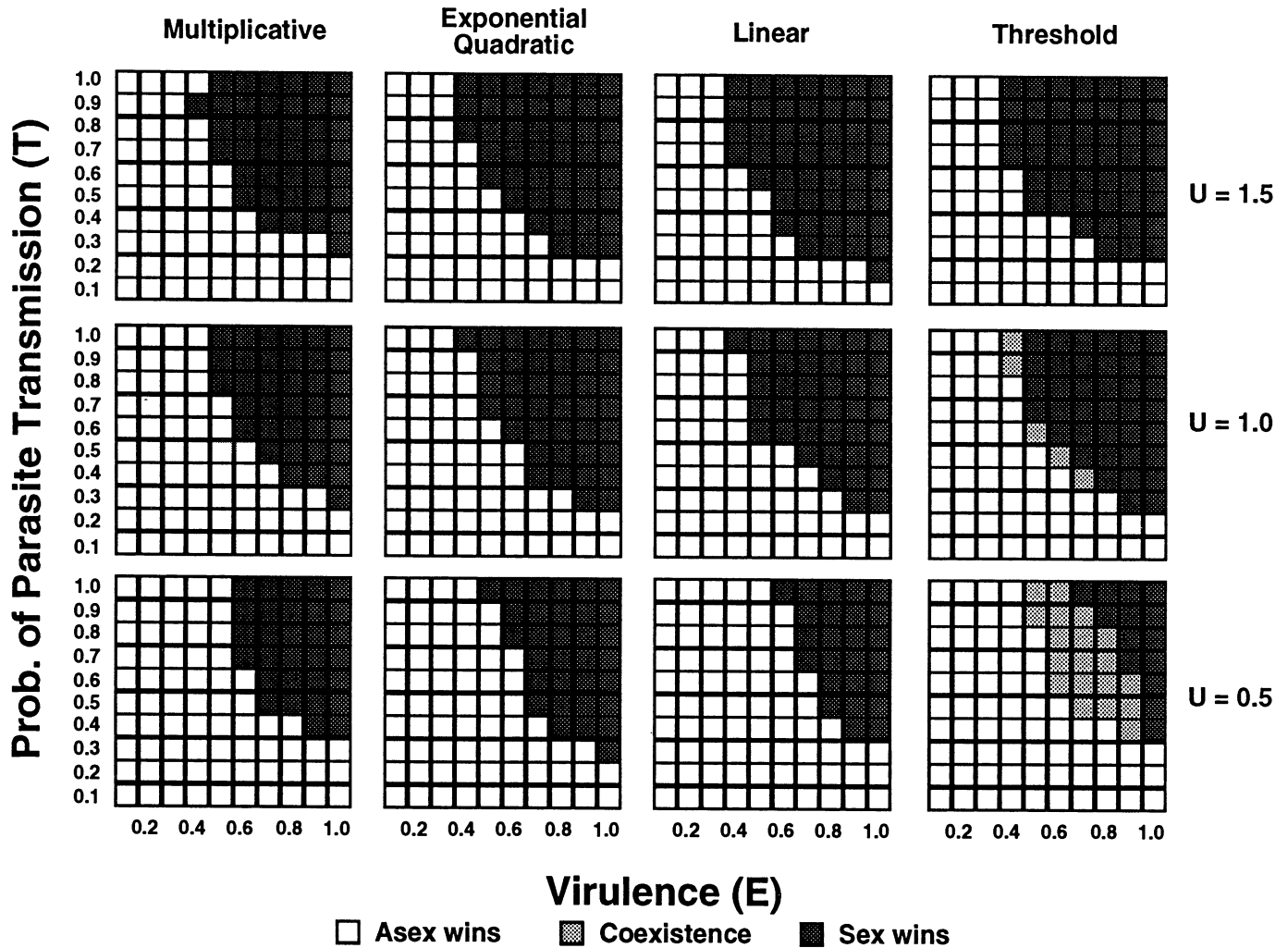


FIG. 2. Results from computer simulations in which sexual populations were challenged by asexual lineages in the presence of coevolving parasites and selection against harmful recurrent mutations. Each block in the grids represents the majority outcome from five replicate runs of the simulation for a single combination of parasite transmission probability (T) and effect of parasitism (E). The parameters for these runs included mutation rates of 0.5, 1.0, and 1.5 per genome per generation under threshold selection, linear, and exponential-quadratic fitness functions. The values used for these functions are the same as those given in Figure 1.

rates of 0.5 generated an advantage to sex over 32% of the parameter space (Table 1). Parasite effects (E) of 0.5 led to protection for sex when the probability of parasite transmission (T) was greater than 0.9. For the case of extreme virulence ($E = 1.0$), sex won out for values of T larger than 0.2. An increase in the magnitude of U to 1.0 generated an advantage to sex 40% of the time. Sex won outright for parasite effects as low as 0.4 when probabilities of parasite transmission were greater than 0.9. For highly virulent parasites ($E = 1.0$), sex was protected for values of T greater than 0.2. Mutation rates of 1.5 led to protection for sex over 45% of the parameter space. Parasite transmission probabilities of 0.8 were sufficient to generate an advantage to sex for parasite effects as low as $E = 0.4$, and extreme virulence ($E = 1.0$) favored sex when transmission probabilities were greater than 0.2.

For the case of linear selection for $U = 0.5$, sex won outright over 25% of the total parameter space (Table 1). Parasite effects (E) as low as 0.6 generated an advantage to

sex when coupled with transmission probabilities greater than 0.9. For the case of extreme virulence ($E = 1.0$), sex was protected for parasite transmission probabilities greater than 0.3. Increasing the mutation rate to 1.0 resulted in sex winning over 40% of the parameter space. As for exponential-quadratic selection, sex was favored for parasite effects of 0.4 when probabilities of parasite transmission were greater than 0.9. For high levels of parasite virulence ($E = 1.0$), an advantage to sex was generated provided parasite transmission probabilities exceeded 0.2. Increasing the mutation rate to 1.5 generated an advantage to sex over 49% of the parameter space. Parasite transmission probabilities of 0.7 resulted in protection for sex when parasite effects were as low as $E = 0.4$, and parasite effects of $E = 1.0$ favored sex when transmission probabilities were greater than 0.1.

Finally, for the case of threshold selection under mutation rates of 0.5, sex won outright 14% of the time (Table 1). Parasite effects (E) of 0.7 resulted in an advantage to sex when transmission probabilities were greater than 0.8. For

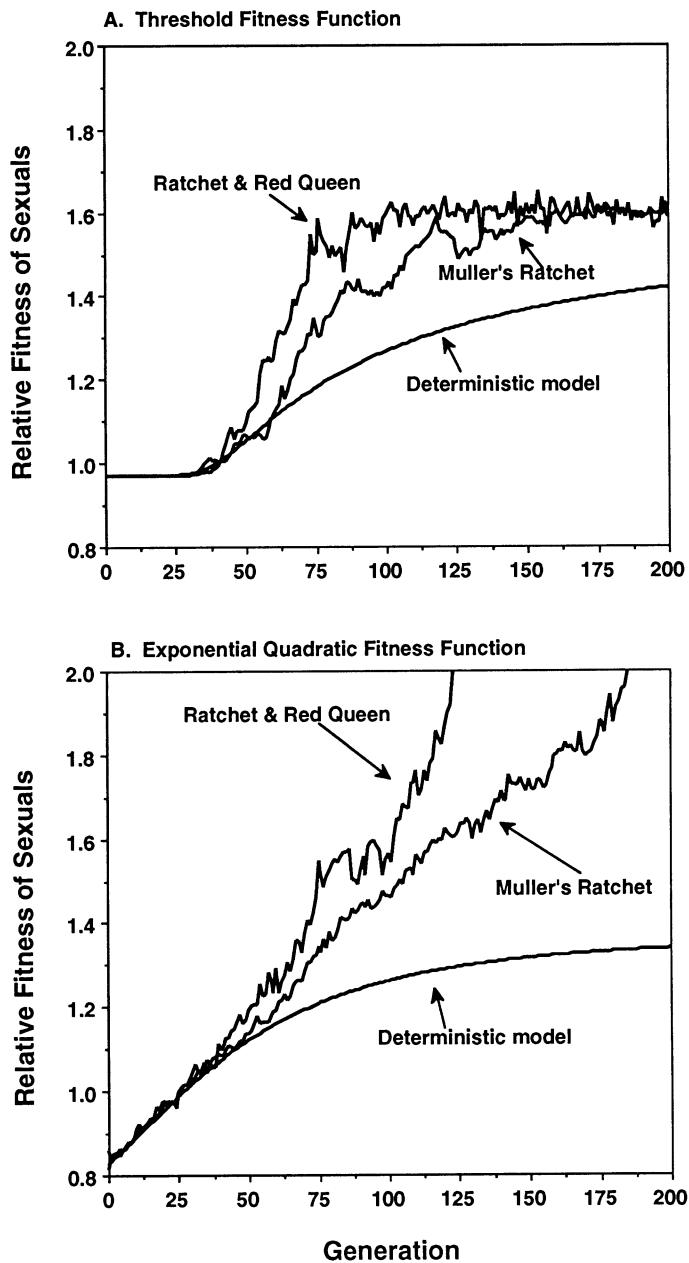


FIG. 3. Erosion of the twofold reproductive advantage of asexual lineages under mutational deterministic, Muller's ratchet, and the ratchet-plus-Red-Queen models of mutation accumulation. Parameters for these runs included a genomic mutation rate (U) of 0.5 under threshold (A) and exponential-quadratic (B) fitness functions. For the coevolutionary model, the effect of parasitism (E) was set at 0.6 and probability of parasite transmission was set at 0.9. At the start of each generation, the mutation load (L) of the sexual and asexual populations was evaluated, and the ratio $(1 - L_{\text{sex}})/(1 - L_{\text{asex}})$ computed as a measure of the advantage to sexual reproduction. For exponential-quadratic and threshold fitness functions, mutation accumulation acting alone is incapable of generating an advantage to sex under the deterministic model. The same result holds for the mutational stochastic model (Muller's ratchet), but the rate at which fitness declines in the asexual population is accelerated compared to the deterministic model; we attribute this to the combined effects of stochastic loading and stochastic elimination components of Muller's ratchet. The addition of parasites to the model results in protection for sex under the exponential quadratic fitness function, but not under threshold selection. Under threshold selec-

TABLE 1. Advantage of sex under multiplicative, exponential-quadratic, linear, and threshold fitness functions. Variables include: U = mutation rate/genome/generation; n = approximate equilibrium number of mutations for a sexual population; i = minimum probable number of mutations in founders of asexual lineages; and percent of parameter space occupied by sexuals, asexuals, and populations consisting of both types (coexistence).

U	n	i	% sex	% asex	% coexistence
Multiplicative selection					
0.5	20	11	30%	70%	0%
1.0	40	27	36%	64%	0%
1.5	60	45	40%	60%	0%
Exponential-quadratic selection					
0.5	24	14	32%	68%	0%
1.0	35	23	40%	60%	0%
1.5	43	30	45%	55%	0%
Linear selection					
0.5	23	13	25%	75%	0%
1.0	30	19	40%	60%	0%
1.5	36	23	49%	51%	0%
Threshold selection					
0.5	48	34	14%	67%	19%
1.0	50	38	38%	57%	5%
1.5	51	39	47%	53%	0%

highly virulent parasites ($E = 1.0$), an advantage to sex was generated for parasite transmission probabilities greater than 0.3. Interestingly, long-term coexistence (> 300 generations) occurred over a substantial (19%) region of parameter space. An increase in U to 1.0 led to protection for sex over 38% of the parameter space, and for parasite effects of 0.5 when probabilities of transmission exceeded 0.6. For extreme parasite virulence ($E = 1.0$), sex won outright provided that parasite transmission probabilities exceeded values of 0.2. A region of coexistence remained under $U = 1.0$, covering 5% of the parameter space. A mutation rate of 1.5 generated a decisive advantage to sex over 47% of the parameter space, and the region of coexistence was eliminated. Protection for sex occurred for parasite transmission probabilities of 0.7 coupled with parasite effects of $E = 0.4$. Highly virulent parasites ($E = 1.0$) generated protection for sex when transmission probabilities were greater than 0.2.

In addition to testing for an advantage to sex under different combinations of parasite intensity and fitness functions, we examined the rate of fitness decline due to mutation accumulation in asexual lineages under threshold and exponential-quadratic fitness functions (Fig. 3). In both cases, relaxing the assumption of infinite population size leads to an accelerated rate of fitness decline in parasite-free populations. Addition of parasites to the model resulted in an even faster rate of fitness decline. This apparently results from an increased efficiency of the ratchet as clonal host populations are driven through periodic bottlenecks. A major difference

←

tion, Muller's ratchet is halted as the asexual population approaches the point where all individuals have exactly $K - 1$ mutations, and the terminal mutation load equilibrates to that obtained under the deterministic model.

between the exponential-quadratic and threshold fitness models is that, under most of the parameter space investigated, threshold selection brings the ratchet to a halt as the population approaches $K - 1$ mutations. In such situations, the terminal mutation load of asexual populations is equivalent to that of infinite populations, and the elimination of clones by Kondrashov's mechanism requires mutation rates greater than 1.0 per genome per generation (Howard 1994).

DISCUSSION

Muller's ratchet operates on asexual populations when the class of individuals containing the fewest mutations is lost by drift, which can happen in two ways. One is through chance loss of all individuals in the class having the fewest number of mutations. Since this class is unlikely to be recreated by back mutation, the "ratchet" clicks one notch. The rate of clicking depends on the number of individuals in the least-loaded class, which depends in part on population size. We refer to the chance loss of all individuals in the least-loaded class as "stochastic elimination." The second way the least-loaded class can be lost is through mutation pressure; if all progeny of the least-loaded individuals receive at least one additional mutation, the ratchet will click one notch. For example, if there are six offspring produced by the individuals in the least-loaded class, the probability that they all get at least a single mutation is $(1 - e^{-U})^6$, which is 0.064 for $U = 1.0$. We refer to this mechanism (which depends on mutation rate and population size) as "stochastic loading." Clicking of the ratchet will most often result from some combination of the two mechanisms. For example, the ratchet will click one notch when half the individuals in the least-loaded class fail to breed (stochastic elimination) and the other half produce progeny that gain at least one additional mutation (stochastic loading). Our results suggest that, independent of the shape of the fitness function, both aspects contribute to mutational gains in a clonal lineage during its early spread.

Kondrashov's (1982, 1988) mechanism can be envisioned as follows. When the function that maps mutation number onto fitness is strictly truncated, a large clonal population will come into mutation-selection balance at exactly $K - 1$ mutations, where K is the threshold number of mutations. If the probability of an offspring receiving a new mutation is Poisson distributed with a mean of one, then about two-thirds ($1 - e^{-U} = 0.632$) of the clonal progeny will exceed the threshold and die. This can generate a decisive advantage to sex because recombination maintains a higher variance in mutation number and enhances the efficiency of selection against deleterious mutations. For mutation rates of greater than one, a decrease in the population mutation load of a sexual population can offset the inherent twofold reproductive advantage of invading clones (Kondrashov 1988). Muller's ratchet will not operate under Kondrashov's assumption of infinite population size, and its efficiency will be severely retarded even in small populations when selection against deleterious mutations act synergistically. In particular, the action of the ratchet should cease once all members of a clonal population contain exactly $K - 1$ mutations (Fig. 3). The reason is that the least-loaded class now consists of the entire

set of clonal individuals; also in all but the smallest populations, this class is unlikely to be lost by either stochastic loading or stochastic elimination. Hence, under threshold selection, large and small asexual populations should equilibrate at the same terminal mutation load.

The ratchet, however, will operate up until the finite clonal population reaches its terminal mutation load; the time it takes to reach this point is therefore crucial. Consider a clone, founded from a single individual, that was randomly sampled from the sexual population. It is extremely unlikely that this clone will be at mutation-selection balance ($K - 1$ mutations). For example, given a mutation rate of one, 92% of the members of a sexual population will contain fewer than the threshold number of mutations. Hence, 92% of the time, a clone derived from this sexual population will initially have a relative fitness of one and a full twofold advantage of not producing males. If the clone fixes before it reaches mutation-selection balance, then there are no sexual individuals left to "save." Hence it is important to relax Kondrashov's (1982) original assumption that the asexual population begins in mutation-selection balance and examine the fates of asexual lineages initialized with fewer than the equilibrium number of mutations (Charlesworth 1990).

Following Charlesworth (1990), we initiated clones at two standard deviations less than the mean number of mutations in the sexual population. We then followed the fate of these rare clones under different fitness functions where the effects of parasites and the probability of encounter with parasites were variables. When parasites had low rates of transmission or minor effects on fitness, we found that the asexual population replaced a sexual population of 1000 individuals under all types of fitness functions, even for mutation rates as high as 1.5 per genome per generation (for a similar result using the exponential quadratic function see Charlesworth 1990). As parasite virulence and transmission were increased, we found that sex became increasingly favored by selection.

For example, under the multiplicative fitness function, sex is increasingly likely to be favored as parasite virulence and transmission rates increase and as the mutation rate increases (Fig. 2, Table 1). Higher virulence by parasites drives clones through steeper cycles, which aids both aspects of the ratchet, while higher mutation rates fuel the stochastic-loading aspect of the ratchet. Nonetheless, the conditions for sex (in terms of parameter space) were reduced here under the more challenging assumption that clones are initialized at two standard deviations lower than the mean number of mutations for the sexual population (cf. Fig. 2 to fig. 2d in Howard and Lively 1994). The most surprising aspect of the present results is that they seem to be little affected by the shape of the fitness function. Increasing the level of synergism among mutations did not greatly alter the outcome of selection (Fig. 2), at least for mutation rates of one and greater. In general, higher parasite virulence and transmission rates led to selection for sex, and this effect was enhanced at higher mutation rates.

The result obtained for truncated fitness functions deserves closer scrutiny, however, because the ratchet is unlikely to work at mutation-selection balance under our assumption that all mutations have equal effects. But, as noted above, clones are unlikely to begin in mutation-selection balance. The present results suggest that parasites will exacerbate the effects

of the ratchet as the clone spreads from its initially rare state until each individual in the clonal population contains exactly $K - 1$ mutations (Fig. 3). Once the clone acquires its terminal mutation load, it is driven extinct by Kondrashov's mechanism without further effects of parasites, provided mutation rates exceed one per genome per generation. An infrequent but interesting exception to this pattern occurs over a small region of parameter space in which sexual and asexual populations coexist for more than 300 generations (Fig. 3). Here, for a mutation rate of one, the clone is able to persist with a terminal mutation load that completely eliminates its twofold reproductive advantage. The advantage to a sex, however, is relatively small ($\bar{W}_{\text{sex}} / \bar{W}_{\text{asex}} = 2.5$), and can be offset as parasites evolve away from rare clones to attack common sexual genotypes. In such situations, parasites can act to prevent Kondrashov's mechanism from eliminating the clone by periodically depressing the fitness of the sexual population. In regions of the parameter space where sex wins outright, parasites prevent the fixation of clones in the short term and then operate together with the ratchet to drive the clone to mutation-selection balance before it eliminates the parent sexual population. Hence, under these conditions, three separate mechanisms are acting to prevent the elimination of sexuals: the ratchet and the Red Queen drive the clone to mutation-selection balance at $K - 1$ mutations, whereupon it is eliminated by the effects of mutation accumulation.

For mutation rates of less than one, Kondrashov's mechanism is not sufficient to eliminate clones, but is aided by the addition of parasites to the model. In some situations, the coevolutionary dynamics that arise from parasitism can apparently restore the ability of Muller's ratchet to operate in populations at mutation-selection balance under threshold selection. This occurs when highly transmissible, highly virulent parasites act to drive asexual populations through bottlenecks of extremely low population size. Here, all members of the least-loaded class contain $K - 1$ mutations, and a single click of the ratchet dooms the asexual population to extinction. In cases where parasitism is less intense (lower E and T), the demographic cycles are less steep and the action of the ratchet is severely restricted if not eliminated altogether. In this situation, Kondrashov's mechanism acting alone is incapable of eliminating the clone. Instead, parasites can select for clonal diversity, which should eventually lead to the elimination of the ancestral sexual population (Lively and Howard 1994). When the synergism between mutations is reduced, Kondrashov's mechanism becomes less important in actually eliminating clones and Muller's ratchet becomes more important.

In summary, our results suggest that moderate to severe effects of parasites can act in combination with mutation accumulation to provide a short-term advantage to sex. This basic result is robust to the shape of the function that maps the number of mutations onto fitness. In all cases, parasites aid the accumulation of mutations during the early spread of the clone by driving common genotypes through bottlenecks. Under multiplicative, exponential-quadratic, and linear fitness functions, the ratchet and the Red Queen will then also eliminate the clone in less than 300 generations. Under threshold selection, the clone is eliminated by Kondrashov's mechanism after it comes into mutation-selection balance,

provided mutation rates are on the order of one per genome per generation. These results suggest that models of host-parasite coevolution and mutation accumulation are not mutually exclusive.

ACKNOWLEDGMENTS

We thank L. Delph, P. Mathis, S. Weeks, M. Wells, and S. West for comments on the manuscript. This study was supported by a faculty summer research grant from Middle Tennessee State University to RSH and by a National Science Foundation grant (DEB-9629489) to CML. Additional grant support from the Underwood Fund of the BBSRC and the Marsden Fund of New Zealand are gratefully acknowledged (CML).

LITERATURE CITED

- BELL, G. 1982. The masterpiece of nature: the evolution and genetics of sexuality. Univ. of California Press, Berkeley.
- BREMERMAN, H. J. 1980. Sex and polymorphism as strategies in host-pathogen interactions. *J. Theor. Biol.* 87:641-702.
- BURT, A., AND G. BELL. 1987. Mammalian chiasma frequencies as a test of the two theories of recombination. *Nature* 326:803-805.
- BUTCHER, D. 1995. Muller's ratchet, epistasis, and mutation effects. *Genetics* 141:431-437.
- CHARLESWORTH, B. 1990. Mutation-selection balance and the evolutionary advantage of sex and recombination. *Genet. Res.* 55:199-221.
- CHARLESWORTH, D., M. T. MORGAN, AND B. CHARLESWORTH. 1993. Mutation accumulation in finite outbreeding and inbreeding populations. *Genet. Res.* 61:39-56.
- CLARKE, B. 1976. The ecological genetics of host-parasite relationships. Pp. 87-103 in A. E. R. Taylor and R. Muller, eds. Genetic aspects of host-parasite relationships. Vol. 14. Blackwell Scientific, Oxford.
- GEMMILL, A. W., M. E. VINEY, AND A. F. READ. 1997. Host immune status determines sexuality in a parasitic nematode. *Evolution* 51:393-401.
- GLESNER, R. R., AND D. TILMAN. 1978. Sexuality and the components of environmental uncertainty: clues from geographic parthenogenesis in terrestrial animals. *Am. Nat.* 112:659-673.
- HAMILTON, W. D. 1980. Sex versus non-sex versus parasite. *Oikos* 35:282-290.
- HAMILTON, W. D., R. AXELROD, AND R. TANESE. 1990. Sexual reproduction as an adaptation to resist parasites (a review). *Proc. Nat. Acad. Sci.* 87:3566-3573.
- HOULE, D., D. K. HOFFMASTER, S. ASSIMACOPOULOS, AND B. CHARLESWORTH. 1992. The genomic mutation rate for fitness in *Drosophila*. *Nature* 359:58-60.
- HOWARD, R. S. 1994. Selection against deleterious mutations and the maintenance of biparental sex. *Theor. Popul. Biol.* 45:313-323.
- HOWARD, R. S., AND C. M. LIVELY. 1994. Parasitism, mutation accumulation, and the maintenance of sex. *Nature* 367:554-557.
- JAENIKE, J. 1978. An hypothesis to account for the maintenance of sex within populations. *Evol. Theory* 3:191-194.
- JOKELA, J., AND C. M. LIVELY. 1995. Parasites, sex, and early reproduction in a mixed population of freshwater snails. *Evolution* 49:1268-1271.
- KONDRASHOV, A. S. 1982. Selection against harmful mutations in large sexual and asexual populations. *Genet. Res.* 40:325-332.
- . 1988. Deleterious mutations and the evolution of sexual reproduction. *Nature* 336:435-440.
- . 1993. Classification of hypotheses on the advantage of amphimixis. *J. Hered.* 84:372-387.
- . 1994. Muller's ratchet under epistatic selection. *Genetics* 136:1469-1473.

- LIVELY, C. M. 1987. Evidence from a New Zealand snail for the maintenance of sex by parasitism. *Nature* 328:519–521.
- . 1992. Parthenogenesis in a freshwater snail: reproductive assurance versus parasitic release. *Evolution* 46:907–913.
- LIVELY, C. M., AND R. S. HOWARD. 1994. Selection by parasites for clonal diversity and mixed mating. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 346:271–281.
- LIVELY, C. M., C. CRADDOCK, AND R. C. VRIJENHOEK. 1990. Red Queen hypothesis supported by parasitism in sexual and clonal fish. *Nature* 344:864–866.
- LOYD, D. G. 1980. Benefits and handicaps of sexual reproduction. *Evol. Biol.* 13:69–111.
- MAY, R. M., AND R. ANDERSON. 1983. Epidemiology and genetics in the coevolution of parasites and hosts. *Proc. R. Soc. Lond. B Biol. Sci.* 219:281–313.
- MAYNARD SMITH, J. 1978. *The evolution of sex*. Cambridge Univ. Press, Cambridge.
- MUKAI, T., S. T. CHIGUSA, L. E. METTLER, AND J. F. CROW. 1972. Mutation rate and dominance of genes affecting viability in *Drosophila melanogaster*. *Genetics* 72:335–355.
- MULLER, H. J. 1964. The relation of recombination to mutational advance. *Mutat. Res.* 1:2–9.
- PECK, J. R., AND A. EYRE-WALKER. 1997. The muddle about mutations. *Nature* 387:135–136.
- SCHMITT, J., AND J. ANTONOVICS. 1986. Experimental studies on the evolutionary significance of sexual reproduction. IV. Effect of neighbor relatedness and aphid infestation on seedling performance. *Evolution* 40:830–836.
- SCHRAG, S. J., A. O. MOOERS, G. T. NDIFON, AND F. A. READ. 1994. Ecological correlates of male outcrossing ability in a simultaneous hermaphrodite snail. *Am. Nat.* 143:636–655.

Corresponding Editor: L. Nunney

Evolution, 52(2), 1998, pp. 610–613

ADAPTATION TO COMPETITION BY NEW MUTATION IN CLONES OF *ALEXANDRIUM MINUTUM*

EDUARDO COSTAS,¹ BLANCA NIETO,¹ VICTORIA LOPEZ-RODAS,¹ CONCHITA SALGADO,¹ AND MIGUEL TORO²

¹Departamento de Producción Animal, Facultad de Veterinaria, Universidad Complutense, 28040, Madrid, Spain

²Area de Mejora Genética, CIT-INIA, Carretera La Coruña km. 7, 28040, Madrid, Spain

E-mail: toro@inia.es

Abstract.—We describe two competition experiments between clones of the dinoflagellate *Alexandrium minutum*. In the first experiment, two clones originating from a single haploid cell competed until one of the clones was almost driven to extinction. In the second experiment, these two clones were allowed to compete with the original populations, which were previously kept as cysts. The results indicate that an improvement of the competitive ability in both clones has occurred during the history of competition. This adaptation to competition must be attributed to selection acting on the new genetic variation that has arisen by mutation.

Key words.—*Alexandrium minutum*, competition, spontaneous mutation.

Received March 26, 1997. Accepted January 9, 1998.

The understanding of changes that occur when two species or two clones compete is still an unsolved problem in ecological genetics. In classical population biology several questions on this topic have been addressed both from theoretical and experimental approaches. The first is related to the productivity of mixed genotypes, which can be greater than the average production of their pure components in monoculture as a consequence of complementary resource utilization or of facilitation between genotypes. This phenomenon has importance in agricultural practice and is also relevant to the maintenance of polymorphism and sexual reproduction (Pérez-Tomé and Toro 1982; Bell 1991).

The second refers to the result of competitive interaction. The classical principle of competitive exclusion postulates that if two species compete for the same limited resource, they cannot coexist. However, this has been rejected as a general principle (Ayala 1971). In a more general setting, there have been many laboratory experiments addressing whether a history of previous coexistence can alter the competitive outcome. If additive variance exists for competitive ability, natural selection can increase its value during the first phase of coexistence and, therefore, modify the result of an

a posteriori competitive interaction (Dawson 1983; Goodnight and Craig 1996).

A third issue is related to the Red Queen hypothesis (van Valen 1973). Under this hypothesis, selection would act simultaneously in both competing species, resulting in a matched increase in their competitive ability; therefore, the result of competition would remain unchanged.

Dinoflagellate species are particularly suitable for evolution experiments (Brand 1981). Their rapid growth rates allow the study of changes brought about by selection or adaptation during many generations in only a few months. Because they reproduce asexually, replicated, genetically identical populations (consisting of a single genotype) can be obtained from an isolated cell. Therefore, evolutionary change in these populations depends entirely on new mutations. Furthermore, dinoflagellates produce temporary cysts (dormancy stages without cell division), which can be stored at low temperature over several months and then revived (Pfiester and Anderson 1987). Thus, the ancestral (obtained from revived cysts) and derived genotypes (from exponentially growing cultures) can be compared directly. In the present experiment, the species studied was *Alexandrium minu-*