

Cyclical dynamics under constant selection against mutations in haploid and diploid populations with facultative selfing

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Summary

We have found that constant selection against mutations can cause cyclical dynamics in a population with facultative selfing. When this happens, the distribution of the number of deleterious mutations per genotype fluctuates with the period $\sim 1/s_{He}$ generations, where s_{He} is the coefficient of selection against a heterozygous mutation. The amplitude of oscillations of the mean population fitness often exceeds an order of magnitude. Cyclical dynamics can occur under intermediate selfing rates if selection against heterozygous mutations is weak and selection against homozygous mutations is much stronger. Cycling is possible without epistasis or with diminishing-returns epistasis, but not with synergistic epistasis. Under multiplicative selection, cycling might happen if the haploid mutation rate exceeds 1.9 in the case of selfing of haploids, and if this diploid mutation rate exceeds 4.5 in the case of selfing of diploids. We propose a heuristic explanation for cycling under facultative selfing and discuss its possible relevance.

1. Introduction

Cyclical dynamics of the population size are ubiquitous in ecology. By contrast, the genetic composition of a population usually approaches equilibrium, as long as selection remains invariant. So far, only a few exceptions to this rule have been found. Hastings (1981) and Akin (1982) have shown that stable cycling can happen under strong, highly epistatic viability selection acting on two linked loci, as long as the parameters of the model (coefficients of selection and the recombination rate) are within an extremely narrow range. Doebeli & de Jong (1998) investigated cycles of length 2 that occur under fertility selection. Gavrillets (1998) has found cycling caused by strong viability selection with both maternal and paternal effects. Thus, genetic cycling under constant selection always requires rather restrictive conditions. Here, we report another case of such cycling that occurs when selection in the diploid phase removes deleterious mutations from a population with partial selfing in either haploid or diploid phase.

2. Models

We use a standard deterministic numerical model of mutation–selection balance (Kimura & Maruyama, 1966). In the case of haploid selfing (possible, for example, in ferns and fungi, in which the haploid phase is represented by independent organisms), the life cycle is mutation–mating–syngamy–selection–meiosis. In the case of diploid selfing, the life cycle is mutation–mating–meiosis–syngamy–selection (Fig. 1). In the case of haploid selfing, the population at the beginning of the haploid phase is described by $p(i)$, the frequency of individuals carrying i mutations. After mutation with haploid genomic rate U_{Hapl} , this frequency becomes (Kimura & Maruyama, 1966, eqn 3.1)

$$p'(i) = \sum_{j=0}^i p(j) e^{-U_{Hapl}} \frac{U_{Hapl}^{i-j}}{(i-j)!}. \quad (1)$$

If the fraction C of zygotes is formed after haploid selfing (i.e. by syngamy of two identical gametes), the population of newborn diploids consists of two cohorts. Fraction C , produced by selfing, carry no heterozygous mutations and i homozygous mutations with probability $p_s(i) = p'(i)$. The rest, produced by outcrossing, carry no homozygous mutations (assuming

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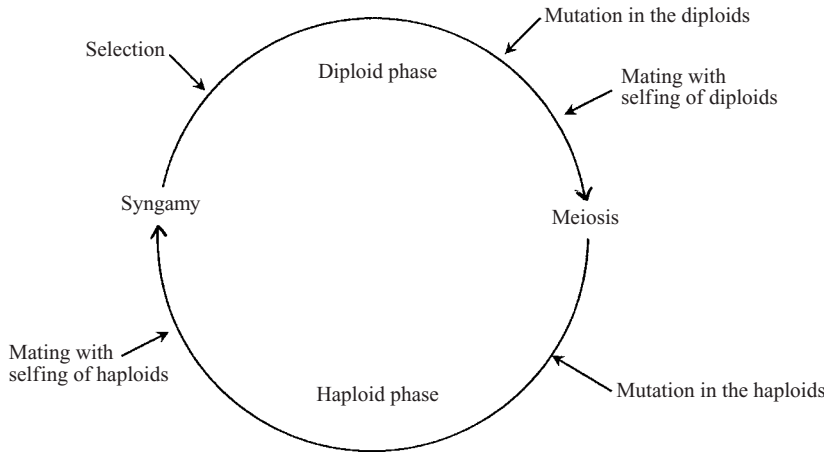


Fig. 1. Life cycle with haploid and diploid selfing.

that mutant alleles are rare) and i heterozygous mutations with probability

$$p_o(i) = \sum_{j=0}^i p'(j)p'(i-j). \tag{2}$$

Selection leads to the following transformations of genotype frequencies within the selfed and outcrossed cohorts,

$$p'_s(i) = p_s(i)w_s(i)/W_s; W_s = \sum_j p_s(j)w_s(j); \tag{3}$$

$$p'_o(i) = p_o(i)w_o(i)/W_o; W_o = \sum_j p_o(j)w_o(j); \tag{4}$$

where $w_s(i)$ and $w_o(i)$ are the fitnesses of individuals with i homozygous or heterozygous mutations, respectively, and W_s and W_o are the mean fitnesses of the selfed and outcrossed cohorts, respectively. Selfed and outcrossed cohorts compose fractions $CW_s/[CW_s + (1-C)W_o]$ and $(1-C)W_o/[CW_s + (1-C)W_o]$ of the population after selection, respectively.

After meiosis, a diploid organism produced by haploid selfing and carrying i mutations produces only meiospores with exactly i mutations, whereas diploid organisms produced by outcrossing transmit to a meiospore each of its mutations with probability 0.5, independent of other mutations. Thus, at the beginning of the next haploid phase, the distribution of the number of mutations in the newborn haploids is

$$P(i) = \left[CW_s p'_s(i) + (1-C)W_o \sum_j \sum_k p'_o(j)p'_o(k) \right] [Mei(j+k, i)] / [CW_s + (1-C)W_o]; \tag{5}$$

$$Mei(j+k, i) = \binom{j+k}{i} \left(\frac{1}{2}\right)^{j+k}.$$

Eqns 1–5 completely describe the dynamics under haploid selfing in the course of one generation.

The Kimura–Maruyama model was applied to selfing of diploids by Kondrashov (1985). Before

mutation, the population of diploids is described by $p(i, j)$, the frequency of individuals carrying i heterozygous and j homozygous mutations. Mutation with diploid genomic rate U_{Dipl} increments only the number of heterozygous mutations

$$p'(i, j) = \sum_{n=0}^i p(n, j) e^{-U_{Dipl}} \frac{U_{Dipl}^{i-n}}{(i-n)!}. \tag{6}$$

If a fraction C of offspring is produced by selfing after a succession of mutation, meiosis and syngamy, the frequency of newborn diploids in the population becomes,

$$p''(i, j) = Cp_s(i, j) + (1-C)p_o(i, j), \tag{7}$$

where $p_s(i, j)$ and $p_o(i, j)$ are the frequencies of selfed and outcrossed offspring with i heterozygous and j homozygous mutations, respectively.

Obviously,

$$p_s(i, j) = \sum_k \sum_l Self_{ij}(k, l) p'(k, l), \tag{8}$$

where

$$Self_{ij}(k, l) = \binom{k}{i} \binom{k-i}{j-l} \left(\frac{1}{2}\right)^{2k-i}, \tag{9}$$

is the probability of producing an offspring with i heterozygous and j homozygous mutations from self-fertilization of an individual with k heterozygous and l homozygous mutations.

Similarly,

$$p_o(i, j) = \sum_k \sum_l \sum_m \sum_n Out_{i,j}(k, l, m, n) p'(k, l) p'(m, n), \tag{10}$$

where

$$Out_{i,j,o}(k, l, m, n) = \binom{k+m}{i-l-n}, \tag{11}$$

is the probability of producing an offspring with i heterozygous and no homozygous mutations from

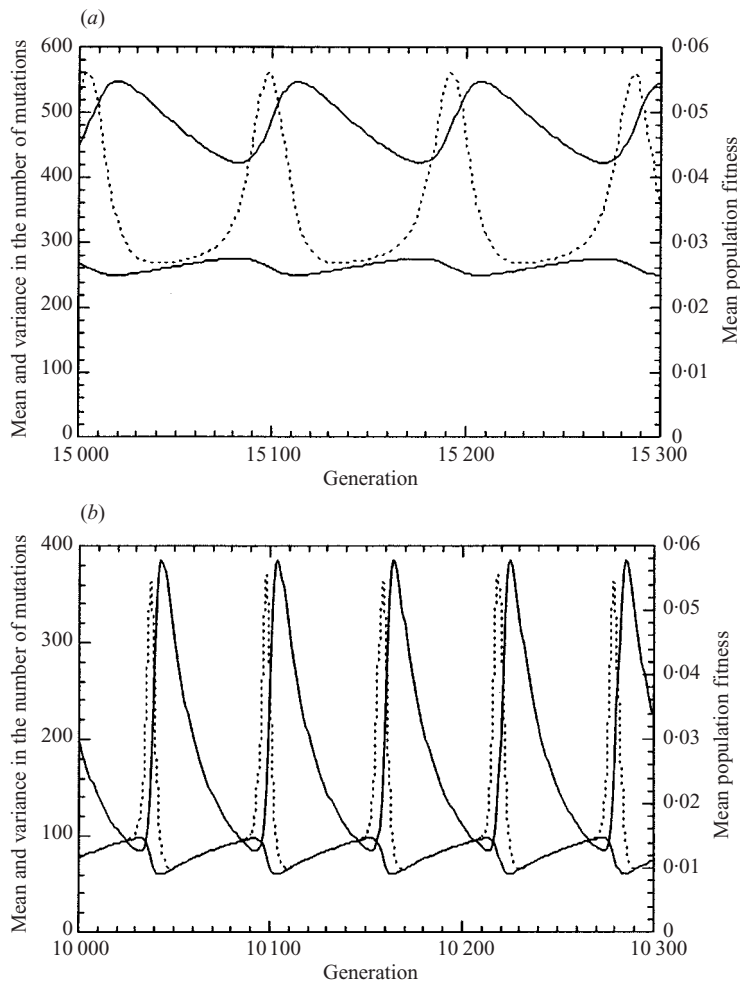


Fig. 2. Cyclical dynamics of the mean population fitness (thick line) and the mean (thin line) and variance (dashed line) of the number of mutations per individual under haploid selfing: (a) $U_{Hapl}=1.9$, $C=0.32$, $s_{He}=0.005$, and $s_{Ho}=0.9$; (b) $U_{Hapl}=2.5$, $C=0.30$; $s_{He}=0.02$, and $s_{Ho}=0.5$.

parents with k heterozygous and l homozygous, and with m heterozygous and n homozygous mutations; of course, $Out_{i,j \neq 0} = 0$ as long as individual mutations are rare. Finally, after selection,

$$P(i, j) = p''(i, j)w(i, j) / W; W = \sum_i \sum_j p''(i, j)w(i, j), \tag{12}$$

where $w(i, j)$ is the fitness of individuals carrying i heterozygous and j homozygous mutations, and W is the mean population fitness.

The models have been implemented as Metrowerks C programs, which can be downloaded at <ftp://ftp.ncbi.nih.gov/pub/kondrashov/selfing>.

3. Results

Figures 2 and 3 provide examples of indefinite cycling, revealed by oscillations with nearly constant amplitude after 6000 generations from the beginning of a run, under haploid selfing with multiplicative selection; that is, $w_o(i) = (1 - s_{He})^i$ and $w_s(j) = (1 - s_{Ho})^j$. In this

case, the model contains four parameters: U_{Hapl} , C , s_{Ho} and s_{He} . A survey of the parametric space revealed that cycling is favoured by high U_{Hapl} , low s_{He} and intermediate C . Cycling does not depend strongly on s_{Ho} as long as $s_{Ho} \gg s_{He}$. When U_{Hapl} declines and/or s_{He} increases, cycling requires C to fit into progressively narrower ranges (Table 1). The minimal U_{Hapl} under which cycling definitely happens is 1.9 (Fig. 3). Finding the exact critical value of U_{Hapl} is difficult because, when an initially low U_{Hapl} increases, cycling apparently developed through Andronov–Hopf bifurcation (Bazykin, 1998). When a parameter changes gradually, an initially small stable limit cycle becomes an attractor instead of focus equilibrium. Thus, stable oscillations replace damped oscillations, and long runs are required to determine when the oscillations become permanent. Convergence to equilibrium becomes oscillating starting from $U_{Hapl} > 1.5$. Cycling, if present, always occurs regardless of the initial state of the population.

Cycling with diploid selfing under multiplicative selection $w(i, j) = (1 - S_{He})^i (1 - S_{Ho})^j$ occurs under

Table 1. Dependence of the possibility of cycling under haploid selfing on U_{Hapl} , C and s_{He} with $s_{Ho}=0.9$ ('+' : cycling; '-' : no cycling)

		C							
		0.26	0.28	0.30	0.32	0.34	0.36	0.38	0.40
$U_{Hapl}=2.00$	$s_{He}=0.005$	+	+	+	+	+	+	+	+
	$s_{He}=0.01$	-	+	+	+	+	+	+	-
$U_{Hapl}=1.95$	$s_{He}=0.005$	-	+	+	+	+	+	+	+
	$s_{He}=0.01$	-	-	-	+	-	-	-	-
$U_{Hapl}=1.90$	$s_{He}=0.005$	-	-	+	+	+	+	-	-
	$s_{He}=0.01$	-	-	-	-	-	-	-	-
$U_{Hapl}=1.85$	$s_{He}=0.005$	-	-	-	-	-	-	-	-
	$s_{He}=0.01$	-	-	-	-	-	-	-	-

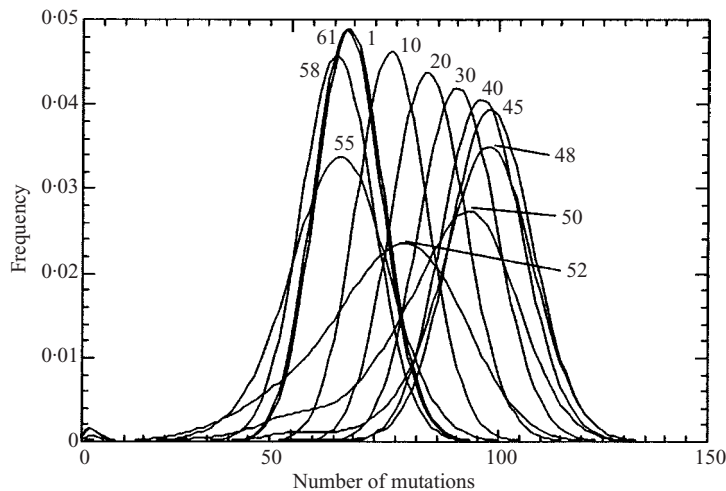


Fig. 3. Cyclical dynamics of the distribution of the number of mutations per individual with haploid selfing in a run shown in Fig. 2b. The number of the generation since a moment when the variance in the number of mutations per individual is minimal (generation 10048 of the run) is marked on each distribution.

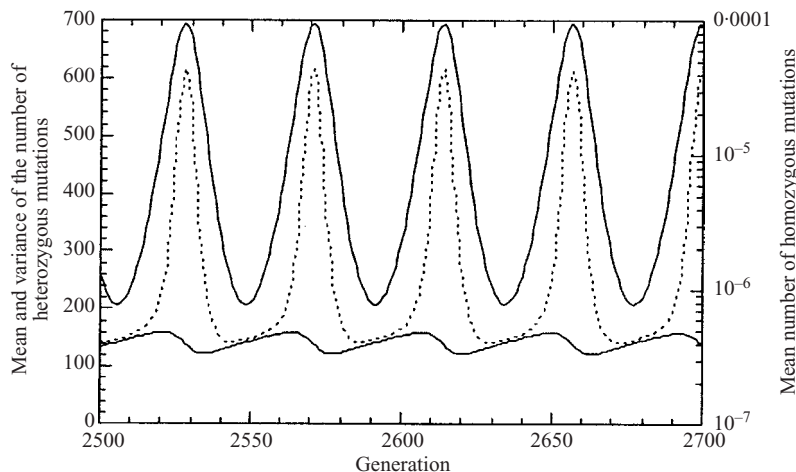


Fig. 4. Cyclical dynamics of the mean number of homozygous mutations (thick line) and the mean (thin line) and variance (dashed line) of the number of heterozygous mutations per individual under diploid selfing with $U_{Dipl}=4.5$, $C=0.35$, $s_{He}=0.02$ and $s_{Ho}=0.99$. Mean population fitness (not shown) fluctuates between 0.025 and 0.053.

conditions similar to those necessary for cycling with haploid selfing, but the required U_{Dipl} is about two times larger than U_{Hapl} (Table 2, Fig. 4). With either haploid or diploid selfing, we never observed cycling

under synergistic epistasis (Shnol & Kondrashov, 1993). By contrast, diminishing-returns epistasis, which might be biologically unrealistic, led to cycling under a wider range of parameters (data not reported).

Table 2. Dependence of the possibility of cycling under diploid selfing on U_{Dipl} and C with $s_{He}=0.02$ and $s_{Ho}=0.99$ ('+' : cycling; '-' : no cycling)

	C						
	0.50	0.55	0.60	0.65	0.70	0.75	0.80
$U_{Dipl}=5.0$	+	+	+	+	+	+	+
$U_{Dipl}=4.50$	–	–	+	+	+	+	–
$U_{Dipl}=4.00$	–	–	–	–	–	–	–

4. Discussion

We observed cycling in models of constant selection against mutations in haploid and diploid populations reproducing by facultative selfing. Diploid selfing is common in flowering plants (Charlesworth & Charlesworth, 1987) and in conifers (Sorensen, 1973; Sakai *et al.*, 1989; Ågren & Willson, 1991; Hitchcock & Cronquist, 1984; Godfrey & Wooten, 1981). Haploid selfing occurs in homosporous ferns (McCauley *et al.*, 1985; Soltis & Soltis, 1987) and filamentous ascomycetes (Nauta & Hoekstra, 1992) owing to fusion of gametes produced by the same haploid gametophyte. If selection occurs during the haploid phase, haploid selfing leads to the same population-level consequences as haploid apomixis. However, if selection occurs during the diploid phase, as was assumed in our model, haploid selfing is not identical to haploid apomixis.

Cycling requires high mutation rates and, thus, strong selection and low mean population fitness. Estimates of mutation rates remain controversial (Drake *et al.*, 1998; Kondrashov, 1998; Lynch *et al.*, 1999; Keightley & Eyre-Walker, 1999; Nachman & Crowell, 2000). Still, many estimates, including those for plants, indicate high mutation rates (Charlesworth, 1989; Klekowski & Godfrey, 1989; Klekowski, 1984). Also, cycling requires intermediate selfing rates, weak selection against heterozygous mutations and much stronger selection against homozygous mutations. These conditions are realistic (Charlesworth *et al.*, 1990; Charlesworth & Charlesworth, 1987; Soltis & Soltis, 1987, 1992; Simmons & Crow, 1977).

Cycling under facultative selfing is caused by the following mechanism. With $s_{Ho} \gg s_{He}$, the population usually consists effectively of two cohorts, produced by outcrossing and selfing. Most of the population consists of individuals that carry many ($\sim U/s_{He}$) mutations. These have mostly had only outcrossing in their ancestry for a long time, because the reproduction of such individuals by selfing produces very few viable offspring. However, there are also rare individuals carrying far fewer ($\sim U/s_{Ho}$) mutations that have had only selfing in their recent ancestry.

Mean fitness of obligate selfers is $\exp(-U_{Hapl})$ with haploid selfing and $\sim \exp(-U_{Dipl}/2)$ with diploid

selfing (Kondrashov, 1985; Charlesworth *et al.*, 1990). The mean fitness of obligate outcrossers under multiplicative selection in the diploid phase is $\exp(-2U_{Hapl})$ with haploid selfing and $\exp(-U_{Dipl})$, respectively (Kimura & Maruyama, 1966). Thus, in the absence of epistasis, selfing provides a population-level advantage. This advantage is even higher with diminishing-returns epistasis, whereas selfing might be disadvantageous under synergistic epistasis (Kondrashov, 1985; Charlesworth *et al.*, 1990).

If, at some moment, the cohort with selfed ancestry is very rare, mating with individuals from this cohort (all individuals outcross with probability $1-C$) does not substantially affect the mean fitness of those with outcrossed ancestry. Because selfing leads to a higher mean fitness, the fraction of individuals with selfed ancestry increases, as long as C exceeds the disadvantage of outcrossing, which, under multiplicative selection equals $\exp(-U_{Hapl})$ or $\exp(-U_{Dipl}/2)$. When this fraction becomes high enough, mating with them increases the variance in the number of mutations in those of outcrossed ancestry, making selection among them more efficient and reducing the number of mutations and increasing their mean fitness. As a result, the fraction of individuals with selfed ancestry drops, which completes the cycle (Fig. 3). Obviously, this phenomenon depends on the advantage of selfing and thus is impossible under synergistic epistasis.

The length of the cycle is always $\sim 1/s_{He}$. This is not surprising, because the mean number of mutations per individual fluctuates between 0 and U/s_{He} , and, after selection becomes inefficient, this number is incremented by $\sim U$ per generation.

A similar analysis of the dynamics under facultative selfing has been proposed by Lande *et al.* (1994) in order to explain data from plant species with high inbreeding depression caused by early expression of recessive lethal mutations under intermediate selfing rates. However, Lande *et al.* (1994) did not consider the possibility of cycling.

Our results provide the fourth known case of genetic cycling under constant selection. Evaluating a possible role of cycling in the dynamics of natural population requires better knowledge of parameters of mutation and selection.

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