

## A deterministic model of cyclical selection

By ROLF F. HOEKSTRA

*Biological Centre, Department of Genetics, University of Groningen,  
Haren (GN), The Netherlands*

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### SUMMARY

A deterministic model of cyclical selection in randomly mating populations is studied. Sufficient conditions for a protected polymorphism, which are for the special case of alternating selection also necessary conditions, are obtained using a simple graphical approach. The most important condition requires 'marginal overdominance' (Wallace, 1968); the other conditions seem hard to satisfy in a natural situation. Furthermore it is shown that the cyclical selection model can be regarded as a special case of a frequency-dependent selection model (Cockerham *et al.* 1972). Using this property, a mean fitness function for the cyclical selection model is derived. Generally, the mean fitness will not be maximized under cyclical selection. The relevance of the model to the problem of the role of cyclical selection in the maintenance of genetic polymorphism in natural populations is discussed. It is concluded that this relevance is probably rather limited with regard to the creation of protected polymorphism, but that the influence of cyclical selection on transient polymorphisms might be more significant. An approximate formula for the time needed for a given change in gene frequency under cyclical selection is derived. It appears that cyclical selection can extend considerably the time during which a transient polymorphism persists, especially if the selective differences in the different environments are of the same order of magnitude and of opposite sign.

### 1. INTRODUCTION

Since the discovery that a large proportion of loci in natural populations are polymorphic, as revealed by electrophoretic studies of proteins (e.g. Lewontin & Hubby, 1966; Prakash, Lewontin & Hubby, 1969; Selander & Yang 1969; Harris, Hopkinson & Luffman, 1968), considerable discussion has been devoted to the mechanisms responsible for maintaining such large amounts of genetic polymorphism. Some authors suggest that most electrophoretic variation is selectively neutral or nearly neutral (e.g. Kimura, 1968; King & Jukes, 1969), while others stress the importance of some type of balancing selection (e.g. Prakash *et al.* 1969; Ayala, 1972; Wills, 1973). The maintenance of a single-locus polymorphism can be explained by a variety of selection models, covering situations of overdominance, frequency-dependent selection, density-dependent selection, and differential selection due to environmental heterogeneity in space or in time. Relatively little attention has been paid to the latter class of models, namely those in which temporal

variation in selection intensities is assumed. Environmental variables relevant to fitness may vary in a stochastic manner, for example diseases, or (in some cases) numbers of parasites and predators, or they may vary regularly, for example those correlated with seasons. Models applicable to the first situation were studied by (among others) Kimura (1954), Ohta (1972) and Gillespie (1973), while a deterministic model which fits the second situation was given by Haldane & Jayakar (1963).

In this paper we will study a deterministic model of cyclical selection. It fits, for example, species living in a seasonal environment where generation-time is short relative to the duration of a season, a situation faced by for example many insects and small rodents. In this study we are primarily interested in the question to what extent genetic polymorphism may be maintained by cyclical selection.

## 2. THE MODEL

Consider, in a diploid organism, a single autosomal locus with two alleles  $A_1$  and  $A_2$ , segregating in a very large population (so that random variation in gene frequency is negligible), in which mating is at random, and generations are discrete. Mutation and migration are ignored. The population is subjected to cyclical selection with cycle length  $n$ . Let  $w_i$ ,  $v_i$  denote the relative fitness values of the three genotypes  $A_1A_1$ ,  $A_1A_2$  and  $A_2A_2$  respectively in generation  $i + kn$  ( $i = 1, 2, \dots, n$ ;  $k = 0, 1, 2, \dots$ ). The parameters  $w_i$  and  $v_i$  specify the  $i$ th environment. It is clear that not all environments making up a cycle need to be different: for example a population having three generations in the summer and one in the winter has a cycle of four environments, the first three of which are the same. Thus the simplest case of cyclical selection is when  $n = 2$ : we then have an alternation from generation to generation of two environments, and will call this case alternating selection. For simplicity, we will start exploring the alternating selection model.

## 3. GRAPHICAL ANALYSIS OF ALTERNATING SELECTION

We denote the relative frequencies of  $A_1$  and  $A_2$  prior to selection by  $p$  and  $q = 1 - p$ . Considering just one cycle, the gene frequency after one generation of selection  $p_1$  is related to the gene frequency before selection  $p_0$  by the familiar recurrence relation

$$p_1 = p_0 \left( \frac{p_0 w_1 + q_0}{\bar{w}_1} \right) \equiv \theta_1(p_0), \quad (1)$$

where  $\bar{w}_1 = w_1 p_0^2 + 2p_0 q_0 + v_1 q_0^2$  is the mean (relative) fitness.

Similarly, the gene frequency after the second generation of selection is given by

$$p_2 = p_1 \left( \frac{p_1 w_2 + q_1}{\bar{w}_2} \right) \equiv \theta_2(p_1), \quad (2)$$

with  $\bar{w}_2 = w_2 p_1^2 + 2p_1 q_1 + v_2 q_1^2$  being the mean fitness prior to the onset of selection in the second generation. Depending on the selective values  $w_i$  and  $v_i$ , the graph

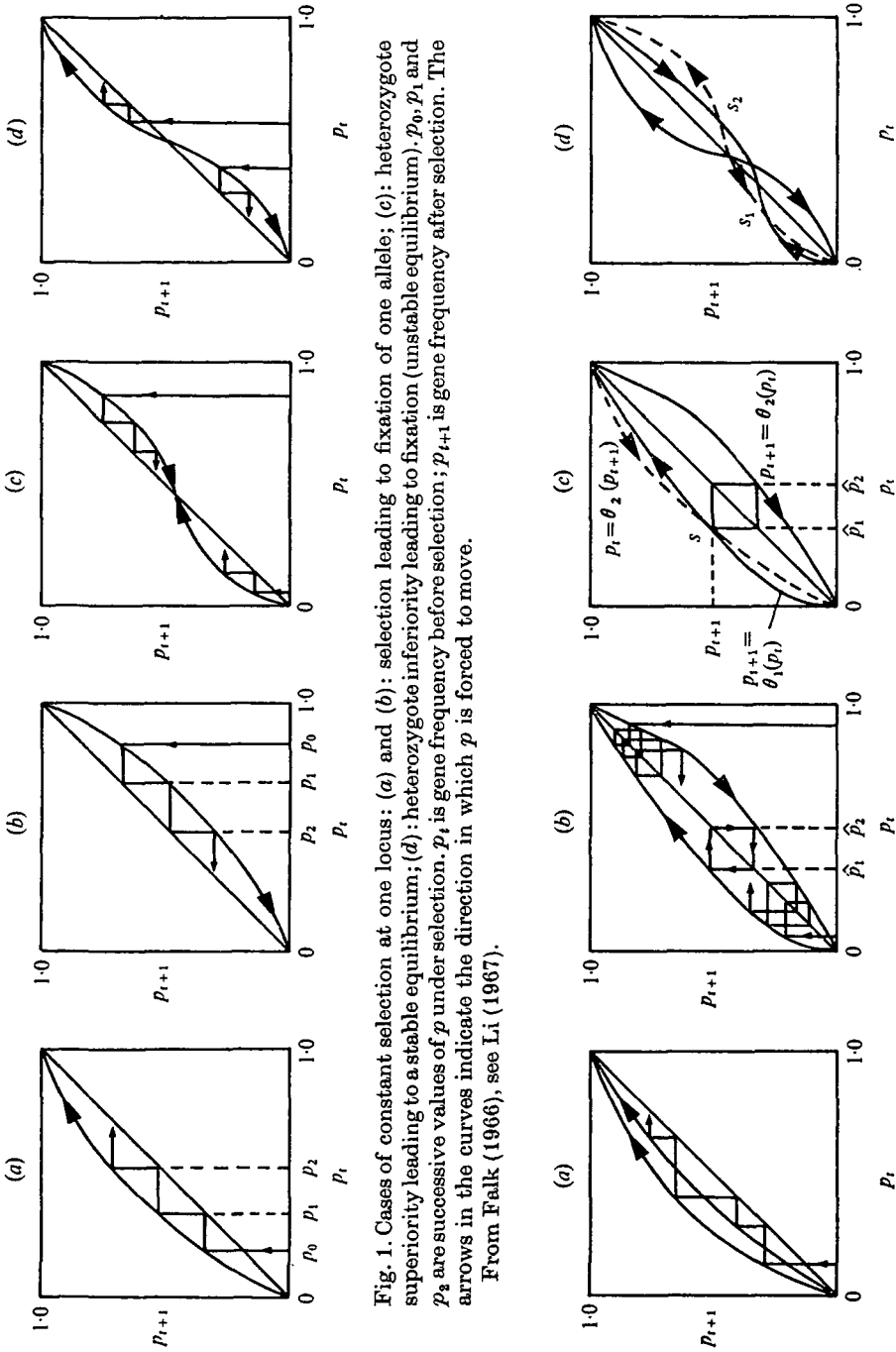


Fig. 1. Cases of constant selection at one locus: (a) and (b): selection leading to fixation of one allele; (c): heterozygote superiority leading to a stable equilibrium; (d): heterozygote inferiority leading to fixation (unstable equilibrium).  $p_0, p_1$  and  $p_2$  are successive values of  $p$  under selection;  $p_t$  is gene frequency before selection;  $p_{t+1}$  is gene frequency after selection. The arrows in the curves indicate the direction in which  $p$  is forced to move.  
From Falk (1966), see Li (1967).

Fig. 2. Some cases of alternating selection; same legends as Fig. 1. For explanation, see text.

of the function  $\theta_i$  is one of the four possible types, sketched in Fig. 1 (adapted from Falk (1966) and Li (1967); see also Cannings (1969)). This graphic representation can be used to show the successive values of  $p$  from generation to generation in the selection process. In Fig. 2 some cases of alternating selection are represented by plotting the functions  $\theta_1$  and  $\theta_2$  together in the same diagram, and constructing the successive values of  $p$  under selection in the same manner as in Fig. 1. In Fig. 2(a) alternating selection ultimately leads to fixation of the  $A_1$ -allele because this allele is favoured in both environments; in Fig. 2(b) there is a stable equilibrium situation in which  $p$  fluctuates from generation to generation between two fixed values  $\hat{p}_1$  and  $\hat{p}_2$ .

Now suppose that the actual parameters in a given case are such that the graph of the functions  $\theta_1$  and  $\theta_2$  are as plotted in Fig. 2(c); (however, the following argument is not confined to the case given in Fig. 2(c), but also applies to the general case). If the curve  $p_{t+1} = \theta_2(p_t)$  is mirrored with respect to the line  $p_{t+1} = p_t$ , the graph of  $p_t = \theta_2(p_{t+1})$  is obtained.

It is easy to see that a point of intersection  $S$  between the curves of  $p_{t+1} = \theta_1(p_t)$  and  $p_t = \theta_2(p_{t+1})$  represents an equilibrium, the coordinates of  $S$  being the equilibrium frequencies of  $p$ . The converse is also true: any equilibrium point will correspond with a point of intersection between the curves of  $p_{t+1} = \theta_1(p_t)$  and  $p_t = \theta_2(p_{t+1})$ . The stability of an equilibrium can be inferred from the graph by looking at the slope of the two curves in their point(s) of intersection in  $(0, 1)$ . An equilibrium, represented by a point  $S$  lying above the diagonal  $p_{t+1} = p_t$  will be stable if the slope at  $S$  of the curve which forces  $p$  to increase is smaller than the slope of the other curve, while for a point  $S$  lying below the diagonal the reverse holds (see Fig. 2(d):  $S_1$  represents a stable equilibrium,  $S_2$  an unstable one).

This graphic approach finally enables us to find sufficient conditions for a 'protected polymorphism' (Prout, 1968), which refers to the situation that the two alleles  $A_1$  and  $A_2$  cannot be lost or fixed by selection (see also Bodmer & Parsons, 1960). This will be the case if the two trivial points  $p = 0$  and  $p = 1$  are unstable, therefore if (see Fig. 2(c)):

$$\left. \frac{d\theta_1(p_t)}{dp_t} \right|_{p_t=0,1} > \left. \frac{d\theta_2(p_{t+1})}{dp_t} \right|_{p_t=0,1},$$

or

$$\left. \frac{d\theta_1(p_t)}{dp_t} \right|_{p_t=0,1} \frac{d\theta_2(p_t)}{dp_t} \Big|_{p_t=0,1} > 1,$$

which is equivalent to

$$\left. \frac{d\theta_1(\theta_2(p_t))}{dp_t} \right|_{p_t=0,1} > 1,$$

or, using the notation of equations (1) and (2):

$$\left. \frac{dp_2}{dp_0} \right|_{p_0=0,1} > 1. \quad (3)$$

Further conditions can be found by considering the cases

$$\left. \frac{dp_2}{dp_0} \right|_{p_0=0} = 1, \quad \left. \frac{dp_2}{dp_0} \right|_{p_0=1} = 1 \quad \text{and} \quad \left. \frac{dp_2}{dp_0} \right|_{p_0=0,1} = 1.$$

Then the points  $p_0 = 0$  and  $p_0 = 1$  are unstable if (in terms of the geometrical approach of Figs. 1 and 2) the curve of  $p_2 = \theta_2(\theta_1(p_0))$  is concave at  $p_0 = 0$  and/or convex at  $p_0 = 1$ .

Therefore the additional sufficient conditions for a protected polymorphism are:

$$\left. \frac{dp_2}{dp_0} \right|_{p_0=0} = 1, \quad \left. \frac{dp_2}{dp_0} \right|_{p_0=1} > 1, \quad \left. \frac{d^2p_2}{dp_0^2} \right|_{p_0=0} > 0; \tag{4}$$

$$\left. \frac{dp_2}{dp_0} \right|_{p_0=0} > 1, \quad \left. \frac{dp_2}{dp_0} \right|_{p_0=1} = 1, \quad \left. \frac{d^2p_2}{dp_0^2} \right|_{p_0=1} < 0; \tag{5}$$

$$\left. \frac{dp_2}{dp_0} \right|_{p_0=0,1} = 1, \quad \left. \frac{d^2p_2}{dp_0^2} \right|_{p_0=0} > 0, \quad \left. \frac{d^2p_2}{dp_0^2} \right|_{p_0=1} < 0. \tag{6}$$

Generalization of these sufficient conditions to a cycle-length of  $n$  generations is straightforward: for the general case,  $p_2$  in the expressions (3) to (6) has to be replaced by  $p_n = \theta_n\{\theta_{n-1}(\dots[\theta_2\{\theta_1(p_0)\}]\dots)\}$ . After working out, which involves application of the chain rule for derivatives and some rearranging, the sufficient conditions for a protected polymorphism in the cyclical selection model with cycle length  $n$  become:

$$\left. \begin{aligned} \text{(i)} \quad & \prod_{i=1}^n v_i < 1, \quad \prod_{i=1}^n w_i < 1; \\ \text{(ii)} \quad & \prod_{i=1}^n v_i = 1, \quad \prod_{i=1}^n w_i < 1, \quad \sum_{j=1}^n \left[ (w_j - 1) \prod_{i=j}^n v_i \right] > 0; \\ \text{(iii)} \quad & \prod_{i=1}^n v_i < 1, \quad \prod_{i=1}^n w_i = 1, \quad \sum_{j=1}^n \left[ (v_j - 1) \prod_{i=j}^n w_i \right] > 0; \\ \text{(iv)} \quad & \prod_{i=1}^n v_i = 1, \quad \prod_{i=1}^n w_i = 1, \quad \sum_{j=1}^n \left[ (w_j - 1) \prod_{i=j}^n v_i \right] > 0, \quad \sum_{j=1}^n \left[ (v_j - 1) \prod_{i=j}^n w_i \right] > 0. \end{aligned} \right\} \tag{7}$$

Condition (i) and a special case of (ii, iii), namely the case of complete dominance, were already obtained by Haldane & Jayakar (1963), using a different approach. In principle, further conditions may be found by examining subsequently higher derivatives, but since the conditions thus obtained will be extremely hard to satisfy, it does not seem worthwhile to do so.

The first condition of (7), is fulfilled in a situation where there is some kind of generalized heterosis, or, as Wallace (1968) called it, ‘marginal overdominance’. There is no need for heterosis in all the different environments: for example, if both homozygotes have a very low relative fitness once in a cycle, this condition could be satisfied rather easily while in the other environments of the cycle there is dominance or even heterozygote inferiority.

The other conditions of (7) are less likely to be met. Fig. 3 shows for the alternating selection case ( $n = 2$ ) the region in which a point, representing a set of relative fitness values, has to be situated to give a protected polymorphism. Fig. 3(a) gives the region in which the special case of complete dominance ( $v_1 = v_2 = 1$ ) of

condition (ii) is satisfied; Fig. 3(b) applies to the general formulation of condition (ii), and Fig. 3(c) shows the points satisfying condition (iv).

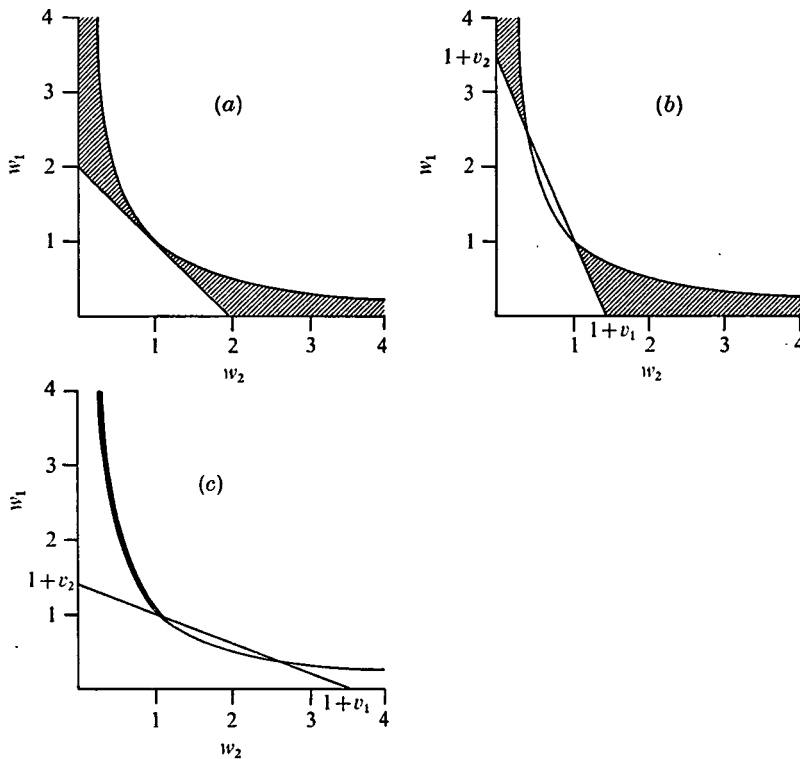


Fig. 3. A protected polymorphism in the alternating selection model is established if the point  $(w_1, w_2)$  is on the shaded area in (a) and (b) or on the heavily drawn part of the curve in (c). The relative fitnesses of  $A_1A_1$ ,  $A_1A_2$  and  $A_2A_2$  in the two environments are respectively: (a):  $w_1, 1, 1$ , and  $w_2, 1, 1$ ; (b):  $w_1, 1, v_1$  and  $w_2, 1, v_2$ , with  $v_1v_2 = 1$ ; (c):  $w_1, 1, v_1$  and  $w_2, 1, v_2$ , with  $w_1w_2 = v_1v_2 = 1$  and  $w_1 \neq w_2, v_1 \neq v_2$ .

#### 4. THE CYCLICAL SELECTION MODEL AS A SPECIAL CASE OF A FREQUENCY-DEPENDENT SELECTION MODEL

An interesting feature of the cyclical selection model is that it can be regarded as a special case of the frequency-dependent selection model of Cockerham *et al.* (1972). In order to show this, we first give very briefly an outline of their model.

##### (i) *Brief description of the Cockerham model*

Relative fitness values are defined for pairwise associations of genotypes; this applies to situations where for instance competitive ability, mating success or viability of a given genotype depend on what other genotype(s) are present. Thus an individual of genotype  $i$  has a relative fitness value  $w_{ij}$  when in association with an individual of genotype  $j$ , where in our notation  $i$  and  $j$  refer to the number of

$A_1$  alleles in the genotype. For one autosomal locus with two alleles the following matrix of fitness values results:

$$\begin{array}{c}
 \text{In association with} \\
 \overbrace{A_1 A_1 \quad A_1 A_2 \quad A_2 A_2} \\
 \text{Genotype} \left\{ \begin{array}{l} A_1 A_1 \\ A_1 A_2 \\ A_2 A_2 \end{array} \right. \begin{array}{l} w_{22} \quad w_{21} \quad w_{20} \\ w_{12} \quad w_{11} \quad w_{10} \\ w_{02} \quad w_{01} \quad w_{00} \end{array} \left. \begin{array}{l} \bar{w}_2 \\ \bar{w}_1 \\ \bar{w}_0 \end{array} \right\}
 \end{array} \quad (8)$$

With random mating and random association of individuals, the mean relative fitness of genotype  $i$  is  $\bar{W}_i = p^2 w_{i2} + 2pq w_{i1} + q^2 w_{i0}$ , and the overall mean fitness is  $\bar{W} = p^2 \bar{W}_2 + 2pq \bar{W}_1 + q^2 \bar{W}_0$ . The gene frequency after selection is

$$p' = \frac{p(p\bar{W}_2 + q\bar{W}_1)}{\bar{W}}, \quad \text{and the change in gene frequency,}$$

$$\Delta p = p' - p = \frac{pq}{\bar{W}} [p(\bar{W}_2 - \bar{W}_1) + q(\bar{W}_1 - \bar{W}_0)] \equiv \frac{pq}{\bar{W}} K(p, w).$$

When studying equilibria it is more convenient to consider the so-called competitive comparisons  $d_{ij} = w_{ij} - w_{jj}$  instead of the relative fitness values  $w_{ij}$ . The resulting matrix of comparisons is

$$\begin{array}{ccc}
 0 & d_{21} & d_{20} \\
 d_{12} & 0 & d_{10} \\
 d_{02} & d_{01} & 0
 \end{array} \quad (9)$$

and

$$\Delta p = \frac{pq}{\bar{W}} [p(\bar{d}_2 - \bar{d}_1) + q(\bar{d}_1 - \bar{d}_0)] \equiv \frac{pq}{\bar{W}} K(p, d). \quad (10)$$

A non-trivial equilibrium frequency  $\hat{p}$  ( $0 < \hat{p} < 1$ ) will satisfy the equation

$$K(p, d) = 0, \quad \text{or} \quad (\text{see formula (10)}):$$

$$\begin{aligned}
 K(p, d) = & p^3(-2d_{12} + d_{02} - 2d_{21} - 2d_{01} + d_{20} - 2d_{10}) \\
 & + p^2(2d_{21} + 4d_{01} - 2d_{20} + 5d_{10} + d_{12} - d_{02}) \\
 & + p(d_{20} - 4d_{10} - 2d_{01}) + d_{10} = 0.
 \end{aligned} \quad (11)$$

Cockerham *et al.* (1972) give the necessary and sufficient conditions for a protected polymorphism in their frequency-dependent model. These are six mutually exclusive conditions in terms of the comparisons  $d_{ij}$ , easily derived from (11) using endpoint analysis:

$$\left. \begin{array}{l}
 (1) \quad d_{10} > 0, \quad d_{12} > 0, \\
 (2) \quad d_{10} = 0, \quad d_{12} > 0, \quad d_{20} > 2d_{01}, \\
 (3) \quad d_{10} > 0, \quad d_{12} = 0, \quad d_{02} > 2d_{21}, \\
 (4) \quad d_{10} = 0, \quad d_{12} = 0, \quad d_{20} > 2d_{01}, \quad d_{02} > 2d_{21}, \\
 (5) \quad d_{10} = 0, \quad d_{12} > 0, \quad d_{20} = 2d_{01}, \quad d_{02} < d_{21} + 2d_{21}, \\
 (6) \quad d_{10} > 0, \quad d_{12} = 0, \quad d_{02} = 2d_{21}, \quad d_{20} < d_{10} + 2d_{01}.
 \end{array} \right\} \quad (12)$$

(ii) *The cyclical selection model as a special case of the Cockerham model*

In order to incorporate the cyclical selection model into the framework of the Cockerham model, we first derive the relative genetic contribution of each genotype to the population after one cycle of selection. This is a measure of the relative fitness when a cycle is taken as the time-unit of the selection process, instead of a single generation, which is usually regarded as the time-unit in selection models.

Table 1. *Derivation of the relative fitnesses over a cycle of selection (r.f.c. functions) for the case of alternating selection*

Genotypes ...	$A_1A_1$	$A_1A_2$	$A_2A_2$
Frequencies before selection	$p^2$	$2pq$	$q^2$
Relative fitness values in environment 1	$w_1$	1	$v_1$
Mean relative fitness	$\bar{w}_1 = w_1p^2 + 2pq + v_1q^2$		
Frequencies after selection and random mating	$\frac{(w_1p+q)^2}{\bar{w}_1^2} p^2$	$\frac{(w_1p+q)(v_1q+p)}{\bar{w}_1^2} 2pq$	$\frac{(v_1q+p)^2}{\bar{w}_1^2} q^2$
Relative fitness values in environment 2	$w_2$	1	$v_2$
Mean relative fitness	$\bar{w}_2 = \frac{w_2(w_1p+q)^2}{\bar{w}_1^2} p^2 + \frac{(w_1p+q)(v_1q+p)}{\bar{w}_1^2} 2pq + \frac{v_2(v_1q+p)^2}{\bar{w}_1^2} q^2$		
R.f.c. functions	$\frac{w_2(w_1p+q)^2}{\bar{w}_1^2}$	$\frac{(w_1p+q)(v_1q+p)}{\bar{w}_1^2}$	$\frac{v_2(v_1q+p)^2}{\bar{w}_1^2}$
or	$w_2c_2$	1	$\frac{v_2}{c_2}$
with	$c_2 = \frac{w_1p+q}{v_1q+p}$		

These relative fitnesses covering a cycle of selection will be called *relative-fitness-cycle functions* (r.f.c. functions). The r.f.c. functions for the case of  $n = 2$  (alternating selection model) are derived in Table 1. The r.f.c. functions for cases of  $n > 2$  can be obtained in an analogous way: cyclical selection with a cycle length of 3 generations can be interpreted as an alternation in the following scheme:

	$A_1A_1$	$A_1A_2$	$A_2A_2$
Environment 1, 2	$w_2c_2$	1	$\frac{v_2}{c_2}$
Environment 3	$w_3$	1	$v_3$

Similarly, for  $n = 4$  there is an alternation between environments 1, 2, 3 and environment 4, and so on.

The r.f.c. functions for  $n \geq 2$  are given in Table 2. The r.f.c. functions appear to be frequency-dependent, which is not surprising: if a cycle were to consist of  $n$  identical environments (the case of constant selection), the r.f.c. functions would be frequency-dependent too; it merely reflects the fact that the magnitude of the selection response depends on the gene frequency. Nevertheless, the cyclical



selection model can now be analysed as a special case of the frequency-dependent selection model of Cockerham *et al.*

First, consider the case of alternating selection ( $n = 2$ ). Clearly, the r.f.c. functions derived in Table 1 correspond to the mean relative fitnesses  $\bar{W}_i$  in (8). Therefore, a set of  $w_{ij}$  (see (8)) can be found from the following equations in which the left-hand

Table 2. Relative-fitness-cycle functions for different cycle-lengths

Cycle-length in generations	R.f.c. functions of genotypes		
	$A_1A_1$	$A_1A_2$	$A_2A_2$
2	$w_2c_2$	1	$\frac{v_2}{c_2}; c_2 = \frac{w_1p+q}{v_1q+p}$
3	$w_3c_3$	1	$\frac{v_3}{c_3}; c_3 = \frac{w_2c_2p+q}{(v_2/c_2)q+p}$
⋮	⋮	⋮	⋮
$n$	$w_nc_n$	1	$\frac{v_n}{c_n}; c_n = \frac{w_{n-1}c_{n-1}p+q}{(v_{n-1}/c_{n-1})q+p}$

sides represent the r.f.c. functions from table 1 and the right-hand sides the  $\bar{W}_i$  from (8).

$$\left. \begin{aligned} w_2(w_1p+q)^2 &= w_{22}p^2 + 2w_{21}pq + w_{20}q^2 \\ (w_1p+q)(v_1q+p) &= w_{12}p^2 + 2w_{11}pq + w_{10}q^2 \\ v_2(v_1q+p)^2 &= w_{02}p^2 + 2w_{01}pq + w_{00}q^2 \end{aligned} \right\} \tag{13}$$

The following matrix of fitness values  $w_{ij}$  satisfies the equations (13):

$$\left. \begin{aligned} w_2w_1^2 & & w_2w_1 & & w_2 \\ w_1 & & \frac{w_1v_1+1}{2} & & v_1 \\ v_2 & & v_2v_1 & & v_2v_1^2 \end{aligned} \right\} \tag{14}$$

and the corresponding matrix of comparisons (5) becomes

$$\left. \begin{aligned} 0 & & w_2w_1 - \frac{w_1v_1+1}{2} & & w_2 - v_2v_1^2 \\ w_1(1-w_2w_1) & & 0 & & v_1(1-v_2v_1) \\ v_2 - w_2w_1^2 & & v_2v_1 - \frac{w_1v_1+1}{2} & & 0 \end{aligned} \right\} \tag{15}$$

These values can be substituted in (11); the resulting cubic equation reduces to a quadratic equation in a number of special cases of which the two biologically most interesting ones will now be examined (see (11 and (15)).

*Special case 1.*  $d_{10} = 0$ , or  $v_1(1 - v_2v_1) = 0$ ; (the same applies to  $d_{12} = 0$ , as can be seen for example from writing  $K$  as a function of  $q$ ). This includes the following two cases: (1) one homozygote is lethal in one environment ( $v_1 = 0$ ), and (2) one allele is fully dominant in both environments ( $v_1 = v_2 = 1$ ). The derivation of the equi-

brum frequencies from (11) is straightforward: for example, in the case  $v_1 = v_2 = 1$ , one obtains

$$\left. \begin{aligned} \hat{p} &= \frac{w_2 - 1 + \sqrt{(1 - w_1 w_2)}}{w_2(1 - w_1)} && \text{if } w_1 > 1 \\ \hat{p} &= \frac{w_2 - 1 - \sqrt{(1 - w_1 w_2)}}{w_2(1 - w_1)} && \text{if } w_1 < 1. \end{aligned} \right\} \tag{16}$$

and

By interchanging  $w_1$  and  $w_2$  in (16), the other equilibrium frequency in the alternating system can be calculated.

*Special case 2.* For the symmetric model:  $w_1 = v_2 = 1 + x$ ;  $w_2 = v_1 = 1 - x$ , the coefficient of  $p^3$  in (11) equals zero, and the solution of the resulting quadratic equation is

$$\hat{p} = \frac{3x - 2 + \sqrt{(4 - 3x^2)}}{6x}. \tag{17}$$

We now turn to the general case of cyclical selection with cycle-length  $n$ . The matrix of fitness values  $w_{ij}$  becomes (see (14) and Table 2):

$$\left. \begin{array}{ccc} c_{n-1}^2 w_{n-1}^2 w_n & c_{n-1} w_{n-1} w_n & w_n \\ c_{n-1} w_{n-1} & \frac{w_{n-1} v_{n-1} + 1}{2} & \frac{v_{n-1}}{c_{n-1}} \\ v_n & \frac{v_{n-1} v_n}{c_{n-1}} & \frac{v_{n-1}^2 v_n}{c_{n-1}^2} \end{array} \right\} \tag{18}$$

To include in this general formulation the case of alternating selection ( $n = 2$ ) we put by definition:

$$c_1 = \frac{w_0 p + q}{v_0 q + p} = \frac{p + q}{q + p} = 1.$$

Now the  $w_{ij}$  in (18) and therefore also the corresponding  $d_{ij}$  are no longer constants (as in (14)) but are complicated functions of  $p$ . We therefore extend the Cockerham model to account for higher-order interactions. Thus, for second-order interactions we have to define

$$\bar{w}_{ij} = p^2 w_{ij2} + 2pq w_{ij1} + q^2 w_{ij0},$$

and

$$\begin{aligned} \bar{d}_{ij} &= \bar{w}_{ij} - \bar{w}_{jj} \\ &= p^2 d_{ij2} + 2pq d_{ij1} + q^2 d_{ij0} \quad \text{and so forth.} \end{aligned}$$

Equation (11) and the conditions (12) can be modified to account for these higher-order interactions, while the  $d_{ij...}$  can be calculated from the above defined relations, and the  $w_{ij...}$  in turn can be obtained in a similar manner as the  $w_{ij}$  were obtained from the equations (13).

It can be shown that from conditions (12) (or the higher-order equivalents of (12)) the same conditions for a protected polymorphism result as formulated in (7). Moreover, for  $n = 2$  (though not for larger  $n$ ) the conditions (5) and (6) of (12) appear to be (internally) contradictory, from which it follows that for the alter-

nating selection model conditions (7) are not only sufficient but also necessary for a protected polymorphism.

Finally it may be noted that it is not surprising that the alternating selection model can be fitted within the Cockerham *et al.* model, since both models give rise to

$$\frac{p'}{q'} = \frac{p(f(p, q))}{q(g(p, q))},$$

where  $f$  and  $g$  are arbitrary homogeneous cubics in  $p$  and  $q$ ; similar arguments apply for the general case of cyclical selection and the Cockerham model extended to higher-order interactions. In fact, the Cockerham *et al.* scheme can be used even when  $f$  and  $g$  are not homogeneous in  $p$  and  $q$ , which illustrates the generality of this model.

### 5. MEAN FITNESS

It is not at first sight clear how to define a mean fitness function in the cyclical selection model. In a cycle of  $n$  different environments there are  $n$  different single-generation mean fitness functions, and the change in mean fitness within a cycle cannot be approximated with some continuous function. When considering a cycle as the time-unit of the selection process one could define a mean fitness function by constructing some average of the single generation mean fitnesses.

However, a possibility for defining a mean fitness function over a cycle of selection arises naturally in our approach, namely by using the r.f.c. functions derived in Tables 1 and 2. Thus for a cycle-length of  $n$  generations the mean fitness is

$$\bar{W} = w_n c_n p^2 + 2pq + \frac{v_n}{c_n} q^2. \quad (19)$$

This is the same function as the overall mean fitness  $\bar{W}$  from the matrix of fitness values (8).

Two important conclusions result from this definition. First, the mean fitness will generally not be maximized under cyclical selection, and therefore the mean fitness may decrease during the selection process. This is a well-known characteristic of frequency-dependent selection models and can be shown by putting

$$d\bar{W}/dp = 0,$$

as is done by Cockerham *et al.* (1972) for the frequency-dependent selection model applied in this study. The second conclusion is that for a given cycle of environments the mean fitness (19) depends on the starting point in the cycle.

In the case of a cycle of environments 1, 2, ...,  $n$  (with fixed sequence), the cycle can start at  $n$  different environments, which gives rise to  $n$  different descriptions of essentially the same process. A particular fitness matrix (8) is associated with each of these mean fitness functions and consequently also a particular function  $K(p, d)$  (11) with its equilibrium-solution(s).

## 6. DISCUSSION

The conditions which must be satisfied in order to obtain protected polymorphism in the cyclical selection model are severe, except for the first condition, which requires 'marginal overdominance' (Wallace, 1968): if we assume that the actual selective differences between genotypes and between different environments are mostly small (that is, if we assume that the  $w_i$  and  $v_i$  mostly do not differ greatly from 1), then the most important region in the diagrams of Fig. 3 is around the point (1, 1). It is clear from Fig. 3 that the area of protected polymorphism in this region is quite small. Therefore the relevance of cyclical selection to the maintenance of genetic polymorphism in natural populations seems to be rather limited, at least in those cases where the action of natural selection on a single locus is independent of other loci. This probably will be true in some instances, but evidence is accumulating concerning selection acting on correlated blocks of genes rather than on single genes (e.g. Franklin & Lewontin, 1970; Mukai, Mettler & Chigusa, 1971; Allard & Kahler, 1972).

If strong linkage disequilibrium between polymorphic loci is a common phenomenon, the role of cyclical selection in the maintenance of genetic variation might be more important, but this cannot be explored with the present model.

There are a few reports in the literature of regularly fluctuating gene frequencies in natural populations: Timoféeff-Ressovsky (1940) found cyclic changes in the frequencies of colour morphs of the ladybird *Adalia bipunctata* correlated with the seasons. Especially well known are the seasonal changes in frequencies of inversion types in *Drosophila* (Dobzhansky, 1943, 1956; Dubinin & Tiniakov, 1945). There is also some evidence of cyclical changes in enzyme polymorphisms in *Drosophila* (Dobzhansky & Ayala, 1973).

Gershenson (1945) described seasonal changes in the frequencies of the black and grey morphs in the Russian population of the hamster. In vole populations, allelic frequencies of some enzyme loci are fluctuating regularly, correlated with the fluctuating population density (e.g. Semeonoff & Robertson, 1968; Tamarin & Krebs, 1969; Gaines & Krebs 1971). In some of these cases cyclical selection may be the cause of the observed changes in frequency, especially when they are seasonal. However, regular cycles in gene frequencies can also occur in populations with overlapping generations and fluctuations in age structure, due to causes which are non-specific with respect to genotype (Charlesworth & Giesel, 1972*a*), or when there is density-dependent selection (Charlesworth & Giesel, 1972*b*).

Cyclical selection may influence the amount of genetic polymorphism present in natural populations at a given time by creating protected polymorphisms (the relevance of which we have just discussed), but also by changing the time till fixation. If in a cyclical selection situation no stable equilibrium exists, the population will become monomorphic for the locus under consideration. However, the time till fixation, that is, the time that the so-called transient polymorphism lasts, may vary considerably, depending on the fitness values in the different environments.

To get some information on the number of generations of selection needed for a given change in gene frequency we use the following approximations; we consider only the alternating selection case ( $n = 2$ ), but the result is easily extended for cycle-lengths greater than 2. The alternating selection model is approximated by a model in which the population faces the different selection regimes within one

Table 3. Number of generations required for a given change in gene frequency in the alternating selection model compared with the rate of change in the environments separately

Fitness values	From 0.5 to 0.05 (or from 0.5 to 0.95)	
	Exact	Approximated with (21)
0.9 1 1.1 } 1.1 1 1 } 0.9 1 1.1 } 1.1 1 1 }	80	75
0.98 1 1.02 } 1.02 1 1 }	390	386
0.98 1 1.02 } 1.02 1 1 }	150	—
1.02 1 1 } 0.98 1 1.02 }	196	—
0.98 1 1.02 } 1.02 1 0.99 }	788	783
1.02 1 0.99 }	168	—

generation (e.g. in two different stages in the life-cycle), the fitnesses being multiplicative. So the model

$$\begin{matrix} A_1 A_1 & A_1 A_2 & A_2 A_2 \\ w_1 & 1 & v_1 \\ w_2 & 1 & v_2 \end{matrix}$$

is approximated by the model

$$\begin{matrix} A_1 A_1 & A_1 A_2 & A_2 A_2 \\ w_1 w_2 & 1 & v_1 v_2 \end{matrix} \tag{20}$$

If in model (20)  $1 - s_1$  is substituted for  $w_1 w_2$  and  $1 - s_2$  for  $v_1 v_2$ , and second and higher order terms in  $s_1$  and  $s_2$  are neglected, then the change in gene frequency per cycle is

$$\Delta p = p(1 - p)(-(s_1 + s_2)p + s_2).$$

By putting  $\Delta p = dp/dt$  and solving the resulting differential equation, one gets the following approximate formula for the number of cycles (which is in this case half the number of generations) required to change the gene frequency from  $p_0$  to  $p_k$ :

$$k = \frac{1}{s_2(1+r)} \left[ \log \frac{p_k(p_0+r)}{p_0(p_k+r)} + r \log \frac{p_k(1-p_0)}{p_0(1-p_k)} \right], \tag{21}$$

where  $s_2 = 1 - v_1 v_2$  and  $r = \frac{-s_2}{s_1 + s_2} = \frac{v_1 v_2 - 1}{2 - w_1 w_2 - v_1 v_2}$ .

The approximation appears to be sufficiently close as can be seen from a few examples shown in Table 3.

The transient polymorphism in the alternating selection situation may last considerably longer than in the different environments separately, especially if the selective forces in the two environments are in opposite directions and approximately equally strong.

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