BALANCED POLYMORPHISMS WITH UNLINKED LOCI

By P. A. P. MORAN*

[*Manuscript received August* 16, 1962]

Summary

The stationary states of a genetic population whose fitness is controlled by two independent loci, with two alleles each, are considered. It is shown that apart from degenerate cases there are at most five such states. It is also shown that there are at most three stationary states which are stable. Examples are given where these bounds are attained.

I. INTRODUCTION

Consider a randomly mating population whose fitness is dependent on the situations at two unlinked loci at each of which there are two alleles which we denote by A, a, and B, b, respectively. Suppose that the gene frequency of A is p, and that of B is P.

If the relative fitnesses, i.e. the relative contributions to a subsequent generation, are given by constants w_{ij} as in the following tabulation

	AA	Aa	aa
BB	w_{11}	w_{12}	w_{13}
Bb	w_{21}	w_{22}	w_{23}
bb	w_{31}	w_{32}	w_{33}

then the mean fitness of the population is defined by

$$\begin{aligned} W = {} & w_{11}P^2p^2+2w_{12}P^2p(1-p)+w_{13}P^2(1-p)^2+2w_{21}P(1-P)p^2+4w_{22}P(1-P)p(1-p) \\ & +2w_{23}P(1-P)(1-p)^2+w_{31}(1-P)^2p^2+2w_{32}(1-P)^2p(1-p)+w_{33}(1-P)^2(1-p)^2. \end{aligned} \tag{1}$$

If this is plotted as a function of p and P in the square $(0 \leqslant p \leqslant 1, 0 \leqslant P \leqslant 1)$ we obtain a surface which was called by Wright an "adaptive topography". If we suppose that the replacement of one generation by another is a continuous process so that time can be taken as continuous, it is easy to set up differential equations giving the rates of change of p and P with time in terms of W and its derivatives. From these it is easy to deduct that if (p,P) is an internal point of the square then:

(i) if the population is stationary, i.e. does not change with time, we must have

$$\partial W/\partial p = \partial W/\partial P = 0, \tag{2}$$

(ii) if such a stationary state is also to be stable, i.e. such that small deviations in p and P only result in the population returning to the stationary value, we must also have

$$\partial^2 W/\partial p^2 < 0, \quad \partial^2 W/\partial P^2 < 0, \tag{3}$$

$$(\partial^2 W/\partial p^2)(\partial^2 W/\partial P^2) > (\partial^2 W/\partial P \partial p)^2. \tag{4}$$

* Department of Statistics, Institute of Advanced Studies, Australian National University, Canberra.

This amounts to saying that a stationary state corresponds to a level point in the adaptive topography, and that a stable stationary point corresponds to a local maximum.

It is, however, possible to obtain stationary or stable points on the boundaries of the square, i.e. when one or more of p and P are equal to 0 or 1. Such cases require no special investigation since they reduce to the situation for a single locus which is well known. As an example we may consider the set of fitnesses

$$\begin{matrix} 1 & 2 & 1 \\ 2 & 0 & 2 \\ 1 & 2 & 1 \end{matrix}$$

which has four stationary stable points, namely $(0,\frac{1}{2})$, $(1,\frac{1}{2})$, $(\frac{1}{2},0)$, $(\frac{1}{2},1)$ at each of which only one of the equations (2) are satisfied. Clearly not more than four such stationary stable states are possible.

It is also clear that it is possible for stationary points to form a whole continuum of values as for example if the w_{ij} are independent of one or both of their suffixes. We shall, however, only consider cases where the stationary points are isolated, and the conditions on the w_{ij} which are necessary and sufficient for this to happen will appear later.

II. The Number of Stationary Points

Let N be the largest number of isolated stationary points strictly inside the unit square, and N_m the largest number of such points which are maxima. We shall show that $N = 5$, $N_m = 3$.

W is a quartic polynomial in p and P with the further restriction that powers of p and P greater than two do not occur. Somewhat simpler formulae are obtained if we write it in the form

$$\begin{aligned} W = {} & a_{00}+a_{01}p+a_{02}p^2 \\ & +a_{10}P+a_{11}pP+a_{12}p^2P \\ & +a_{20}P^2+a_{21}pP^2+a_{22}p^2P^2. \end{aligned} \tag{5}$$

The a_{ij} can be expressed in terms of the w_{ij} by sets of linear equations which are easily written down.

From the meaning of fitness we must have $w_{ij} \geqslant 0$. However, the conditions (2), (3), and (4) are unaltered by adding any finite positive or negative constant to all the W_{ij}, or by multiplying all the W_{ij} by the same positive constant. Hence we need impose no restrictions on the W_{ij} or the a_{ij}.

Equations (2) then become, using (5),

$$(a_{01}+a_{11}P+a_{21}P^2)+2p(a_{02}+a_{12}P+a_{22}P^2) = 0, \tag{6}$$

and

$$(a_{10}+a_{11}p+a_{12}p^2)+2P(a_{20}+a_{21}p+a_{22}p^2) = 0. \tag{7}$$

Similarly the conditions (3) and (4) become

$$\begin{aligned} a_{02}+a_{12}P+a_{22}P^2 < 0, \\ a_{20}+a_{21}p+a_{22}p^2 < 0, \end{aligned}$$

and

$$(a_{02}+a_{12}P+a_{22}P^2)(a_{20}+a_{21}p+a_{22}p^2) > (a_{11}+2a_{12}p+2a_{21}P+4a_{22}pP)^2. \quad (8)$$

We next show that the restrictions $0 < p < 1$, $0 < P < 1$ can be ignored. For suppose the function (5) has n stationary points of specified character in the whole plane $-\infty < p < \infty$, $-\infty < P < \infty$. Let L be a positive constant such that all the values of p and P at the n stationary points satisfy $|p| < L$, $|P| < L$. Then by transferring the origin to $(-L, -L)$ and rescaling we obtain a new set of values for the a_{ij} such that the corresponding W has the same number of stationary points of the same character in the square $(0 < p < 1,\ 0 < P < 1)$. Thus in determining N and N_m we can ignore these restrictions.

Suppose that W has exactly n stationary points of prescribed character. W is a continuous function of the a_{ij} and by considering its behaviour on circles of sufficiently small radii about each of these stationary points when the a_{ij} vary slightly, it is clear that there exists a constant $\delta > 0$ such that all W's defined by constants a'_{ij} satisfying

$$|a'_{ij}-a_{ij}| < \delta,$$

will have at least as many maxima, minima, and stationary points, in general, as the original W.

Given p, W is a quadratic function of P in general. However, it is only linear in P when p takes a value equal to one of the roots of the equation

$$a_{20}+a_{21}p+a_{22}p^2 = 0. \quad (9)$$

Similarly W becomes linear in p when P takes a value equal to one of the roots of

$$a_{02}+a_{12}P+a_{22}P^2 = 0. \quad (10)$$

By altering a_{01} and a_{10} if necessary, we can ensure that the equations (6) and (7) cannot be satisfied when p is a root of (9), or when P is a root of (10).

Equations (5) and (6) are cubic equations in the two unknowns. By the standard theorem of Bézout if these equations do not have a continuum of values they can have at most nine roots (van der Waerden 1931), and therefore $N_m \leqslant N \leqslant 9$. We shall show in fact, however, that $N \leqslant 5$.

To do this we solve (6) for p in terms of P, obtaining

$$p = -\tfrac{1}{2}(a_{01}+a_{11}P+a_{21}P^2)(a_{02}+a_{12}P+a_{22}P^2)^{-1}.$$

Substituting this in (7) and using the fact that (10) does not hold for any value of P corresponding to a stationary point we obtain an equation in P of the fifth degree. Whatever the number of stationary points there can be at most five distinct values of P corresponding to them. Furthermore for all these values of P, W is a strictly quadratic function of p, and has a unique stationary point. p is therefore determined uniquely in terms of P and there can be at most five stationary points.

N is in fact equal to 5, and this is shown by constructing a numerical example in which W actually has five stationary points. For this we take the w_{ij} as equal to

22	1	21
1	31	1
21	1	22

It can be verified that there are stationary points at (0·29487, 0·29487), (0·70513, 0·70513), (0·27201, 0·72799), (0·72799, 0·27201), and (0·5, 0·5). It is also easy to verify that the first four of these are saddle-points and the last a maximum.

III. The Number of Local Maxima

We now prove that $N_m = 3$. W can be written in the form

$$\begin{aligned} W &= (a_{00}+a_{10}P+a_{20}P^2)+p(a_{01}+a_{11}P+a_{21}P^2)+p^2(a_{02}+a_{12}P+a_{22}P^2) \\ &= k(P)+p\,h(P)+p^2\,g(P), \end{aligned} \tag{11}$$

where $k(P)$, $h(P)$, and $g(P)$ are quadratic functions of P. We assume as before that there is no stationary point with a value of P such that $g(P) = 0$.

For each value of P, other than the two roots of $g(P) = 0$, W will be a function of p with a single maximum or minimum at a finite value of p given by

$$\partial W/\partial p = h(P)+2p\,g(P) = 0, \tag{12}$$

so that

$$p = -\tfrac{1}{2}h(P)\,g(P)^{-1}.$$

Substituting this in (11) we obtain

$$W(P) = \tfrac{1}{4}g(P)^{-1}[4k(P)\,g(P)-h(P)^2], \tag{13}$$

which is a formula for the value $W(P)$, of W at the unique stationary point on the section of the surface W given by P constant and not a root of $g(P) = 0$.

Considered as a function of P, $W(P)$ will have a stationary value at, and only at, those values of P which are the values of P at the stationary points of W, the fitness surface. We have already seen that there can be at most five of these and we have arranged that none are roots of $g(P) = 0$. Moreover at these roots $h(P)$ is necessarily non-zero, and we can, by the previous argument, suppose that the roots are distinct.

It follows that on opposite sides of a root $g(P)$ will have different signs, and hence if $W(P)$ is increasing (or decreasing) in the left-hand neighbourhood of the root, it will be increasing (decreasing) in the right-hand neighbourhood. Although $W(P)$, as given by (13), can thus take infinite values it follows that maxima must be separated by minima, and since five stationary points are possible, not more than three of these can be maxima. Thus $N_m \leqslant 3$.

To show that $N_m = 3$ we construct an example to show that three maxima are actually possible, which is somewhat surprising. This is given by the values of w_{ij}:

0·79440	0·82880	0·79020
0·82880	0·79920	0·81410
0·79020	0·81410	0·80625

It can be verified that with these values of w_{ij}, W has maxima at exactly the points (0·2, 0·2), (0·6, 0·8), (0·8, 0·6), the values of the second derivatives being given by

	$\partial^2 W/\partial p^2$	$\partial^2 W/\partial P^2$	$\partial^2 W/\partial P \partial p$
(0·2, 0·2)	−0·018	−0·018	0
(0·6, 0·8)	−0·0675	−0·02	−0·036
(0·8, 0·6)	−0·02	−0·0675	−0·036

so that the conditions (3) and (4) are satisfied at all three points. Thus $N_m = 3$.

IV. General Remarks

The above methods unfortunately do not seem to extend to the corresponding problem with more than two unlinked loci. For a simple locus with more than two alleles it is already well known (Kimura 1956; Mandel 1959) that only one non-trivial stationary state is possible. For two alleles at two linked loci the dynamics of the system has been studied in detail by Lewontin and Kojima (1960) but not the number of possible maxima.

V. References

Kimura, M. (1956).—*Proc. Nat. Acad. Sci., Wash.* **42**: 336.

Lewontin, R. C., and Kojima, K. (1960).—*Evolution* **14**: 458.

Mandel, S. P. H. (1959).—*Heredity* **13**: 289.

Waerden, B. L. van der (1931).—"Moderne Algebra." (Springer: Berlin.)