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The study of multiallelic genetic systems by matrix methods

By C. CANNINGS*
Department of Statistics, University of Aberdeen

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1. INTRODUCTION

The study of the effect of natural selection on multiallelic loci presents problems of considerable complexity. Even when we confine our attention to a large random mating population, to one locus and to constant fertilities and viabilities from generation to generation we may find the problem intractable.

Studies of such systems must rely for the present on one of two approaches: (i) the development of results of a general nature (such as that of Cormack (1964), which is essentially equivalent to the solution given by Littlewood (1957) to a mechanical problem) which can be demonstrated using topological concepts, or (ii) the use of special features of the system under consideration, such as the increasing nature of the mean viability for the autosomal locus (Mandel, 1959).

In this paper we shall utilize the second approach. A general matrix notation for autosomal and sex-linked loci will be developed. This representation will enable us to recognize the similarities between each system, or special cases of the system, and the autosomal system treated by Mandel (1959*a*), Mulholland & Smith (1959) and Kingman (1961). We shall then be able to utilize the special features of the autosomal system, and the results thus derived, to make statements about the sex-linked locus, and various more general problems connected with the autosomal locus (e.g. differential viabilities for the two sexes).

2. THE AUTOSOMAL LOCUS

Notation

(i) The gametic arrays for the males and females will be represented by diagonal matrices. Thus in the case of a diallelic locus with alleles A and a and gametic array R.A. + S.a we shall simply write

$$\begin{pmatrix} \mathrm{R} & \mathrm{O} \\ \mathrm{O} & \mathrm{S} \end{pmatrix}.$$

These matrices will not in general be written in expanded form, but will be denoted by E and G for the females and males respectively.

(ii) The genotypic arrays will in general also be represented in the above manner, being denoted by P and Q for the females and males respectively.

* Present address: International Laboratory of Genetics and Biophysics, Pavia Section, c/o Istituto di Genetica, Università di Pavia, Italy.

(iii) U will denote a matrix for which $U_{ij} = 1$ for all i and j, I the unit matrix and $\mathbf{1}$ the unit vector.

3. FERTILITIES, VIABILITIES AND ASSORTATIVE MATING

Suppose we consider the population just before pairs are formed. As above the genotypic arrays are diagonal matrices P and Q. We may represent the array of pairs formed under a random mating system at PUQ, where the (i, j) element is P_iQ_j, the proportion of matings between a female of the ith genotype and a male of the jth. If mating now takes place, and the fertility of a pair formed by a female of the ith genotype, and a male of the jth is F_{ij} (where k, j are an ordered pair), then we simply weight each mating by its fertility so that the array

$$X = PFQ$$

represents the effective proportion of each mating (F being the matrix of F_{ij} elements). It should be pointed out that this system includes a type of assortative mating. The frequency of a particular mating has been given above as P_iQ_j, and the effective frequency due to fertility F_{ij} as $F_{ij}P_iQ_j$. We could, however, have considered the frequency of the mating as $F_{ij}P_iQ_j$, due to assortative mating, and treated the fertility as unity (or indeed any intermediate position). This has been pointed out by Cannings (1968*a*) for a system with two alleles. Although somewhat artificial this representation may allow meaningful investigation of complete assortative mating.

It is now necessary to decide what genotype frequencies will result from the mating array X. An example will best illustrate one way in which this might be done.

Suppose we have alleles A_1 and A_2, and hence three genotypes A_1A_1, A_1A_2 and A_2A_2. The array X is now

$$\begin{pmatrix} F_{11}P_1Q_1 & F_{12}P_1Q_2 & F_{13}P_1Q_3 \\ F_{21}P_2Q_1 & F_{22}P_2Q_2 & F_{23}P_2Q_3 \\ F_{31}P_3Q_1 & F_{32}P_3Q_2 & F_{33}P_3Q_3 \end{pmatrix}.$$

The X_{11} element contributes $A_1A_1'S$ alone, X_{12} and X_{21} contribute $\frac{1}{2}A_1A_1'S$, and X_{22} contributes $\frac{1}{4}A_1A_1'S$. If we pre- and post-multiply X by

$$\begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

we obtain

$$\begin{pmatrix} X_{11} & \frac{1}{2}X_{12} & 0 \\ \frac{1}{2}X_{21} & \frac{1}{4}X_{22} & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

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and so the sum of the elements of this matrix is the relative proportion of A_1A_1 genotypes. Thus we may write our recurrence formulae (a dashed symbol pertaining to the subsequent generation), as

$$\lambda P_1' = \mathbf{1}^T \left\{ \begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{pmatrix} \mathbf{x} \begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{pmatrix} \right\} \mathbf{1},$$

where λ is such that $\mathbf{1}^T P' \mathbf{1} = 1$; and

$$\lambda P_2' = \mathbf{1}^T \left\{ \begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{pmatrix} \mathbf{x} \begin{pmatrix} 0 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 1 \end{pmatrix} \right\} \mathbf{1},$$

and

$$\lambda P_3' = \mathbf{1}^T \left\{ \begin{pmatrix} 0 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 1 \end{pmatrix} \mathbf{x} \begin{pmatrix} 0 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 1 \end{pmatrix} \right\} \mathbf{1}.$$

As will be easily seen, the diagonal elements of the matrix

$$\begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

simply correspond to the proportion of A_1 gametes produced by A_1A_1, A_1A_2, that is 1, $\frac{1}{2}$, 0, and pre- and post-multiplication by such matrices specifies both segregation and the union of gametes. We could thus introduce non-random segregation of gametes by adjusting these matrices. For example, pre- and post-multiplication by

$$\begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{3} & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad \begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{2}{3} & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

would correspond to the situation in which the female heterozygote produced $\frac{1}{3}A_1$ and $\frac{2}{3}A_2$, while the male produced $\frac{2}{3}A_1$ and $\frac{1}{3}A_2$. The relevance of this to the union of gametes will be seen later in connexion with the sex-linked locus. The generalization of this method to multiallelic systems is straightforward and needs no elaboration here.

The addition of differential viabilities to this representation is straightforward. If we regard the genotype matrix P as being at birth then in order to obtain that at maturity we simply take VP, where V is a diagonal matrix of viabilities. Thus we have

$$X^* = VPFQY, \tag{1}$$

where Y is the matrix of viabilities for the males. Separation of the genotype frequencies can be carried out as above.

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This representation has two possible uses. It may be of value in computer studies of models involving fertilities when subroutines for matrix multiplication are available, and it may also allow special cases to be treated, one such case will be considered below.

If $F = U$ in (1) then we have a system in which selection is exerted through the viabilities alone. Similarly, when $F = JUH$, for J and H diagonal, we have

$$X^* = (VPJ)\ U(HQX) \tag{2}$$

and this is essentially the same as (1) with $F = U$, and viability matrices VJ and HX. Thus we see that this special case (that of multiplicative fertilities) gives rise to a system of equations equivalent to that of viabilities alone, where these viabilities differ for the two sexes. This result was given by Bodmer (1965).

(i) *Viabilities*

We shall now ignore fertility differences, except in as much as some of the models below have been shown already to be equivalent to special cases of fertility differences.

As before our gametic arrays are taken as the diagonal matrices E and G. These are taken to be the arrays at maturity; that is, after viability differences have had their effect. The viabilities will be represented as matrices A and B for the females and males respectively. Thus the genotype consisting of the ith and jth alleles will have viabilities A_{ij} and B_{ij} in the females and males respectively (we shall assume $A_{ij} = A_{ji}$ and $B_{ij} = B_{ji}$).

In the subsequent generation at maturity

$$KE'\mathbf{1} = \tfrac{1}{2}(EAG + GAE)\ \mathbf{1} \tag{3}$$

and

$$MG'\mathbf{1} = \tfrac{1}{2}(EBG + GBE)\ \mathbf{1}, \tag{4}$$

where K and M are such that $\mathbf{1}^T E'\mathbf{1} = 1$ and $\mathbf{1}^T G'\mathbf{1} = 1$. These equations must be equivalent to (2).

We may derive these two relationships in an analogous manner to that used with fertility differences. Random pairing of genotypes followed by selection in the form of fertilities led to an array PFQ. Similarly random pairing of gametes followed by selection in the form of viabilities leads to an array EAG. For two alleles the array $\frac{1}{2}(EAG + GAE)$ becomes

$$\begin{pmatrix} A_{11}E_1G_1 & A_{12}(E_1G_2 + E_2G_1) \\ A_{12}(E_1G_2 + E_2G_1) & A_{22}E_2G_2 \end{pmatrix}.$$

Collection together of all terms corresponding to one allele involves addition of all the elements in the corresponding row. This is done by post-multiplying by $\mathbf{1}$ to give (3). Equation (4) is similarly derived.

We shall denote equilibrium by use of $\hat{}$ above the appropriate symbol. For equilibrium we simply require that $E = E' = \hat{E}$ and $G = G' = \hat{G}$ so (3) and (4) become

$$\left.\begin{aligned} \hat{K}\hat{E}\mathbf{1} &= \tfrac{1}{2}(\hat{E}A\hat{G} + \hat{G}A\hat{E})\ \mathbf{1} \\ \text{and} \qquad \hat{M}\hat{G}\mathbf{1} &= \tfrac{1}{2}(\hat{E}B\hat{G} + \hat{G}B\hat{E})\ \mathbf{1} \end{aligned}\right\}. \tag{5}$$

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It is unclear how a solution of these equations might be obtained, and indeed there will in many cases be no unique solution (Owen, 1953). Some insight may be gained by considering special cases.

We first consider the problem of stability.

Consider $KE'\mathbf{1} = \frac{1}{2}(EAG+GAE)\,\mathbf{1}$. Suppose that the frequencies E and G are $\hat{E}+\delta$ and $\hat{G}+\Delta$ respectively, where δ and Δ are diagonal matrices, $\mathbf{1}^T\delta\mathbf{1} = 0$ and $\mathbf{1}^T\Delta\mathbf{1} = 0$. We shall neglect terms of the second, and higher, orders in δ and Δ (i.e. δ^2, Δ^2 and $\delta\Delta$). Then

$$\begin{aligned}(EAG+GAE) &= (\hat{E}+\delta)\,A(\hat{G}+\Delta)+(\hat{G}+\Delta)\,A(\hat{E}+\delta),\\ &= (\hat{E}A\hat{G}+\hat{G}A\hat{E})+(\delta A\hat{G}+\hat{G}A\delta)+(\Delta A\hat{E}+\hat{E}A\Delta)\\ &\qquad +\text{higher-order terms.}\end{aligned}$$

It follows that K, which we shall write as $\hat{K}+\delta K$, is equal to

$$\begin{aligned}\hat{K}+\delta K &= \tfrac{1}{2}\mathbf{1}^T(EAG+GAE)\,\mathbf{1},\\ &= \tfrac{1}{2}\mathbf{1}^T(\hat{E}A\hat{G}+\hat{G}A\hat{E})\mathbf{1}+\tfrac{1}{2}\mathbf{1}^T\,(\delta A\hat{G}+GA\delta)\\ &\qquad +\tfrac{1}{2}\mathbf{1}^T(\Delta A\hat{E}+\hat{E}A\Delta)\,\mathbf{1}+\text{higher-order terms},\end{aligned}$$

the first term of the right-hand side corresponding to K, the rest to δK. Thus if we write $E' = \hat{E}+\delta'$ we have

$$(\hat{K}+\delta K)\,(\hat{E}+\delta')\mathbf{1} = \tfrac{1}{2}(EAG+GAE)\,\mathbf{1}$$

and so

$$\begin{aligned}(\hat{K}\delta')\mathbf{1} &= \tfrac{1}{2}(\delta A\hat{G}+\hat{G}A\delta)\,\mathbf{1}-\tfrac{1}{2}\hat{E}\,\{\mathbf{1}^T(\delta A\hat{G}+\hat{G}A\delta)\,\mathbf{1}\}\;\mathbf{1}\\ &\qquad +\tfrac{1}{2}(\Delta AE+EA\Delta)\,\mathbf{1}-\tfrac{1}{2}E\{\mathbf{1}^T(\Delta AE+GA\Delta)\,\mathbf{1}\}\,\mathbf{1}. \qquad (6)\end{aligned}$$

There will be another equation in which $\hat{M}$ is substituted for $\hat{K}$, Δ for δ', $\hat{E}$ for $\hat{G}$, $\hat{G}$ for $\hat{E}$ and B for A.

The second half of the right-hand side of (6) is identical to the first half if $\hat{E} = \hat{G}$ except for Δ replacing δ. Rearrangement of (6) into an expression of the form

$$\boldsymbol{\delta}' = (C \quad C)\,\boldsymbol{\delta} \qquad (7)$$

is then possible, where $\boldsymbol{\delta}'$, $\boldsymbol{\delta}$ and $\boldsymbol{\Delta}$ are vectors containing the same elements as the diagonals of the corresponding matrices, and C is a matrix defined so as to make (6) and (7) equivalent. There will be a further equation for $\boldsymbol{\Delta}'$ of the same form so that

$$\begin{pmatrix}\boldsymbol{\delta}'\\ \boldsymbol{\Delta}'\end{pmatrix} = \begin{pmatrix}C & C\\ D & D\end{pmatrix}\;\begin{pmatrix}\boldsymbol{\delta}\\ \boldsymbol{\Delta}\end{pmatrix},$$

where D is defined in terms of $\boldsymbol{\Delta}'$ in a similar way to C in terms of $\boldsymbol{\delta}'$.

This special form will be of considerable importance in the consideration of special cases.

C and D will be referred to as generation matrices, and differ only by a factor of $\frac{1}{2}$ from the generation matrices obtained in the corresponding autosomal cases when A is the viability matrix for both sexes, and when B is the viability matrix for both sexes. That this is so can be seen quite simply from equation (6). The con-

sideration of the case of equal viabilities in the sexes reduces equations (3) and (4) to the form

$$KE' = KG' = EAE\mathbf{1},$$

a case discussed in some detail below. If in (6) we put $\hat{G} = \hat{E}$, $\delta = \Delta$, we have

$$K\delta'\mathbf{1} = EA\delta + \delta AE - E(\mathbf{1}^T(EA\delta + \delta AE)\mathbf{1})\mathbf{1},$$

which can clearly be written as

$$\boldsymbol{\delta}' = 2C\boldsymbol{\delta},$$

where C is identical to that defined above.

The stability of the system may now be determined in the usual way, by evaluating the latent roots of the generation matrix, in conjunction with the conditions $\mathbf{1}^TE\mathbf{1} = \mathbf{1}^TG\mathbf{1} = 1$, although in practice this may be intractable. However, we have shown that when $\hat{E} = \hat{G}$ the generation matrix takes a special form closely related to the simpler case of equal viabilities in the two sexes. This will allow us to utilize the results on the stability of the latter system to study the stability of special cases of the former.

(ii) *Special cases*

(i) $A = B$ reduces the system to identical viabilities for the two sexes. We obtain:

$$KE'\mathbf{1} = \tfrac{1}{2}(EAG + GAE)\,\mathbf{1} = MG'\mathbf{1}$$

and hence after one generation the gametic arrays in the two sexes are identical. Equation (5) then reduces to

$$KE'\mathbf{1} = EAE\mathbf{1},$$

and so for equilibrium

$$K\hat{E}\mathbf{1} = \hat{E}A\hat{E}\mathbf{1}. \tag{8}$$

The solution of this can be obtained using Cramers' rule (Mirsky (1955), p. 134; Birkhoff & MacLane (1959), p. 306). Thus

$$\hat{E}\mathbf{1} = \frac{A^{-1}\mathbf{1}}{\lambda},$$

where

$$\lambda = \mathbf{1}^TA^{-1}\mathbf{1}.$$

Tallis (1966) has obtained this result independently and by a somewhat different method. The equation is of course equivalent to that of Mandel (1959, equation 6).

The conditions for stability and convergence of the gene frequencies have been obtained by Mandel (1959), Mulholland & Smith (1959) and Kingman (1961). These conditions correspond to the conditions for K to be maximized at equilibrium, that is for

$$K = \mathbf{1}^T(EAE)\,\mathbf{1}$$

to be maximized, and are equivalent to the condition that the latent roots of the generation matrix lie in $(-1, +1)$.

(ii) $B = U$ is equivalent to selection acting amongst the females only. From equation (4) we obtain

$$MG'\mathbf{1} = \tfrac{1}{2}(EUG+GUE)\mathbf{1} \tag{9}$$

and so $M = 1$. Further expansion of (9) shows that $G'_i = \frac{1}{2}(G_i+E_i)$ and so

$$G' = \tfrac{1}{2}(G+E). \tag{10}$$

Equilibrium occurs when $G' = G = \hat{G}$ which implies, from (10), that $\hat{E} = \hat{G}$.

Thus

$$K\hat{E}\mathbf{1} = \hat{E}A\hat{E}\mathbf{1}$$

which is equivalent to equation (8). Thus

$$\hat{E}\mathbf{1} = \frac{A^{-1}\mathbf{1}}{\mathbf{1}^T A^{-1}\mathbf{1}}$$

and K^* is maximized at equilibrium, where $K = \mathbf{1}^T EAE\mathbf{1}$.

In a situation where $\hat{E} = \hat{G}$ we have argued that the generation matrix can be written as

$$\begin{pmatrix} C & C \\ D & D \end{pmatrix},$$

where C and D are one-half of the generation matrices obtained for equal selection in the two sexes.

In this case $B = U$, i.e. $B_{ij} = 1$ and since no changes will occur in gamete frequencies when no selection is acting in either sex $D = \frac{1}{2}I$. Thus we have a generation matrix

$$\begin{pmatrix} C & C \\ \frac{1}{2}I & \frac{1}{2}I \end{pmatrix} \quad \text{or more simply} \quad \frac{1}{2}\begin{pmatrix} C & C \\ I & I \end{pmatrix},$$

where C is now exactly equivalent to the generation matrix for equal selection in the two sexes.

We can now apply Theorem 1 of the Appendix. The non-zero latent roots of

$$\begin{pmatrix} C & C \\ I & I \end{pmatrix} \quad \text{are} \quad \lambda_i = 1+\mu_i,$$

where μ is a latent root of C for $i = 1, \ldots, n$. Thus the non-zero latent roots of

$$\frac{1}{2}\begin{pmatrix} C & C \\ I & I \end{pmatrix} \quad \text{are} \quad \tfrac{1}{2}\lambda_i = \tfrac{1}{2}(1+\mu_i) \quad (i = 1, 2, \ldots, n).$$

If $\mu_i \in (-1, +1)$ then $\frac{1}{2}\lambda_i \in (0, +1)$ and conversely. Stability in the corresponding autosomal case implies that all $\mu_i \in (-1, +1)$ and this in term implies that $\frac{1}{2}\lambda_i \in (0, +1)$ and hence $\frac{1}{2}\lambda \in (-1, +1)$. Thus the conditions on the viability matrix A which Mandel (1959*a*), Mulholland & Smith (1959) and Kingman (1961) have derived as necessary and sufficient for stability are sufficient in this case. However, $\frac{1}{2}\lambda_i \in (-1, +1)$ implies only that $\mu_i \in (-3, +1)$ and so the conditions on A for stability in the associated case are not necessary for stability (at least not as demonstrated by the above treatment).

If, however, we can demonstrate that λ_i is necessarily positive then the necessary and sufficient conditions for stability must be identical. This situation arises in the case of two alleles, when indeed the conditions are also sufficient for convergence. This result has been proved by the author (Cannings, 1969) using a generalization of a monotonicity argument previously applied to the sex-linked locus (Cannings, 1967).

(iii) *A and B diagonal. Heterozygote elimination in both sexes*

Thus $a_{ij} = b_{ij} = 0$ if $i \neq j$ and we write a_{ii} as a_i, $b_{ii} = b_i$. Since A and B are diagonal matrices we may write

$$KE' = AEG \quad \text{and} \quad MG' = BEG.$$

Putting $L = KM$ and $H = EG$ (L being a constant and H a diagonal matrix) we have on multiplying the two forms together.

$$LH' = (AB)\,H^2, \tag{11}$$

which is essentially a matrix equivalent of a geometric progression. Using a subscript to denote the generation under consideration we have

$$L_n H_{n+1} = (AB)^{2^n-1} H_1^{2n} \quad \text{for} \quad n \geqslant 1.$$

Note that equation (11) is precisely the form we should obtain with heterozygote elimination in one sex only (the diagonal elements being simply $a_i b_i$). Now

$$K_{n+1} E_{n+2} = A E_{n+1} G_{n+1} = A H_{n+1},$$

and so

$$\left(\frac{K_n + 1}{L_n}\right) E_{n+2} = A(AB)^{2^n-1} (E_1 G_1)^{2^n} \quad \text{for} \quad N \geqslant 1 \tag{12}$$

with a similar expression for G_{n+2}.

For equilibrium we have

$$M\hat{E} = A\hat{E}\hat{G} \quad \text{and} \quad N\hat{G} = B\hat{G}\hat{E}$$

and hence (denoting the ith and jth elements of $\hat{E}$ and $\hat{G}$ by $\hat{E}_i^*$, etc.

$$\frac{\hat{E}_i^*}{\hat{E}_j^*} = \frac{b_j}{b_i} \quad \text{and} \quad \frac{\hat{G}_i^*}{\hat{G}_j^*} = \frac{a_j}{a_i}$$

provided $\hat{E}_i$, $\hat{E}_j$, $\hat{G}_i$, $\hat{G}_j$ are non-zero. Suppose that for $R \in S_R$ (a set of integer) $\hat{E}_R^*$ and $\hat{G}_R^*$ are non-zero and for $R \notin S_R$ $\hat{E}_R^* = \hat{G}_R^* = 0$. Thus for $R \in S_R$

$$\hat{E}_R = \frac{1/b_R}{\sum\limits_{R \in S_R} \frac{1}{a_R}} \quad \text{and} \quad \hat{G}_R = \frac{1/a_R}{\sum\limits_{R \in S_R} \frac{1}{a_R}}. \tag{13}$$

To investigate to which equilibrium the system will converge (i.e. to specify the set S_R) is a simple matter if we rearrange (11) as

$$L_n H_{n+1} = (ABH_1)^{2n-1} H_1 \quad \text{for} \quad n \geqslant 1.$$

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It is now clear that $\hat{H}$ will have non-zero elements on the diagonal corresponding to the dominant latent roots of ABH_1, and zeros elsewhere. Thus S_R is specified by the set of integers R such that

$$a_R b_R H^*_{IR} = \max_{\text{All } i} (a_i b_i H^*_{1i}),$$

where H^*_{1R} and H^*_{1i} denote the Rth and ith values from the initial gametic arrays.

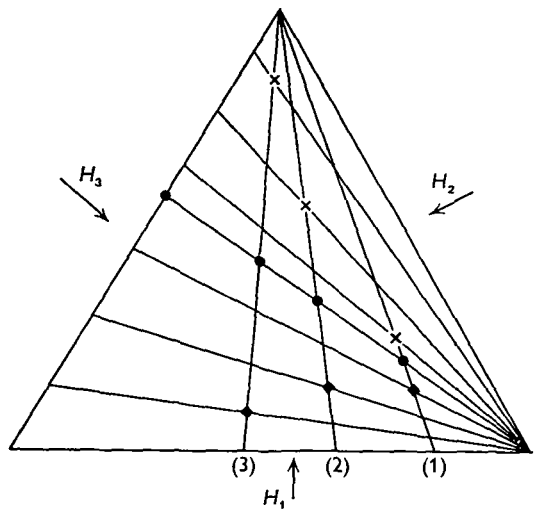

Fig. 1. Heterozygote elimination in both sexes. Three generations for initial values such that ×, $A_1B_1H_1 > A_2B_2H_2 > A_3B_3H_3$; ●, $A_1B_1H_1 = A_2B_2H_2 > A_3B_3H_3$; ◆, $A_2B_2H_2 > A_1B_1H_1 > A_3B_3H_3$.

Moreover, for $i, j \in S_R (H^*_i/H^*_j)$ is a constant from generation to generation and $\sum_{R \in S_R} H^*_R$ increases monotonically. The ratio H^*_l/H^*_m may also be constant for l, $m \notin S_R$.

The equilibrium to which the system converges may not be stable. A slight perturbation to H will cause a change in ABH which may produce a new set of maximum latent roots. The only stable equilibria are those for which only one allele exists (not necessarily the one with the highest value $a_i b_i$).

Example: 3 alleles

Suppose we use a slight modification of the Streng diagram, plotting H_1, H_2 and H_3 as the homogeneous co-ordinates. Then we obtain a picture such as Fig. 1.

(iv) *No additive dominance in fitness*

We consider now the situation in which the viability of a genotype is composed of a contribution from each of the gametes constituting that genotype. The contributions will be added, and this situation is referred to as that of no additive

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dominance. Thus $A_{ij} = B_{ij} = A_i + A_j$, where A_i, $i = 1, 2, \ldots, K$ (K being the number of alleles). The behaviour of this system is to some extent covered by the results of Mandel (1959*a*), Mulholland & Smith (1959) and Kingman (1961).

We have

$$\begin{aligned} VE'\mathbf{1} &= EAE\mathbf{1} \\ &= E(\mathbf{A}\mathbf{1}^T + \mathbf{1}\mathbf{A}^T)\, E\mathbf{1}, \end{aligned}$$

where $\mathbf{A}^T = (A_1, A_{21}, \ldots, A_k)$.

Thus

$$\begin{aligned} VE'\mathbf{1} &= E\mathbf{A}\,(\mathbf{1}^T E\mathbf{1}) + E(\mathbf{1}^T \mathbf{A} E\mathbf{1}) \\ &= E(\mathbf{A} + \Delta\mathbf{1}), \end{aligned}$$

since $\mathbf{1}^T E\mathbf{1} = 1$ and defining $\Delta = \mathbf{1}^T \mathbf{A} E\mathbf{1}$, the mean value of A_i. Also we have

$$\begin{aligned} V &= \mathbf{1}^T EAE\mathbf{1} \\ &= \mathbf{1}^T\, E\mathbf{A}\mathbf{1} + \mathbf{1}^T \Delta\mathbf{1} \\ &= 2\Delta \end{aligned}$$

and so

$$E'\mathbf{1} = E\left\{\frac{A + \Delta\mathbf{1}}{2\Delta}\right\}.$$

This implies that an allele, for which the corresponding A_i exceeds the mean of the A_i'S, will have an increased frequency in the next generation. Thus only one allele (corresponding to the largest A_i) can exist at equilibrium. Convergence of the gene frequencies will be monotonic for the gametes corresponding to the largest and to the smallest A_i'S, but need not be so for other alleles.

(v) *The sex-linked locus*

(*a*) *Notation*

For convenience we shall consider the female to be the homogametic sex.

(i) As for the autosomal locus we shall represent both gametic arrays and genotypic arrays by diagonal matrices. The symbols P and Q will be used for genotypic arrays, and E and G will be used for gametic arrays.

(ii) As before, the viability matrices for the females and males will be denoted by A and B. In this case since the males are the heterogametic sex the viability matrix B will be diagonal.

(*b*) *Fertilities and viabilities*

In the case of a sex-linked locus there are differing numbers of genotypes for the males and females. Thus the genotypic arrays P and Q will not have the same number of rows, and so F, the matrix of fertilities (defined in a similar way to that for the autosomal locus) will not be a square matrix. This fact does not affect the form of the effective mating array, which is given by

$$X = PFQ.$$

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In order to find the frequency of a specific genotype in the next generation we adopt a similar procedure to that for the autosomal locus. For a diallelic locus we find the three genotypic frequencies by evaluating

$$\lambda P_1' = \mathbf{1}^T \left\{ \begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{pmatrix} PFQ \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \mathbf{1} \right\}, \tag{14}$$

where P_1' corresponds to the frequency of the first genotype (homozygote). As before, non-random segregation in the females can be introduced by suitable adjustment of the matrix

$$\begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

Two similar expressions give the frequencies of the other two genotypes.

The new genotype array for the males is obtained from expressions of the form

$$\lambda Q_1' = \mathbf{1}^T \left\{ \begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{pmatrix} PFQ \right\} \mathbf{1}. \tag{15}$$

As we indicated earlier, the process of pre- and post-multiplication by these matrices corresponds to both segregation and random union of gametes. The male genotypes are formed in this situation simply from the female gametes, and so the segregation of the male gametes is irrelevant. We therefore must pre-multiply by an appropriate matrix, but no post-multiplication is necessary.

The addition of viabilities to the system is performed in a similar manner to the autosomal case. We then have

$$X^* = (VP)\, F(QY),$$

where V and Y are diagonal matrices of viabilities. If we put $F = JUH$ (J and H being diagonal) we obtain

$$X^* = (VPJ)\, U(HQX).$$

Thus multiplicative fertilities are seen to be equivalent to viability differences (the sexes, of necessity, having different viabilities).

(c) Viabilities

We now concentrate on studying the effect of viability differences alone in the absence of fertility differences (other than multiplicative ones). As with the autosomal locus, this will enable us to work in terms of gametic arrays. We can write the expression for the gene frequencies in one generation in terms of those in the previous in the following form

$$KE'\mathbf{1} = \tfrac{1}{2}\{EAG + GAE\}\, \mathbf{1} \tag{16}$$

and

$$MG'\mathbf{1} = BE\mathbf{1}, \tag{17}$$

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where K and M are such that $\mathbf{1}^T E' \mathbf{1} = \mathbf{1}^T G' \mathbf{1} = 1$. The $\mathbf{1}$'s are included in (17) only to retain a similar form to previous expressions. In fact, since G', B and E are diagonal, we may write

$$MG' = BE,$$

and substituting for MG' into the formula for $K'E''$ (the next generation) derived from (16) gives

$$(K'M)\, E''\mathbf{1} = \tfrac{1}{2}\,(E'ABE + EBAE')\,\mathbf{1}. \tag{18}$$

For equilibrium we put $E = E' = E'' = \hat{E}$, and so

$$M\hat{K}\hat{E}\mathbf{1} = \tfrac{1}{2}\hat{E}(AB+BA)\,\hat{E}\mathbf{1}. \tag{19}$$

This equation together with

$$\hat{N}\hat{G} = B\hat{E}$$

is equivalent to equation (4) of Sprott (1957). We can immediately write down an expression for $\hat{E}$ in terms of A and B as we did for equation (8).

We have that

$$\hat{E}\mathbf{1} = \frac{(AB+BA)^{-1}\mathbf{1}}{\mathbf{1}^T(AB+BA)^{-1}\mathbf{1}}. \tag{20}$$

This result has been previously published by the author (Cannings, 1968) and is also contained in Mandel (1959*b*) in summation form.

We can evaluate the equilibrium by recognizing that they are simply those obtained in the autosomal case, with viability matrix $\frac{1}{2}(AB+BA)$ in both sexes. Tallis (1966) has discussed this problem in some detail.

As an example we take a situation related to one discussed by Tallis (1966) and due to Wright (Li, 1955). Suppose we have

(i)
$$A = \begin{pmatrix} 1-S_1 & 1 & 1 \\ 1 & 1-S_2 & 1 \\ 1 & 1 & 1-S_3 \end{pmatrix}, \quad B = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix},$$

and

(ii)
$$A = \begin{pmatrix} 1-S_1 & 2/3 & 1 \\ 2/3 & (1-S_2)/2 & 2/3 \\ 1 & \frac{2}{3} & 1-S_3 \end{pmatrix}, \quad B = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 2 & 0 \\ 0 & 0 & 1 \end{pmatrix}.$$

In both cases

$$\tfrac{1}{2}(AB+BA) = \begin{pmatrix} 1-S_1 & 1 & 1 \\ 1 & 1-S_2 & 1 \\ 1 & 1 & 1-S_3 \end{pmatrix},$$

the viability matrix discussed by Tallis (1966). We have seven possible equilibria

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for the females and two sets of equilibria for the males corresponding to case (i) and (ii). These are given below

(*d*) *Equilibrium gene frequencies*

	Male and female (i)	Male (ii)
(1)	$\hat{E}_1 = 1$	$\hat{G}_1 = 1$
(2)	$\hat{E}_2 = 1$	$\hat{G}_2 = 1$
(3)	$\hat{E}_3 = 1$	$\hat{G}_3 = 1$
(4)	$\hat{E}_1 = \dfrac{S_1^{-1}}{S_1^{-1}+S_2^{-1}}$ and $\hat{E}_2 = \dfrac{S_2^{-1}}{S_1^{-1}+S_2^{-1}}$	$\hat{G}_1 = \dfrac{S_1^{-1}}{S_1^{-1}+2S_2^{-1}}$ and $\hat{G}_2 = \dfrac{2S_2^{-1}}{S_1^{-1}+2S_2^{-1}}$
(5)	$\hat{E}_2 = \dfrac{S_2^{-1}}{S_2^{-1}+S_3^{-1}}$ and $\hat{E}_3 = \dfrac{S_3^{-1}}{S_2^{-1}+S_3^{-1}}$	$\hat{G}_2 = \dfrac{2S_2^{-1}}{2S_2^{-1}+S_3^{-1}}$ and $\hat{G}_3 = \dfrac{S_3^{-1}}{2S_2^{-1}+S_3^{-1}}$
(6)	$\hat{E}_1 = \dfrac{S_1^{-1}}{S_2^{-1}+S_3^{-1}}$ and $\hat{E}_3 = \dfrac{S_3^{-1}}{S_1^{-1}+S_3^{-1}}$	$\hat{G}_1 = \dfrac{S_1^{-1}}{S_1^{-1}+S_3^{-1}}$ and $\hat{G}_3 = \dfrac{S_3^{-1}}{S_1^{-1}+S_3^{-1}}$
(7)	$\hat{E}_i = \dfrac{S_i^{-1}}{S_1^{-1}+S_2^{-1}+S_3^{-1}}$ for $i = 1, 2, 3$	$\hat{G}_1 = \dfrac{S_1^{-1}}{S_1^{-1}+2S_2^{-1}+S_3^{-1}}$, $\hat{G}_2 = \dfrac{2S_2^{-1}}{S_1^{-1}+2S_2^{-1}+S_3^{-1}}$ and $\hat{G}_3 = \dfrac{S_3^{-1}}{S_1^{-1}+2S_2^{-1}+S_3^{-1}}$

(*e*) *Stability*

Since equation (16) is identical to equation (3), the part of the generation matrix corresponding to (16) will be that given by equation (6). Thus

$$(\hat{K}\delta')\,\mathbf{1} = \tfrac{1}{2}(\delta A\hat{G}+\hat{G}A\delta)\,\mathbf{1}-\tfrac{1}{2}\hat{E}\{\mathbf{1}^T(\delta A\hat{G}+\hat{G}A\delta)\,\mathbf{1}\}\,\mathbf{1} + \tfrac{1}{2}(\Delta A\hat{E}+\hat{E}A\Delta)\,\mathbf{1}-\tfrac{1}{2}\hat{E}\{\mathbf{1}^T(\Delta A\hat{E}+\hat{E}A\Delta)\,\mathbf{1}\}\,\mathbf{1} \qquad (21)$$

when we neglect higher terms. Also

$$\hat{M}\Delta' = B\delta-\mathbf{1}^T(B\delta)\,\mathbf{1}\hat{G}. \qquad (22)$$

As before, if $\hat{G} = \hat{E}$ we have an expression of the form

$$\boldsymbol{\delta}' = (C \quad C)\begin{vmatrix}\boldsymbol{\delta}\\ \boldsymbol{\Delta}\end{vmatrix},$$

where $\boldsymbol{\delta}'$ and $\boldsymbol{\Delta}$ are vectors corresponding to the diagonal matrices used immediately above. The matrix C is identical to that in (7), and as there, differs only by a factor of $\frac{1}{2}$ from that obtained for an autosomal locus with equal viabilities in the two sexes.

Equations (21) and (22) are essentially the same as those given by Sprott (1957). He derived a necessary and sufficient condition for stability and also a simpler necessary condition. However, although the latter is dependent only on relative viabilities, the former depends also on the equilibrium position. His necessary condition corresponds to the condition that $\mathbf{1}^T\{\hat{E}(AB+BA)\hat{E}\}\,\mathbf{1}$ should be maximized at equilibrium, as has been pointed out by Li (1967).

We now turn our attention to various special cases.

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(vi) *Selection in the heterogametic sex only: $A = U$*

The only allele which survives is that whose 'viability' is greatest, i.e. corresponding to $B_i = \max_{j=1,N} \{B_j\}$, where N is the number of alleles.

If one examines the matrix $(AB+BA)$ for $A = U$ one obtains

$$\begin{pmatrix} 2B_1 & B_1+B_2 & B_1+B_2 & & B_1+B_N \\ B_1+B_2 & 2B_2 & B_2+B_3 & & . \\ . & . & . & & . \\ . & . & . & & . \\ . & . & . & & . \\ B_1+B_N & . & . & & 2B_N \end{pmatrix}$$

which is the matrix obtained when there is no additive dominance in the autosomal case. However, the behaviour of the system is somewhat different in this situation.

We have on rearranging (16) and (17)

$$E' = \tfrac{1}{2}(E+G),$$

$$G' = \frac{BE}{\mathbf{1}^T(BE)\,\mathbf{1}}.$$

Thus the frequency of ith allele in the females is simply the mean of the male and female frequencies in the previous generation. Also it is clear that for the allele which will ultimately be established in the population (i.e. corresponding to max (Bi's)) $G_i' > E_i$ for every generation and so

$$E_1'' = \tfrac{1}{2}(E_i'+G_i')$$

implies that $E_i'' > \tfrac{1}{2}(E_i'+E_i)$ for all generations.

It follows immediately that at least after the first generation both E_i and G_i will increase monotonically. Similar reasoning will demonstrate that E_j and G_j, corresponding to the minimum of the B_K's, will decrease monotonically after the first generation. The behaviour of other frequencies may be oscillatory for a number of generations before going to zero. In any particular case it is a simple matter to follow this behaviour, though it is difficult to see how any general statements can be made—for example, about how many oscillations occur.

(vii) *Selection in the homogametic sex only, $B = I$*

Equation (18) becomes

$$V''E\,\mathbf{1} = \tfrac{1}{2}(E'AE+EAE')\,\mathbf{1},$$

(17) gives $G' = E$, where V is introduced instead of $(K'M)$ for convenience. The equilibrium is thus the same as that for the autosomal locus with viability matrix A in both sexes. It is of interest to investigate the stability of this equilibrium.

We have seen that a simplification of the generation matrix is possible when $\hat{E} = \hat{G}$. Also, since $B = I$, equation (22) takes the form,

$$\Delta = \delta,$$

M being equal to unity.

The generation matrix is now

$$\begin{pmatrix} C & C \\ I & O \end{pmatrix},$$

where C is as before half the generation matrix obtained in the corresponding autosomal case. The necessary and sufficient conditions for stability are thus that the latent roots lie in $(-1, +1)$ (except for those which equal 1 as a result of the total gene frequencies being 1). We have the determinantal equation

$$\begin{pmatrix} C-\lambda I & C \\ I & -\lambda I \end{pmatrix} = 0 \tag{23}$$

and the expansion of this form has been treated in Theorem 2 of the Appendix. The latent roots of C are $\mu_i/2$ where μ_i derives from the corresponding autosomal case. The latent roots from (23) are given by the roots of the quadratic equation in λ_j

$$2\lambda_j^2 - \lambda_j\mu_j - \mu_j = 0 \quad \text{for} \quad j = 1, 2, \ldots, m, \tag{24}$$

the number of alleles. Thus

$$\lambda_j = \tfrac{1}{4}\{\mu_j \pm \sqrt{(\mu_j^2 + 8\mu_j)}\},$$

which is real for $\mu_j \geqslant 0$ and complex for $\mu_j < 0$.

For $\mu_j \in [0, 1)$ we have that $\lambda_j \in [-\frac{1}{2}, 1]$. If $\mu_j \in [-1, 0)$ put $\mu_j^* = -\mu_j$ then

$$\begin{aligned} |\lambda_j|^2 &= \tfrac{1}{16}|\{\mu_j^{*2} + \mu_j^{*2} - 8\mu_j^*\}| \\ &= \tfrac{1}{16}|2\mu_j^{*2} - 8\mu_j^*|, \end{aligned}$$

since $\mu_j^* \in (0, 1]$, $|\lambda_j| \in (0, \sqrt{(6)}/4)$. Thus $|\mu_j| \in [0, +1]$ implies that $|\lambda_j| \in [0, 1]$ and the necessary and sufficient conditions for stability at the autosomal locus, are sufficient, but not necessary, for stability in this case. Once again the conditions are necessary for the diallelic case since then it is necessary that λ_j should lie in $[0, 1]$.

SUMMARY

A matrix notation is developed to facilitate study of natural selection in large populations. The processes of mating (taking into account differences between genotypes in fertility in both sexes), segregation, and differential viabilities are each expressed in matrix notation. Assortative mating and non-random segregation can also be described by the method. The separate processes can then be combined to give simple equations relating the genic and genotypic frequencies in one generation to those in the previous generation. This will facilitate computer treatment of natural selection processes.

The method can also be used to study equilibria and the conditions of their

stability by examining the latents roots of the matrix. Several special cases of selection at an autosomal locus are examined. The method can be extended to sex-linked loci and two special cases are discussed.

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APPENDIX

Theorem 1

If G is an $n \times n$ matrix with latent roots μ_i; $i = 1, 2, \ldots, n$, then the latent roots of the $2n \times 2n$ matrix

$$\begin{pmatrix} G & G \\ I & I \end{pmatrix}$$

are

$$\lambda_i = 1 + \mu_i \quad (i = 1, 2, \ldots, n) \quad \text{and} \quad \lambda_j = 0 \quad (j = n+1, \ldots, 2n).$$

Proof. Suppose $\mathbf{A}$ and $\mathbf{B}$ are n dimensional vectors such that

$$\begin{pmatrix} G & G \\ I & I \end{pmatrix} \begin{pmatrix} \mathbf{A} \\ \mathbf{B} \end{pmatrix} = \lambda \begin{pmatrix} \mathbf{A} \\ \mathbf{B} \end{pmatrix}$$

(i.e.

$$\begin{pmatrix} \mathbf{A} \\ \mathbf{B} \end{pmatrix}$$

is a latent vector, and λ a latent root).

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Then $G\mathbf{A}+G\mathbf{B} = \lambda\mathbf{A}$ and $\mathbf{A}+\mathbf{B} = \lambda\mathbf{B}$. Adding we obtain

$$(G+I)\ (\mathbf{A}+\mathbf{B}) = \lambda(\mathbf{A}+\mathbf{B}),$$

and so λ is also a latent root of $(G+I)$. Thus λ satisfies the characteristic equation

$$|G+(1-\lambda)I| = 0.$$

The latent roots of G are thus $(1-\lambda_i)$ or μ_i and so $\lambda_i = 1+\mu_i\ i = 1, \ldots, n$. There are also n zero roots since the matrix consists of n pairs of identical columns.

Theorem 2

If G is an $n \times n$ matrix with latent roots $\mu_i\ i = 1, 2, \ldots, n$ then the $2n \times 2n$ matrix

$$\begin{pmatrix} G & G \\ I & O \end{pmatrix}$$

has characteristic roots $\lambda_i,\ i = 1, \ldots, 2n$ where λ_{2j-1} and $\lambda_{2j}, j = 1, 2, \ldots, n$ are the roots of the quadratic equation

$$\lambda^2 - \lambda\mu_j - \mu_j = 0.$$

Proof. Suppose $\mathbf{A}$ and $\mathbf{B}$ are n dimensional vectors such that

$$\begin{pmatrix} G & G \\ I & O \end{pmatrix} \begin{pmatrix} \mathbf{A} \\ B \end{pmatrix} = \lambda \begin{pmatrix} \mathbf{A} \\ \mathbf{B} \end{pmatrix}.$$

Then $G\mathbf{A}+G\mathbf{B} = \lambda\mathbf{A}$ and $\mathbf{A} = \lambda\mathbf{B}$. Therefore

$$G(1+\lambda)\mathbf{A} = \lambda^2\mathbf{A}$$

and so $\mu = \lambda^2/(1+\lambda)$ is a latent root of G.

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