

NOTES AND COMMENTS

AN INEQUALITY IN POPULATION GENETICS

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1. INTRODUCTION

In the theory of population genetics, it is well known that genic equilibrium is possible among a system of alleles at a single locus in a large random mating population, when there is differential viability between the various possible genotypes. In examining the stability of such an equilibrium with respect to chance fluctuations of the gene frequencies (Mandel, 1959) it has been found useful to consider the change in mean viability of the population from one generation to the next. In the case where generations overlap or when selection is infinitesimally slow it is fairly easy to show, by introducing a continuous time parameter, that the mean viability must increase with time (Kimura, 1956; Crow and Kimura, 1956). When the generations are discrete and non-overlapping the problem is more difficult mathematically, and gives rise to an inequality ((21) later) which does not appear to have been proved before. The object of this paper is to establish this inequality and to give a brief account of the way in which it arises out of genetical considerations.

2. STATEMENT OF THE PROBLEM

Consider n alleles A_1, A_2, \dots, A_n at a single genetic locus. Let $a_{ij} \geq 0$ denote the relative viability of the genotype $A_i A_j$ ($i, j = 1, 2, \dots, n$); the a_{ij} thus form a symmetric $n \times n$ matrix (a_{ij}) with non-negative elements. Let p_i be the frequency of gene A_i ($i = 1, 2, \dots, n$) in any one generation so that

$$\sum_{i=1}^n p_i = 1, \quad 0 < p_i < 1. \quad (1)$$

Let

$$V = \sum_{i=1}^n \sum_{j=1}^n a_{ij} p_i p_j. \quad (2)$$

V is called the mean viability of the population.

If random mating takes place among the individuals of this generation, the frequencies p_i' of the alleles A_i in the next generation are given by the relations

$$V p_i' = p_i \sum_{j=1}^n a_{ij} p_j \quad (\text{all } i = 1, 2, \dots, n). \quad (3)$$

The mean viability V' of the population in this generation is

$$V' = \sum_{i=1}^n \sum_{j=1}^n a_{ij} p_i' p_j'. \quad (4)$$

Under certain conditions (see, *e.g.* Mandel, 1959, it is possible for the alleles A_i to be maintained in polymorphic equilibrium, *i.e.* for the gene frequencies p_i to remain constant from generation to generation, with $p_i > 0$ for all i . It has been shown (*ibid.* and Mandel and Hughes, 1958) that when the population is in the neighbourhood of such an equilibrium state the inequality

$$V' - V \geq 0 \quad (5)$$

is true. This result enables the stability of the equilibrium to be investigated. It has been suspected, and will be proved here, that (5) holds for all states of the population, independently of the restriction imposed above.

In the two allele case $n = 2$, it is possible to obtain, by elementary but heavy algebra, an explicit expression for the difference $V' - V$, viz.

$$V' - V = \frac{1}{V^2} \{ p_1(a_{11}p_1 + a_{12}p_2 - V)^2 + p_2(a_{12}p_1 + a_{22}p_2 - V)^2 \} \\ \{ V + a_{11}p_1 + a_{22}p_2 \} \quad (6)$$

and this clearly establishes the validity of (5). The relation (6), however, does not appear to admit any generalisation to $n \geq 3$ and hence the following approach is adopted.

3. PROOF OF THE INEQUALITY

Letting

$$\Phi = (a_{ij}) \quad (i, j = 1, 2, \dots, n) \quad (7)$$

$$P = \text{diag} (p_i) \quad (i = 1, 2, \dots, n) \quad (8)$$

and

$$R^T = (p_1, p_2, \dots, p_n) \quad (9)$$

we have

$$V = R^T \Phi R. \quad (10)$$

Also

$$R'^T = (p'_1, p'_2, \dots, p'_n) = \frac{P\Phi R}{V} \quad (11)$$

and

$$V' = R'^T \Phi R' = \frac{1}{V^2} R^T \Phi P \Phi P \Phi R. \quad (12)$$

It is convenient now to represent the state of the population not by the numbers p_i but by $\sqrt{p_i}$; the vector

$$Q^T = (\sqrt{p_1}, \sqrt{p_2}, \dots, \sqrt{p_n}) \quad (13)$$

is then a vector with unit norm.

We also define the matrix

$$S = \text{diag} (\sqrt{p_i}) \quad (i = 1, 2, \dots, n) \quad (14)$$

so that

$$S^2 = P \quad (15)$$

and the matrix

$$\Psi = S\Phi S. \quad (16)$$

Since Φ is symmetric, so also is Ψ . Noting that

$$R = SQ \quad (17)$$

we obtain from (10), (12) and (16)

$$V = Q^T S \Phi S Q = Q^T \Psi Q \tag{18}$$

$$V' = \frac{1}{\sqrt{2}} Q^T S \Phi S^2 \Phi S^2 \Phi S Q = \frac{1}{\sqrt{2}} Q^T \Psi^3 Q. \tag{19}$$

Thus in order to prove (5) it must be shown that, for any real symmetric matrix Ψ with non-negative elements, and any vector Q with positive elements and unit norm

$$Q^T \Psi^3 Q \geq (Q^T \Psi Q)^3. \tag{20}$$

We shall actually prove the slightly more general inequality

$$Q^T \Psi^r Q \geq (Q^T \Psi Q)^r \tag{21}$$

under the same restrictions, for all integral $r > 0$.

Let the matrix Ψ have eigenvalues $\alpha_i (i = 1, 2, \dots, n)$ and let the components of Q referred to a set of mutually orthogonal eigenvectors of Ψ as a base be $X_i (i = 1, 2, \dots, n)$. Since Ψ is symmetric, all the α_i are real.

We now invoke the following theorem due to Frobenius (1908, 1909, 1912).

3.1. *Theorem.* If Ψ is a matrix with non-negative elements, and $\Psi \neq 0$, then there is an eigenvalue, α_1 say, of Ψ with the following properties :

(i) α_1 corresponds to an eigenvector of Ψ which has non-negative components when referred to the axes of Q ;

(ii) $\alpha_1 > 0$; (22)

(iii) $\alpha_1 \geq |\alpha_i|$ (all $i = 1, 2, \dots, n$). (23)

[For a particularly lucid discussion of these results see Debreu and Herstein (1953) ; also Wielandt (1950), Perron (1907).]

Suppose now that (21) holds when Q has $(n-1)$ components and Ψ is an $(n-1) \times (n-1)$ matrix.

3.2. *Lemma.* Then (21) also holds on the boundaries of the region for which $q_i > 0$, i.e. it holds when one of the q_i is zero.

Proof. Suppose that $q_n = 0$. Then

$$\begin{aligned} Q^T \Psi^r Q &= (q_1, q_2, \dots, q_{n-1}, 0 \left\{ \left(\begin{array}{cccc} \psi_{11} & \psi_{12} & \dots & \psi_{1, n-1} & 0 \\ \psi_{21} & \psi_{22} & \dots & \psi_{2, n-1} & 0 \\ \dots & \dots & \dots & \dots & \dots \\ \psi_{n-1, 1} & \psi_{n-1, 2} & \dots & \psi_{n-1, n-1} & 0 \\ 0 & 0 & \dots & 0 & 0 \end{array} \right) \right. \\ &+ \left. \left(\begin{array}{cccc} 0 & 0 & \dots & 0 & \psi_{1n} \\ 0 & 0 & \dots & 0 & \psi_{2n} \\ \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & \dots & 0 & \psi_{n-1, n} \\ \psi_{n1} & \psi_{n2} & \dots & \psi_{n, n-1} & \psi_{nn} \end{array} \right) \right\}^r \begin{pmatrix} q_1 \\ q_2 \\ \vdots \\ q_{n-1} \\ 0 \end{pmatrix} \\ &\geq (q_1, q_2, \dots, q_{n-1}) \left(\begin{array}{cccc} \psi_{11} & \psi_{12} & \dots & \psi_{1, n-1} \\ \psi_{21} & \psi_{22} & \dots & \psi_{2, n-1} \\ \dots & \dots & \dots & \dots \\ \psi_{n-1, 1} & \psi_{n-1, 2} & \dots & \psi_{n-1, n-1} \end{array} \right)^r \begin{pmatrix} q_1 \\ q_2 \\ \vdots \\ q_{n-1} \end{pmatrix} \tag{24} \end{aligned}$$

the extra terms being all non-negative, since the q_i and ψ_{ij} are all non-negative.

Furthermore

$$\begin{aligned}
 Q^T \Psi Q &= (q_1, q_2, \dots, q_{n-1}, 0) \begin{pmatrix} \psi_{11} & \psi_{12} & \dots & \psi_{1n} \\ \psi_{21} & \psi_{22} & \dots & \psi_{2n} \\ \dots & \dots & \dots & \dots \\ \psi_{n1} & \psi_{n2} & \dots & \psi_{nn} \end{pmatrix} \begin{pmatrix} q_1 \\ q_2 \\ \vdots \\ q_{n-1} \\ 0 \end{pmatrix} \\
 &= (q_1, q_2, \dots, q_{n-1}) \begin{pmatrix} \psi_{11} & \psi_{12} & \dots & \psi_{1, n-1} \\ \psi_{21} & \psi_{22} & \dots & \psi_{2, n-1} \\ \dots & \dots & \dots & \dots \\ \psi_{n-1, 1} & \psi_{n-1, 2} & \dots & \psi_{n-1, n-1} \end{pmatrix} \begin{pmatrix} q_1 \\ q_2 \\ \vdots \\ q_{n-1} \end{pmatrix} \quad (25)
 \end{aligned}$$

Thus, using (24), (25) and the inductive hypothesis, the inequality $Q^T \Psi^r Q \geq (Q^T \Psi Q)^r$ holds when $q_n = 0$, which proves the lemma.

Writing

$$F = Q^T \Psi^r Q - (Q^T \Psi Q)^r \quad (26)$$

we have

$$F \geq 0 \quad (27)$$

on the boundaries of the region $q_i > 0$.

Suppose now that $F < 0$ for some Q inside the region $q_i > 0$. Then there must be a minimum of F inside the region (for F is bounded) which has to be a stationary value for F , since the derivatives of F with respect to the q_i exist and are continuous. We therefore examine the stationary values of F .

Expressing Ψ and Q with the eigenvectors of Ψ as base, we have

$$F = \sum_{i=1}^n X_i^2 a_i^r - \left(\sum_{i=1}^n X_i^2 a_i \right)^r \quad (28)$$

with

$$\sum_{i=1}^n X_i^2 = |Q|^2 = 1. \quad (29)$$

Using Lagrange's method of undetermined multipliers, there must exist a λ such that

$$\frac{\partial F}{\partial X_i} - \partial \frac{\partial}{\partial X_i} \left\{ \sum_{i=1}^n X_i^2 - 1 \right\} = 2X_i a_i^r - r \left\{ \sum_{i=1}^n X_i^2 a_i \right\}. \quad 2X_i a_i - 2\lambda X_i = 0 \quad (30)$$

for all $i = 1, 2, \dots, n$.

Hence, for all i , either

$$X_i = 0 \quad (31)$$

or

$$a_i^r - r a_i \left\{ \sum_{i=1}^n a_i X_i^2 \right\}^{r-1} = \lambda. \quad (32)$$

If $X_1 = 0$, the vector Q would be orthogonal to the vector whose components are $(1, 0, 0, \dots, 0)$ when referred to the eigenvectors of Ψ . But this is the eigenvector of Ψ corresponding to the eigenvalue a_1 with non-negative elements when referred to the original set of axes. We would then have $q_i \leq 0$ for some i , and hence Q falls outside the region in question.

Therefore

$$X_i \neq 0 \quad (33)$$

and (32) holds at least for $i = 1$.

Multiplying the latter half of (30) by $\frac{1}{2}X_i$ and summing over i ,

$$\sum_{i=1}^n X_i^2 \alpha_i^{r-1} - r \left\{ \sum_{i=1}^n X_i^2 \alpha_i \right\}^r = \lambda \sum_{i=1}^n X_i^2 = \lambda \tag{34}$$

i.e.

$$F = \lambda + (r-1) \left\{ \sum_{i=1}^n X_i^2 \alpha_i \right\}^r. \tag{35}$$

Hence, noting that

$$\sum_{i=1}^n \alpha_i X_i^2 = Q^T \Psi Q = V > 0 \tag{36}$$

we have

$$\frac{F}{V^r} = \frac{\lambda}{V^r} + (r-1) = \frac{\alpha_1^r - r \alpha_1 V^{r-1}}{V^r} + (r-1) \tag{37}$$

using (32).

Thus

$$\frac{F}{V^r} = \left(\frac{\alpha_i}{V} \right)^r - r \left(\frac{\alpha_i}{V} \right) + (r-1) \tag{38}$$

Moreover, using (23),

$$V = \sum_{i=1}^n \alpha_i X_i^2 \leq \sum_{i=1}^n \alpha_1 X_i^2 = \alpha_1. \tag{39}$$

Thus (38) may be written

$$\begin{aligned} \frac{F^r}{V^r} &= \left(\frac{\alpha_1}{V} \right)^r - \left(\frac{\alpha_1}{V} \right) - (r-1) \left\{ \frac{\alpha_1}{V} - 1 \right\} \\ &= \left(\frac{\alpha_1}{V} - 1 \right) \left\{ \frac{\alpha_1}{V} + \left(\frac{\alpha_1}{V} \right)^2 + \dots + \left(\frac{\alpha_1}{V} \right)^{r-1} \right\} - (r-1) \left\{ \frac{\alpha_1}{V} - 1 \right\} \\ &= \left(\frac{\alpha_1}{V} - 1 \right) \left\{ \frac{\alpha_1}{V} + \left(\frac{\alpha_1}{V} \right)^2 + \dots + \left(\frac{\alpha_1}{V} \right)^{r-1} - (r-1) \right\} \geq 0, \text{ by (39),} \end{aligned}$$

and therefore

$$F \geq 0 \tag{40}$$

holds throughout the region $q_i > 0$ and on its boundaries.

Thus (21) is true in n dimensions if it is true in $(n-1)$. But (21) holds (with equality) for $n = 1$, when Q has the single component 1 and Ψ the single element $\psi_{11} > 0$. Hence (21) is established for all n .

4. DISCUSSION

The inequality obtained above is interesting from two points of view. Genetically, in the form (5), it shows that the multiple allelic system described in 1., starting out from any initial state in which all the alleles are represented, will tend monotonically under natural selection towards a state of maximum mean viability. Mathematically, the inequality, represented in the form (28), (40), is well known (see Hardy, Littlewood and Polya (1934), p. 26) when the α_1 are non-negative. Here the inequality has been established for a different class of α_1 , viz. the latent roots of real, symmetric non-negative matrices.

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