ON THE CHANGE OF POPULATION FITNESS
BY NATURAL SELECTION * †

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1. INTRODUCTION

In *The Origin of Species*, Darwin (1859) put forward the view that natural selection, by preserving and accumulating small inherited modifications advantageous to each organism, is continuously effecting the improvement of the species in relation to its organic and inorganic environment. At that time the mechanism of particulate inheritance was unknown and he could not reject the theory of blending inheritance nor even the inheritance of acquired characters. Nevertheless it is remarkable that he did arrive at the right conclusion on the role of natural selection in evolution.

Later, based on the theory of Mendelian inheritance, Fisher (1930) formulated his "fundamental theorem of natural selection" by equating the rate of increase of population fitness with the genetic variance in fitness. Since the variance is a non-negative quantity, fitness in this formulation always increases with time. This view seems to be compatible with the general picture of evolution which has taken place in the past and may be considered as a quantitative description of an essential feature of evolution. In fact, Fisher (1930) claims that this law should hold the same position among the biological sciences as the second law of thermodynamics in physical sciences. However, if one considers actual cases in which competition with other species or deterioration of environment are involved, additional terms may be necessary and Fisher (1930) derived an equation for the rate of increase of the Malthusian parameter of the population in which the effect of overpopulation (C), genetic variance (W) and the effect of deterioration of environment (D) are included.

The validity of the "fundamental theorem" for the case of variable selection coefficients has been questioned by Wright (1949) who later derived an additional term for such a case (Wright, 1950). Attempts to obtain more general expressions for the rate of increase of population fitness have been made by Crow and Kimura (1956), Wright (1955) and Crow (1955).

The present paper deals with four problems: (1) I shall give a general equation for the role of additive, dominance, and epistatic components of fitness in determining the rate of change in population fitness. No restriction is placed on the mating system. A few of the many interesting special cases are discussed. (2) The process of

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natural selection will be treated from a different view, and a new formulation given which may be called a "maximum principle in the genetic theory of natural selection". (3) A short section is devoted to the change in population variability with selection. (4) Finally these results will be applied to artificial selection, with special reference to the roles of dominance and epistatic components when inbreeding and linkage are involved.

2. MEASUREMENT OF FITNESS WITH TWO MODELS OF GENERATION TIME

Before going into the detailed argument on the main subject, it might be preferable to explain the mathematical models used and to define "fitness" for each model.

2.1. A model with a discrete time parameter

In this model, all the members of the population at a given moment belong to the same generation. After each breeding cycle the population is completely replaced by its progeny to form the next generation. Thus the generation time, t , takes only integral values; 0, 1, 2, etc. The fitness of each genotype is measured by the average number of offspring per individual. The letter w will be used to designate fitness in this sense and following Wright (1942 and later) will be called the selective value of the genotype. The population is stationary in size if the mean fitness ($\bar{w}$) is unity. The selection coefficient of the genotype A_iA_j denoted by s_{ij} will be defined by

$$s_{ij} = w_{ij} - 1,$$

where w_{ij} is the selective value of A_iA_j .

Quite often, an arbitrary value of unity is assigned to one of the genotypes, but this is not meaningful unless the aim of study is restricted to the change of gene frequencies.

Consider an arbitrary number of alleles at one locus and let x_i be the relative frequency of the i^{th} allele A_i . Under this model, the rate of change of the gene frequency per generation, Δx_i , is given by

$$(2.1.1) \quad \Delta x_i = \frac{x_i(w_i - \bar{w})}{\bar{w}},$$

where $w_i = \sum_j w_{ij}P_{ij}/x_i$ and $\bar{w} = \sum_{ij} w_{ij}P_{ij} = \sum_i w_i x_i$. P denotes the zygotic frequency such that P_{ii} is the frequency of the homozygote A_iA_i while $2P_{ij}$ ($i \neq j$) is the frequency of the heterozygote A_iA_j ($P_{ij} = P_{ji}$). The definition of P is complicated for the multi-locus case, but the difficulty may be avoided by saying that P_{ij} (for arbitrary i and j) stands for the frequency of the *ordered genotype* A_iA_j , i.e. for mathematical convenience we distinguish between A_iA_j and A_jA_i .

2.2. A model with a continuous time parameter

In this model a population may contain individuals of different ages as in human populations. For a rigorous treatment of such a problem integral equations are needed (Haldane, 1927).

An appropriate scale for measuring fitness is the Malthusian parameter, m (Fisher, 1930), which measures the rate of population increase or decrease. It is defined as the real root of the equation ;

$$\int_0^{\infty} e^{-mx} l_x b_x dx = 1,$$

where l_x is the proportion of the population which survive to age x , and b_x is the rate of reproduction at that age. To obtain the fitness, m_{ij} , of the genotype $A_i A_j$, the above equation may be applied to a group of individuals of genotype $A_i A_j$, though perhaps differing at other loci. If there are differences in the vital statistics of the two sexes, "we may, certainly in mankind, and with a strong presumption in all other species, effectively average out the sex differences" (Fisher, 1953).

In the present paper, I will designate the fitness measured in Malthusian parameters by the letter a such that a_{ij} is the fitness of $A_i A_j$. Let n_{ij} be the number of individuals with the ordered genotype $A_i A_j$ in the population. Since a_{ij} represents the net reproductive rate of the genotype $A_i A_j$ such that the contribution to the rate of increase of the population number N from $A_i A_j$ individuals is $n_{ij} a_{ij}$, then if N_i is the number of A_i genes such that

$$x_i = N_i / N,$$

we have

$$(2.2.1) \quad \frac{dN_i}{dt} = \sum_j n_{ij} a_{ij} = N \sum_j P_{ij} a_{ij}.$$

Therefore

$$\frac{dN}{dt} = N \sum_{ij} P_{ij} a_{ij}$$

and we obtain

$$\begin{aligned} \frac{dx_i}{dt} &= \frac{d}{dt} \left(\frac{N_i}{N} \right) = \frac{1}{N} \frac{dN_i}{dt} - \frac{N_i}{N^2} \frac{dN}{dt} \\ &= \sum_j P_{ij} a_{ij} - x_i \sum_{ij} P_{ij} a_{ij} \end{aligned}$$

or more simply

$$(2.2.2) \quad \frac{dx_i}{dt} = x_i (a_i - \bar{a}),$$

where $a_i = \sum_j a_{ij} P_{ij} / x_i$ and $\bar{a} = \sum_{ij} a_{ij} P_{ij}$. The quantity $a_i - \bar{a}$ will be called the average excess of the gene A_i and will be designated by $\tilde{a}_i$. Throughout this paper a bar will be used to designate the population mean while a tilde will designate the deviation from the mean. Thus

(2.2.2) is equivalent to saying that the logarithmic rate of increase of gene frequency is equal to the average excess of the gene in fitness, *i.e.*

$$(2.2.3) \quad \dot{x}_i = \bar{a}_i,$$

in which

$$\dot{x}_i = \frac{d}{dt} \log x_i.$$

2.3. Interrelation between the two models

The above two models are both abstractions from reality and each has its advantages and disadvantages. For example, the discrete model might be suitable for an annual plant population while the continuous model would be preferable for the treatment of a human population. Though the scales of fitness for the two models are different, there are certain correspondences between them. Roughly speaking, m_{ij} or a_{ij} is equivalent to $\log w_{ij}$. A formal passage from (2.1.1) to (2.2.2) is attained as follows. Write $w_{ij} = 1 + s_{ij} \Delta t$ and substitute in (2.1.1) to give

$$\frac{\Delta x_i}{\Delta t} = \frac{x_i(s_i - \bar{s})}{1 + \bar{s} \Delta t}.$$

By letting $\Delta t \rightarrow 0$, we have (2.2.2) except that s_{ij} appears instead of a_{ij} . This suggests a formal correspondence between s_{ij} in the discrete model and a_{ij} in the continuous model.

Mathematically, the discrete model requires the calculus of finite differences, while the continuous model permits application of the familiar differential calculus which often leads to a more elegant formulation. In the present paper I shall mainly employ the continuous model for this reason.

3. RATE OF CHANGE IN POPULATION FITNESS

We start by considering a single locus with an arbitrary number, say n , of alleles. No restriction will be imposed on the mating system. The fitness a_{ij} may be expressed in the following form,

$$a_{ij} = \bar{a} + \alpha_i + \alpha_j + d_{ij},$$

where $\bar{a}$ is the mean fitness of the population, α_i and α_j are respectively additive effects of the genes A_i and A_j on fitness and d_{ij} is the dominance deviation from linearity. Following Fisher (1930, 1941) we shall call α_i the average effect of the gene A_i . The α_i 's are determined by minimising

$$\sum_{ij} d_{ij}^2 P_{ij}.$$

By writing $\bar{a}_{ij}$ for $a_{ij} - \bar{a}$, the quantity to be minimised is

$$Q = \sum_{ij} P_{ij} (\bar{a}_{ij} - \alpha_i - \alpha_j)^2.$$

Since $-\frac{1}{2} \frac{\partial Q}{\partial \alpha_k} = 0$ leads to

$$\sum_j P_{kj}(\bar{a}_{kj} - \alpha_k - \alpha_j) + \sum_i P_{ik}(\bar{a}_{ik} - \alpha_i - \alpha_k) = 0,$$

we have the normal equations for α_k 's ;

$$(3.1) \quad 2\alpha_k x_k + 2 \sum_i P_{ki} \alpha_i = 2 \sum_i P_{ki} \bar{a}_{ki}. \quad (k = 1, \dots, n)$$

If we adopt the notation $\bar{a}_k$ for $\sum_i P_{ki} \bar{a}_{ki} / x_k$, the right side of (3.1) is written as $2x_k \bar{a}_k$ and the sum of squares due to the average effects is given by

$$(3.2) \quad V_g = 2 \sum_k \alpha_k x_k \bar{a}_k.$$

If we note (2.2.2) this may also be written as

$$(3.2)' \quad V_g = 2 \sum_i \alpha_i \frac{dx_i}{dt}.$$

It may be convenient to note for later discussion that under random mating α_i is equal to $\bar{a}_i$ and

$$(3.2)'' \quad V_g = 2 \sum_i x_i \bar{a}_i^2.$$

For the derivation of normal equations (3.1) and the extraction of the sum of squares due to α_i 's, the reader may refer to Kempthorne (1957).

We will call V_g the *genic* variance in fitness ; it has also been called the additive genetic variance in fitness. Fisher (1930) called the same quantity the genetic variance.

Now we introduce a new quantity θ_{ij} defined by

$$(3.3) \quad \theta_{ij} = \frac{P_{ij}}{x_i x_j}. \quad (\theta_{ij} = \theta_{ji}).$$

θ_{ij} may be called the coefficient of departure from random combination of alleles and is unity if mating is random. Substituting $P_{ki} = x_k x_i \theta_{ki}$ in (3.1) and dividing both sides of the equation by $2x_k$, we have

$$\alpha_k + \sum_i x_i \theta_{ki} \alpha_i = \bar{a}_k = \sum_i x_i \theta_{ki} \bar{a}_{ki},$$

or

$$(3.4) \quad \sum_j x_j \theta_{ij} \bar{a}_{ij} = \alpha_i + \sum_j \alpha_j \theta_{ij} x_j.$$

Let us now consider the rate of increase in population fitness under natural selection. Since

$$\bar{a} = \sum_{ij} a_{ij} P_{ij},$$

we have

$$\frac{d\bar{a}}{dt} = \sum_{ij} \frac{da_{ij}}{dt} P_{ij} + \sum_{ij} a_{ij} \frac{dP_{ij}}{dt},$$

or more simply, employing the Newtonian method of denoting a time derivative by a superior dot,

$$(3.5) \quad \dot{\bar{a}} = \sum_{ij} \dot{a}_{ij} P_{ij} + \sum_{ij} a_{ij} \dot{P}_{ij}.$$

The first term in the right side is the population average of the rate of change of individual fitness and may be denoted by

$$(3.6) \quad \frac{\overline{da}}{\overline{dt}} \text{ or } \bar{a}.$$

The second term on the right is

$$\sum_{ij} a_{ij} \dot{P}_{ij} = \sum_{ij} (\bar{a} + \tilde{a}_{ij}) \dot{P}_{ij} = \bar{a} \sum_{ij} \dot{P}_{ij} + \sum_{ij} \tilde{a}_{ij} \dot{P}_{ij},$$

and since $\sum_{ij} P_{ij} = 1$ or $\sum_{ij} \dot{P}_{ij} = 0$, it reduces to

$$\sum_{ij} \tilde{a}_{ij} \dot{P}_{ij},$$

which upon substitution of $P_{ij} = x_i x_j \theta_{ij}$ becomes

$$(3.7) \quad \sum_{ij} \tilde{a}_{ij} \dot{x}_i x_j \theta_{ij} + \sum_{ij} \tilde{a}_{ij} x_i \dot{x}_j \theta_{ij} + \sum_{ij} \tilde{a}_{ij} x_i x_j \dot{\theta}_{ij}.$$

If we substitute (3.4) in the first term of the above expression, we have

$$(3.8) \quad \sum_i \dot{x}_i (\alpha_i + \sum_j \alpha_j \theta_{ij} x_j) = \sum_i \alpha_i \dot{x}_i + \sum_{ij} \alpha_j \dot{x}_i x_j \theta_{ij}.$$

It will be immediately seen from (3.2)' that the first term of the last expression is

$$\frac{1}{2} V_g.$$

By definition $\sum_i P_{ij} = x_j$ or $\sum_i x_i x_j \theta_{ij} = x_j$, and we get $\sum_i x_i \dot{\theta}_{ij} = 0$ or differentiating both sides we get $\sum_i \dot{x}_i \theta_{ij} + \sum_i x_i \dot{\theta}_{ij} = 0$. Thus the second term of (3.8) reduces to

$$\sum_j \alpha_j x_j (-\sum_i x_i \dot{\theta}_{ij}) = -\sum_{ij} \alpha_j x_i x_j \dot{\theta}_{ij}.$$

Similarly the second term of (3.7) becomes

$$\frac{1}{2} V_g - \sum_{ij} \alpha_i x_i x_j \dot{\theta}_{ij}.$$

Therefore (3.7) can be written in the form

$$V_g + \sum_{ij} (\tilde{a}_{ij} - \alpha_i - \alpha_j) x_i x_j \dot{\theta}_{ij},$$

or

$$V_g + \sum_{ij} d_{ij} P_{ij} (\dot{\theta}_{ij} / \theta_{ij}).$$

Thus the required expression for the rate of change of population fitness by selection is

$$(3.9) \quad \frac{d\bar{a}}{dt} = V_g + \frac{\overline{da}}{\overline{dt}} + \sum_{ij} P_{ij} d_{ij} \frac{d}{dt} \log \theta_{ij}$$

or in more simple notation

$$(3.10) \quad \dot{\bar{a}} = V_g + \bar{a} + \overline{d \cdot \dot{\theta}},$$

in which the open circle over θ denotes the time derivative of $\log \theta$ as in (2.2.3). Also it is convenient to note that

$$\sum_{ij} P_{ij} d_{ij} \frac{d}{dt} \log (P_{ij}/x_i x_j) = \sum_{ij} P_{ij} d_{ij} \frac{d}{dt} \log P_{ij} = \sum_{ij} d_{ij} \frac{d}{dt} P_{ij}.$$

Thus, as shown in (3.9) or (3.10), the rate of increase of the population fitness is decomposed into three components: (i) Genic variance in fitness. (ii) Average increase in the fitness of individual genotypes. This term is zero if genotypic fitnesses remain constant. (iii) A contribution due to dominance deviations and mating system. This term vanishes under random mating ($\theta_{ij} = 1$), or under any system of mating if there is no dominance. It is interesting to note the simple relation by which dominance components appear in the expression. Each component is weighted by the rate of change of the logarithm of the corresponding coefficient of departure from random combination of alleles. This would suggest a similar relation for epistatic components when two or more loci are involved.

Without going into the details of derivation, the result for the two loci may be summarised as follows. We decompose the fitness of the genotype $A_i A_j B_k B_l$ in the form

$$a_{ijkl} = \bar{a} + A_{ij} + B_{kl} + \epsilon_{ijkl},$$

where A_{ij} is the additive effect of the first locus (a), B_{kl} that of the second locus (b) and ϵ_{ijkl} is the epistatic deviation. Let

$$A_{ij} = \alpha_i + \alpha_j + d_{ij}^{(a)}$$

and

$$B_{kl} = \beta_k + \beta_l + d_{kl}^{(b)}$$

in which α and β stand for the additive effects of the alleles for the first and second loci respectively and $d^{(a)}$ and $d^{(b)}$ are dominance deviations for the two loci. Let P_{ijkl} be the frequency of the ordered genotype $A_i A_j B_k B_l$ and let $P_{ij}^{(a)}$ be the frequency of the ordered genotype $A_i A_j$ in which no attention is paid to the second locus, i.e. $P_{ij}^{(a)} = \sum_{kl} P_{ijkl}$, and $P_{kl}^{(b)}$ be the similar frequency of the ordered genotype $B_k B_l$ at the second locus. If we designate the frequencies of genes A_i and B_k by x_i and y_k respectively, we can define coefficients of departure from random combination of alleles at the two loci by

$$\theta_{ij}^{(a)} = \frac{P_{ij}^{(a)}}{x_i x_j} \text{ and } \theta_{kl}^{(b)} = \frac{P_{kl}^{(b)}}{y_k y_l},$$

respectively. Similarly we introduce the coefficient of departure involving two loci by

$$\theta_{ijkl} = \frac{P_{ijkl}}{P_{ij}^{(a)} P_{kl}^{(b)}}.$$

Then

$$\begin{aligned} \frac{d\bar{a}}{dt} = & V_g + \frac{\bar{da}}{dt} + \sum_{ij} P_{ij}^{(a)} d_{ij}^{(a)} \frac{d}{dt} \log \theta_{ij}^{(a)} \\ & + \sum_{kl} P_{kl}^{(b)} d_{kl}^{(b)} \frac{d}{dt} \log \theta_{kl}^{(b)} + \sum_{ijkl} P_{ijkl} \epsilon_{ijkl} \frac{d}{dt} \log \theta_{ijkl}, \end{aligned}$$

or more simply

$$(3.11) \quad \dot{\bar{a}} = V_g + \bar{a} + \overline{\theta_{ij}^{(a)} d_{ij}^{(a)}} + \overline{\theta_{kl}^{(b)} d_{kl}^{(b)}} + \overline{\theta_{ijkl} \epsilon_{ijkl}}.$$

The epistatic effect may further be subdivided into additive $\times$ additive, additive $\times$ dominance and dominance $\times$ dominance effects. To simplify the following formulation we adopt a rule that the letters i, j, k and l refer respectively to the left gene in the first locus, the right gene in the first locus, the left gene in the second locus and the right gene in the second locus in the ordered genotype $A_i A_j B_k B_l$. With this abbreviation, not only subscripts a and b are unnecessary but also simple expressions like $P_{ik}, P_{ijk}, \dots$, etc. may be used for the frequencies of ordered genotypes $A_i B_k, A_i A_j B_k$, etc.

$$\begin{aligned} \text{Let} \quad \epsilon_{ijkl} = & (\alpha\beta)_{ik} + (\alpha\beta)_{il} + (\alpha d)_{ikl} \\ & + (\alpha\beta)_{jk} + (\alpha\beta)_{jl} + (\alpha d)_{jkl} \\ & + (d\beta)_{ijk} + (d\beta)_{ijl} + (dd)_{ijkl}. \end{aligned}$$

Corresponding to each of the dominance and epistatic components, coefficients of departure from random combination are defined in the obvious way :

$$\begin{aligned} \theta_{ij} &= P_{ij}/x_i x_j, \theta_{ik} = P_{ik}/x_i y_k, \dots, \\ \theta_{ijk} &= P_{ijk}/P_{ij} y_k, \theta_{ijkl} = P_{ijkl}/P_{ij} P_{kl}. \end{aligned}$$

Then

$$(3.12) \quad \begin{aligned} \dot{\bar{a}} = & V_g + \bar{a} + \overline{\theta_{ij} d_{ij}} + \overline{\theta_{kl} d_{kl}} \\ & + \overline{\theta_{ik} (\alpha\beta)_{ik}} + \dots + \overline{\theta_{ijkl} (dd)_{ijkl}}. \end{aligned}$$

The law of formulation of each term is self-evident so no further explanation is necessary.

Thus for an arbitrary number of loci each with an arbitrary number of alleles, we can write the rate of increase in population fitness as follows :

$$(3.13) \quad \frac{d\bar{a}}{dt} = V_g + \frac{\bar{da}}{dt} + \sum \epsilon \frac{d}{dt} \log \theta,$$

in which ϵ stands for an interaction effect (dominance or epistatic) and θ is the corresponding coefficient of departure from random combination. The summation extends over all possible intra- and inter-locus interactions.

4. SOME SPECIAL SITUATIONS

4.1. For constant genotypic fitnesses, $\bar{a} = 0$ and (3.10) becomes

$$\dot{\bar{a}} = V_g + \overline{d \cdot \dot{\theta}}.$$

If there exists a constant λ_{ij} such that

$$\lambda_{ij} = P_{ij}^2 / P_{ii} P_{jj}$$

for all i and j , then $\dot{\bar{a}} = V_g$. This is easily shown as follows :

Since $P_{ij} = x_i x_j \theta_{ij}$, we have $\lambda_{ij} \theta_{ii} \theta_{jj} = \theta_{ij}^2$ or

$$\log \lambda_{ij} + \log \theta_{ii} + \log \theta_{jj} = 2 \log \theta_{ij}.$$

Differentiating both sides with respect to time,

$$\dot{\theta}_{ii} + \dot{\theta}_{jj} = 2 \dot{\theta}_{ij}.$$

Thus

$$\begin{aligned} \overline{d \cdot \dot{\theta}} &= \sum_{ij} d_{ij} \dot{\theta}_{ij} P_{ij} = \frac{1}{2} \sum_{ij} d_{ij} (\dot{\theta}_{ii} + \dot{\theta}_{jj}) P_{ij} \\ &= \frac{1}{2} \sum_i \dot{\theta}_{ii} \sum_j d_{ij} P_{ij} + \frac{1}{2} \sum_j \dot{\theta}_{jj} \sum_i d_{ij} P_{ij} = 0, \end{aligned}$$

because

$$\sum_j d_{ij} P_{ij} = \sum_i d_{ij} P_{ij} = 0.$$

The equivalent result was obtained by Kempthorne (1957) by using matrix algebra. However, Fisher (1941) had already demonstrated such a result for the two allelic case. Extension to the multi-locus case is immediately apparent from (3.13).

In the case of inbreeding in which zygotic frequencies are expressed by gene frequencies and the inbreeding coefficient F , $P_{ii} = Fx_i + (1-F)x_i^2$ for homozygotes and $P_{ij} = (1-F)x_i x_j$ for heterozygotes. Therefore $\theta_{ii} = \frac{1}{x_i} F + (1-F)$ and $\theta_{ij} = (1-F)$ ($i \neq j$).

We will consider this case later in more detail.

4.2 A quantity analogous to the potential function in a conservative physical system may exist in some special cases. Wright (1955) considered such a quantity and termed it the internal selective value. I shall use a similar quantity which may be called the internal fitness (I) in the following way : We say that the internal fitness exists if

$$2 \sum_i \alpha_i dx_i \quad \left(\sum_i x_i = 1 \right)$$

is an exact differential with respect to gene frequencies ($x_1, x_2, \dots, x_n$). In that case there exists a function I such that the above expression is equated with dI . Therefore

$$\frac{dI}{dt} = 2 \sum_i \alpha_i \frac{dx_i}{dt} = V_g,$$

i.e. the rate of increase of internal fitness is equal to the genic variance

at that moment. Thus if the internal fitness is equal to the mean fitness of the population $\bar{a}$ except for an arbitrary constant, the fundamental theorem is satisfied. However, the reverse is not necessarily true and the derivation of Fisher's fundamental theorem does not presuppose or imply the existence of any such potential function.

4.3. When competition between genotypes is involved we sometimes encounter a rather peculiar situation. As an example let us consider three alleles A_1 , A_2 , and A_3 with frequencies x_1 , x_2 , and x_3 . For simplicity we assume no dominance or more conveniently a haplont situation. Suppose an individual with gene A_1 has its fitness decreased by the amount c when it is surrounded by individuals with A_2 , while A_2 if surrounded by the former A_1 gains fitness by the same amount

FIG. 1.

c . Similarly A_2 when surrounded by A_3 individuals loses fitness by c , while the reverse situation would add fitness c to an A_3 individual, and so on cyclically (fig. 1). Then the law of change of gene frequencies will be given by

$$(4.3.1) \quad \begin{cases} \frac{dx_1}{dt} = cx_1(x_3 - x_2) \\ \frac{dx_2}{dt} = cx_2(x_1 - x_3) \\ \frac{dx_3}{dt} = cx_3(x_2 - x_1). \end{cases}$$

The gene frequencies will move perpetually on a closed path * which is the intersection of a plane

$$x_1 + x_2 + x_3 = 1$$

and a surface

$$x_1 x_2 x_3 = C_0,$$

where C_0 is a constant determined by the initial conditions. In the present case $\alpha_1 = \bar{a}_1 = c(x_3 - x_2)$, $\alpha_2 = \bar{a}_2 = c(x_1 - x_3)$, $\alpha_3 = \bar{a}_3 = c(x_2 - x_1)$, and $\bar{a} \equiv 0$. This shows that, while gene frequencies change perpetually, no change in population fitness occurs :

$$\frac{d\bar{a}}{dt} = 0.$$

* With a discrete model, we have a set of finite difference equations $\Delta x_1 = cx_1(x_3 - x_2)$, etc. instead of (4.3.1) and the path is not quite closed. In the neighbourhood of $(1/3, 1/3, 1/3)$, the solution contains a factor $(1 + c^2/3)^{t/2}$ showing that the path is an outwardly proceeding spiral. The author owes to Professor S. Wright and Mr Y. Hiraizumi for calling his attention to this fact.

Nevertheless the population at a given moment may contain plenty of genic variance, for

$$V_g = c^2\{x_1(x_3-x_2)^2 + x_2(x_1-x_3)^2 + x_3(x_2-x_1)^2\}.$$

The reason for this seeming contradiction is that the second term in our formula (3.9) always cancels out the first term, namely

$$\frac{\overline{da}}{dt} = -V_g,$$

so that

$$\frac{d\bar{a}}{dt} = V_g + \frac{\overline{da}}{dt}$$

still holds.

4.4 In our definition of fitness in (2.2.1), sexual difference in fitness for each genotype, if it exists, is in a sense averaged out in the expression. This is reasonable since under a complicated mating system it would not be practicable to analyse contributions due to different sexes. However, under simple circumstances this may be done to give interesting results. Let a_{ij} be the fitness of an A_iA_j female in producing offspring and let c_{ij} be the competitive ability of the A_iA_j male in fertilising females. We assume random mating and no dominance. Then we have

$$(4.4.1) \quad \frac{d\bar{a}}{dt} = \sigma_{aa} + \sigma_{ac},$$

where σ_{aa} is half the genic variance,

$$\sigma_{aa} = \sum_i x_i (a_i - \bar{a})^2$$

and σ_{ac} is the covariance between average excess (or effect in this case) of fitness in females and that of competitive ability in males.

$$\sigma_{ac} = \sum_i x_i (a_i - \bar{a})(c_i - \bar{c}),$$

in which $\bar{c}$ may be chosen to be zero. Let b be the regression coefficient of c_i on a_i , i.e.

$$c_i = \bar{c} + b(a_i - \bar{a}),$$

where $b = \sigma_{ac}/\sigma_{aa}$. Then if b is less than -1 ,

$$\sigma_{ac} < -\sigma_{aa},$$

and therefore

$$\frac{d\bar{a}}{dt} = \sigma_{aa} + \sigma_{ac} < 0,$$

leading to the deterioration of the population. Yet the population may contain genic variance through this process.

$$V_g = 2\sigma_{aa} > 0.$$

In fact, Huxley (1942) put forward an explanation for the extinction

of species due to fixation of genes which enable males to be more successful in competition but make the species less fit to the external environment.

Fisher (1941) considered a hypothetical gene which enables the possessor to be self-fertilised but which has no effect on the seed productivity or cross-fertilising ability of the pollen. This is essentially equivalent to the case in which $\sigma_{aa} = 0$ in the above formulation. For, in this case $\sigma_{aa} = \sigma_{ac} = 0$ and

$$\frac{d\bar{a}}{dt} = 0,$$

which agrees well with what is expected from the fundamental theorem since

$$V_g = 2\sigma_{aa} = 0.$$

4.5. In a natural population there always exists an element of stochastic indeterminacy in the process of change in fitness. We consider here a simple single locus case with random mating.

Let δx_i be the rate of change in the frequency of A_i per unit time interval which may be taken as one generation, we can write

$$\delta x_i = x_i(a_i - \bar{a}) + \delta' x_i,$$

where $\delta' x_i$ is the change due to random sampling of gametes. Then the rate of change in population fitness is

$$\delta \bar{a} = \sum_{ij} \delta a_{ij} x_i x_j + V_g + 2 \sum_i a_i \delta' x_i.$$

Here a_{ij} is a random variable which may fluctuate from generation to generation. $\delta' x_i$'s are variables from multinomial distribution such that their mean, variance and covariance are given respectively by

$$M(\delta' x_i) = 0, \quad V(\delta' x_i) = x_i(1 - x_i)/2N$$

and

$$\text{Cov}(\delta' x_i \delta' x_j) = -x_i x_j / 2N \text{ for } i \neq j,$$

where N is the number of reproducing individuals in the population. Then the mean and variance of $\delta \bar{a}$ are

$$(4.5.1) \quad M(\delta \bar{a}) = \overline{M(\delta a)} + V_g,$$

and

$$(4.5.2) \quad V(\delta \bar{a}) = \overline{\sigma_{\delta a \delta a'}} + V_g / 2N,$$

where

$$\overline{M(\delta a)} = \sum_{ij} M(\delta a_{ij}) x_i x_j$$

and

$$\overline{\sigma_{\delta a \delta a'}} = \sum_{ij i' j'} \text{Cov}(\delta a_{ij} \delta a_{i' j'}) x_i x_j x_{i'} x_{j'}.$$

The last term $V_g/(2N)$ corresponds to Fisher's error variance for his fundamental theorem (Fisher, 1930).

5. A MAXIMUM PRINCIPLE IN THE GENETICAL THEORY OF NATURAL SELECTION

So far we have considered how natural selection increases population fitness, but have paid little attention to how natural selection changes gene frequencies.

Let us start our consideration from a simple case with random mating and constant fitness of individual genotypes. Consider a locus with n alleles, say $A_1, A_2, \dots, A_n$ with respective frequencies $x_1, x_2, \dots, x_n$. First we will establish the following theorem: *For a given short time interval δt , natural selection causes gene frequency changes $\delta x_1, \delta x_2, \dots, \delta x_n$, in such a way that the increase of population fitness, $\delta \bar{a}$, shall be maximum under the restriction*

$$(5.1) \quad \sum_{i=1}^n \frac{(\delta x_i)^2}{x_i} = \frac{1}{2} V_g(\delta t)^2.$$

To prove this theorem, we put $\delta \bar{a} = \eta$, $\delta x_i = \xi_i$ and $\frac{1}{2} V_g(\delta t)^2 = c$. Since

$$\bar{a} = \sum_{ij} a_{ij} x_i x_j,$$

we have, for any small set of gene frequency changes $(\xi_1, \xi_2, \dots, \xi_n)$,

$$\delta \bar{a} = 2 \sum_{i=1}^n a_i \delta x_i$$

or

$$(5.2) \quad \eta = 2 \sum_{i=1}^n a_i \xi_i.$$

The restriction (5.1) is now written as

$$(5.1) \quad \sum_{i=1}^n \frac{\xi_i^2}{x_i} = c.$$

In addition, since the sum of all the gene frequencies is unity, we inevitably have the obvious restriction :

$$(5.3) \quad \sum_{i=1}^n \xi_i = 0.$$

We are going to show that among all possible sets of gene frequency changes which satisfy (5.1)' and (5.3), the one which is caused by natural selection is the set which makes η maximum.

For this purpose we introduce the Lagrange multipliers λ and μ and consider a function

$$(5.4) \quad \psi = \eta - \lambda \left(\sum_{i=1}^n \frac{\xi_i^2}{x_i} - c \right) - \mu \left(\sum_{i=1}^n \xi_i \right).$$

A set of ξ_i 's which make ψ maximum may be obtained from

$$\frac{\partial \psi}{\partial \xi_i} = 2a_i - 2\lambda \frac{\xi_i}{x_i} - \mu = 0,$$

or

$$(5.5) \quad 2a_i x_i - 2\lambda \xi_i - \mu x_i = 0.$$

Summing up both sides of (5.5) from $i = 1$ to n , and noting (5.3), we have

$$2\bar{a} = \mu.$$

Therefore (5.5) yields

$$(5.6) \quad \xi_i = (a_i - \bar{a})x_i/\lambda.$$

By substituting this back into (5.1)' we have

$$\sum_i x_i (a_i - \bar{a})^2 / \lambda^2 = c.$$

The denominator in the left side of the above equation is $\frac{1}{2}V_g$ from (3.2)'', while $c = \frac{1}{2}V_g(\delta t)^2$, so that

$$1/\lambda^2 = (\delta t)^2 \text{ or } 1/\lambda = \delta t,$$

because negative λ is inadequate. Thus (5.6) is

$$\xi_i = x_i(a_i - \bar{a})\delta t$$

or

$$\frac{\delta x_i}{\delta t} = x_i(a_i - \bar{a}), \quad (i = 1, \dots, n)$$

which is equivalent to (2.2.2) and gives the law of change in gene frequencies due to natural selection.

Geometrical consideration may help in understanding the above theorem (fig. 2). We consider an $(n+1)$ dimensional space in which there are n coordinates for gene frequencies and one coordinate for population fitness. A population with a given set of gene frequencies is expressed as a point P in this space. A set of displacements ξ_i 's together with a corresponding change in population fitness η define a vector radiating from P . Projection of this vector on the n dimensional subspace of gene frequencies is inevitably on the hyper plane given by (5.3). Then the theorem states that among all such vectors whose projections on such n dimensional subspace are on the hyper-ellipsoid given by (5.1)', the vector corresponding to the change by natural selection is the one which gives maximum length of projection on the $\bar{a}$ axis.

The theorem can easily be extended to any number of loci. For example for two loci, we designate the displacement of gene frequencies in the second loci having m alleles by $\zeta_1, \zeta_2, \dots, \zeta_m$, then (5.1)' should be replaced by

$$(5.6) \quad \sum_{i=1}^n \frac{\xi_i^2}{x_i} + \sum_{j=1}^m \frac{\zeta_j^2}{x_j} = \frac{1}{2}V_g(\delta t)^2$$

and (5.3) by

$$(5.7) \quad \sum_i^n \xi_i = 0, \sum_j^m \zeta_j = 0$$

respectively.

The theorem may be further extended to cover a quite general situation in which the above restrictions of random mating and constant fitness of genotypes are removed. In what follows we will

FIG. 2.

consider only the case of a single segregating locus, but the argument may easily be extended to any number of loci.

Let $A = (\tilde{a}_1, \tilde{a}_2, \dots, \tilde{a}_n)$

be a vector whose components are average excesses of genes and let

$$D = (\xi_1, \xi_2, \dots, \xi_n)$$

be a displacement vector in the set of gene frequencies. Then natural selection acts in such a way that the product

$$AD' = \sum_i^n \tilde{a}_i \xi_i$$

shall be maximum under the restriction

$$\sum_i^n \xi_i^2 / x_i = \sigma_a^2 (\delta t)^2,$$

where σ_a^2 is the variance of average excess in fitness per ploid, *i.e.*,

$$\sigma_a^2 = \sum_i^n x_i (a_i - \bar{a})^2.$$

In this form the theorem is applicable not only to diploid but also to $2K$ ploid in general in which $K = \frac{1}{2}, 1, 2, 3, \dots$, etc.

The above theorem is somewhat analogous to the principle of least action in physics and may be called the maximum principle in the genetical theory of natural selection. Whereas from the least action principle the laws of motion may be derived, we may from this theorem derive the rules of change in gene frequencies.

6. RATE OF CHANGE OF POPULATION VARIABILITY

Considering the great importance of the genic variance in evolution, it is appropriate to study how quickly the genic variance will be consumed by natural selection for the improvement of the species. Though the following result is quite restricted, it may help our understanding of the problem.

Consider a random mating population and assume constant fitness of genotypes. In this case the average effect is equal to the average excess and we have

$$V_g = 2 \sum_{i=1}^n x_i (a_i - \bar{a})^2.$$

Taking the time derivative we have

$$\dot{V}_g = 2 \sum_i \dot{x}_i (a_i - \bar{a})^2 + 4 \sum_i x_i (a_i - \bar{a}) (\dot{a}_i - \dot{\bar{a}})$$

or

$$\dot{V}_g = 2 \sum_i x_i (a_i - \bar{a})^3 + 4 \sum_{ij} \dot{x}_i \dot{x}_j a_{ij}.$$

The first term in the right side is the third moment in average effect and will be designated by $\mu_{3(g)}$. The second term reduces to

$$4 \sum_{ij} \dot{x}_i \dot{x}_j d_{ij} \text{ or } \overline{4x_i \alpha_j d_{ij}}$$

so that

$$(6.1) \quad \frac{dV_g}{dt} = \mu_{3(g)} + \overline{4x_i \alpha_j d_{ij}}.$$

With no dominance the second term vanishes and we have

$$\frac{dV_g}{dt} = \mu_{3(g)}.$$

If the distribution of fitness among individuals in a population is near normal $\mu_{3(g)}$ will be very small as compared with V_g itself. This result seems to indicate that the additive genetic variance is consumed quite slowly by natural selection. This conclusion may not be much influenced in most cases by the presence of dominance, since the second term in (6.1) will usually be a small quantity.

7. APPLICATION TO ARTIFICIAL SELECTION

Here we consider only mass selection with respect to a quantitative character governed by a large number of factors.

Let $P_{ijkl\dots}$ be the frequency of the ordered genotype $A_i A_j B_k B_l \dots$, whose phenotypic value or yield is $Y_{ijkl\dots}$. Applying (3.13), the increase of population mean per generation becomes

$$(7.1) \quad \begin{aligned} \Delta \bar{Y} = & \sum_{ijkl\dots} (\Delta Y_{ijkl\dots}) P_{ijkl\dots} \\ & + 2 \left(\sum_i \alpha_i \Delta x_i + \sum_k \beta_k \Delta y_k + \dots \right) \\ & + \sum \epsilon \Delta \log \theta, \end{aligned}$$

where $\alpha, \beta, \dots$, are average effects of the genes on yield at the 1st, 2nd, etc., locus, and ϵ denotes an interaction effect on yield.

The first term in the right side of (7.1) gives the increase of yield by improvement of environment.

In order to handle the remaining terms in the right side of (7.1), we have to establish the relation between the yield ($Y_{ijkl\dots}$) and the fitness or selective value ($w_{ijkl\dots}$) of each genotype. For this we will employ the method used by Crow (1955), and based on an earlier finding of Haldane (1932).

Let σ^2 be the total phenotypic variance. Consider various phases in any locus, say the first, and designate the mean genotypic value of individuals with the phase $A_i A_j$ by

$$Y_{ij} = \sum_{kl\dots} P_{ijkl\dots} Y_{ijkl\dots} / \sum_{kl\dots} P_{ijkl\dots}.$$

We assume that the means of these phases have very small variance around $\bar{Y}$ compared with σ^2 , while individuals with a given phase, say $A_i A_j$, distribute normally with variance σ'^2 around the mean Y_{ij} .

Let $\bar{c}$ be the point of truncation measured from the population mean $\bar{Y}$, then the selective value of the phase $A_i A_j$ is

$$(7.2) \quad w_{ij} = \frac{1}{\sqrt{2\pi}\sigma'} \int_{\bar{c}}^{\infty} e^{-\frac{(y - \bar{Y}_{ij})^2}{2\sigma'^2}} dy,$$

where $\bar{Y}_{ij} = Y_{ij} - \bar{Y}$. Now we assume that $(\bar{Y}_{ij}/\sigma')^2$ is a negligible quantity. Thus we have approximately

$$w_{ij} = S + \frac{\bar{Y}_{ij}}{\sigma^2} IS \propto 1 + \frac{\bar{Y}_{ij}}{\sigma^2} I,$$

where

$$S = \frac{1}{\sqrt{2\pi}\sigma} \int_{\bar{c}}^{\infty} e^{-\frac{y^2}{2\sigma^2}} dy$$

or the proportion saved, and

$$I = \frac{1}{\sqrt{2\pi}\sigma} \int_{\bar{c}}^{\infty} ye^{-\frac{y^2}{2\sigma^2}} dy / S$$

or the selection differential.

The average excess in fitness of A_i is

$$\tilde{w}_i = \frac{\tilde{I}_i}{\sigma^2} I.$$

Thus the yield is transformed into fitness by multiplying by the factor I/σ^2 . Therefore

$$(7.3) \quad \Delta x_i = x_i \tilde{I}_i \cdot \frac{I}{\sigma^2},$$

where $\tilde{I}_i$ is the average excess of the gene A_i on yield. Substituting this in the second term of (7.1) we have

$$2 \sum_i \alpha_i \Delta x_i = 2 \frac{I}{\sigma^2} \sum_i \tilde{I}_i \alpha_i x_i = \frac{I}{\sigma^2} \sigma_{g(1)}^2,$$

where $\sigma_{g(1)}^2$ is the additive or genic variance in yield due to the first locus. Thus if we designate by σ_g^2 the total genic variance due to all loci, we have

$$(7.4) \quad 2(\sum_i \alpha_i \Delta x_i + \dots) = \frac{I}{\sigma^2} \sigma_g^2 = h^2 I,$$

where h^2 is the heritability in the narrow sense.

Next we will consider the effect of gene interactions collectively expressed in the last term of (7.1). The effect of dominance in the first locus appears as

$$\sum_{ij} P_{ij} d_{ij} \Delta \log \theta_{ij},$$

or

$$\sum_{ij} x_i x_j d_{ij} \Delta \theta_{ij}.$$

The most important case of non-random mating is inbreeding in which

$$\theta_{ii} = F/x_i + 1 - F \text{ and } \theta_{ij} = 1 - F \text{ for } i \neq j.$$

For this case, we have

$$(7.5) \quad \sum_{ij} x_i x_j d_{ij} \Delta \theta_{ij} = \frac{\Delta F}{1 - F} \sum_i d_{ii} x_i - F \sum_i d_{ii} \Delta x_i,$$

where Δx_i is given by (7.3). The total contribution by dominance is the sum of such terms for all loci.

Next we will consider terms due to epistasis. As pointed out by Fisher (1918), epistasis involving more than two loci may be rather unimportant and we will consider only dual epistacy. Let $\mathcal{J}_{ab}$ be the epistatic contribution due to interaction between the first and the second loci, then

$$\mathcal{J}_{ab} = \sum \overline{\epsilon_{ijkl} \Delta \log \theta_{ijkl}} = \sum_{ijkl} \epsilon_{ijkl} \Delta P_{ijkl},$$

where ϵ_{ijkl} stands for the epistatic effect on yield rather than on fitness. Perhaps the simplest but most important case in which $\mathcal{J}_{ab}$

is not zero is the case in which under random mating the two loci on the same chromosome have not reached linkage equilibrium. Let X_{ik} be the frequency of the chromosome with $A_i B_k$. Then the frequency of the ordered genotype $A_i A_j B_k B_l$ is

$$P_{ijkl} = \frac{1}{2}(X_{ik}X_{jl} + X_{il}X_{jk}).$$

Thus

$$(7.6) \quad \mathcal{J}_{ab} = 2 \sum_{ijkl} \epsilon_{ijkl} \Delta X_{ik} X_{jl} = 2 \sum_{ik} \epsilon_{i \cdot k} \Delta X_{ik},$$

where

$$\epsilon_{i \cdot k} = \sum_{jl} \epsilon_{ijkl} X_{jl}, \quad (\epsilon_{ijkl} = \epsilon_{ijlk} = \epsilon_{jikl} = \epsilon_{jilk}).$$

However

$$(7.7) \quad \Delta X_{ik} = X_{ik} \tilde{w}_{i \cdot k} - c \sum_{jl} \left| \frac{X_{ik} X_{il}}{X_{jk} X_{jl}} \right| w_{ijkl},$$

in which

$$\tilde{w}_{i \cdot k} = \sum_{jl} w_{ijkl} X_{jl} - \bar{w}$$

and w_{ijkl} is the selective value of $A_i A_j B_k B_l$ while c is the recombination fraction between the two loci. For the derivation of (7.7), the reader may refer to my previous paper (Kimura, 1956). Substituting (7.7) in (7.6) noting that fitness may be obtained from yield by multiplying I/σ^2 .

$$(7.8) \quad \mathcal{J}_{ab} = \frac{I}{\sigma^2} \left\{ E - 2c \sum_{ijkl} \epsilon_{i \cdot k} \left| \frac{X_{ik} X_{il}}{X_{jk} X_{jl}} \right| \gamma_{ijkl} \right\},$$

where

$$E = 2 \sum_{ik} \epsilon_{i \cdot k} \tilde{f}_{i \cdot k} X_{ik}.$$

The total contribution may be obtained by adding up terms like $\mathcal{J}_{ab}$ for all relevant pairs of loci. The case of random mating with linkage may also be approached by considering additive chromosomal variance rather than additive genic variance.

8. CONCLUDING REMARKS

Any discussion on the change of population fitness must start from the definition of the term fitness. Though there may be diverse ways of defining fitness, the term, to be useful for population genetics, must be related to organism's ability to leave descendants. If it is defined in terms of Malthusian parameters expressing the geometric rate of population increase, the rate of increase of population fitness, as shown from (3.9) through (3.13), is expressed as the sum of three terms: A term due to genic variance, one due to change in environment, and one due to the joint effect of genetic interaction (dominance and epistasis) and change in mating system:

$$(8.1) \quad \frac{d\bar{a}}{dt} = V_g + \bar{a} + \Sigma \epsilon \bar{\theta}.$$

From the standpoint of the genetical theory of evolution, the first term V_g is by far the most important, since it represents the part of increase in fitness due to the improvement of the *genic* constitution of the species. The effects due to the remaining terms are generally speaking unpredictable from the *genic* constitution of the species and may conveniently be treated as environmental factors. However, if we come down to a specific situation, we may handle these terms to obtain more information as shown in section 4.

In this section we will consider the effect of overpopulation on fitness. Since a given niche can support only a finite number of individuals at a given moment, the population mean of the Malthusian parameters, averaged over the long period that the species has lived, must be very near to zero. Whenever the genic constitution of the species is improved by natural selection, the increase in the Malthusian parameters will soon be cancelled out by the increase of population number. Though the equation (8.1) is general enough to include the above process as a special aspect, it may be interesting to separate it for special consideration.

Let M be the Malthusian parameter of an actual population and let N be the population number at a given moment, then we have

$$(8.2) \quad \frac{1}{N} \frac{dN}{dt} = M$$

by definition. Let $a_{ijkl\dots}$ be the Malthusian parameter of the genotype $A_i A_j B_k B_l \dots$ which would be realised if there were no effect of overcrowding, then $\bar{a}$ is the intrinsic rate of population increase and

$$(8.3) \quad \frac{1}{N} \frac{dN}{dt} = \bar{a} - f(N),$$

where $f(N)$ is a function representing the effect of population number or, when the population is confined to a restricted area, the effect of density. In other words $f(N)$ represents the resistance against population increase due to overcrowding.

From (8.2) and (8.3)

$$M = \bar{a} - f(N)$$

or taking time derivatives of both sides,

$$(8.4) \quad \frac{dM}{dt} = \frac{d\bar{a}}{dt} - \frac{df(N)}{dt}.$$

Since the second term in the right side may be written as

$$\frac{df(N)}{dt} = \frac{df(N)}{dN} \frac{dN}{dt} = MN \frac{df(N)}{dN},$$

(8.4) becomes

$$(8.5) \quad \frac{dM}{dt} + MN \frac{df(N)}{dN} = \frac{d\bar{a}}{dt},$$

where the right side is given by (8.1). Since we are considering the deleterious effect of *overpopulation*, we may assume that $f(N)$ is a monotone non-decreasing function and therefore $f'(N)$ is non-negative. However, it should be kept in mind that in nature extreme low population density is also disadvantageous for population growth (*cf.* Haldane, 1953).

Returning to (8.3), we will consider a few special cases. For the logistic law of growth

$$f(N) = KN,$$

where K is a constant, and therefore $f'(N) = K$. Thus the second term in the left side of (8.5) becomes KMN .

For weaker resistance, we may take

$$f(N) = K \log N.$$

In this case $f'(N) = K/N$ and we can get rid of a troublesome factor N out of the equation (8.5) :

$$(8.6) \quad \frac{dM}{dt} + \frac{M}{C} = V_g + \bar{a} + \Sigma \epsilon \bar{\theta},$$

where $C = 1/K$. (8.6) may be considered to be equivalent to Fisher's formulation :

$$(8.7) \quad \frac{dM}{dt} + \frac{M}{C} = W - D,$$

in which " W is the rate of actual increase in fitness determined by natural selection, and D is the rate of loss due to the deterioration of the environment" (Fisher, 1930). W is equal to our V_g and $-D$ corresponds to

$$\bar{a} + \Sigma \epsilon \bar{\theta}.$$

Thus Fisher's "environment" implies not only physical and biological environment in the usual sense, but also genetical environment the effect of which is represented by

$$\Sigma \epsilon \bar{\theta},$$

in our formulation. Considering the great diversity of ways in which non-genic (non-genetic in Fisher's sense) factors come into play, to treat such factors collectively as an environment is quite adequate. However, it is possible, as shown in the present paper, to represent the contribution by such factors in terms of gene interaction and change in mating system in a rather simple way when these are known.

9. SUMMARY

1. When fitness (a) of individual genotypes is measured in Malthusian parameters, the rate of increase of population fitness due to natural selection is expressed as a sum of the three terms : (i) a term due to *genic* (or additive genetic) variance in fitness (V_g), (ii) one due

to change in environment, and (iii) one due to joint effect of genetic interaction (dominance and epistasis) and change in mating system. Thus we have

$$\frac{d\bar{a}}{dt} = V_g + \frac{d\bar{a}}{dt} + \Sigma \epsilon \frac{d}{dt} \log \theta,$$

in which ϵ stands for an interaction effect in fitness and θ is the corresponding coefficient of departure from random combination. The summation extends over all possible interactions. The above formulation establishes the roles of additive, dominance and epistatic components on the rate of increase of population fitness. It is the reformulation of the results published by Fisher in 1930 under the title *The Fundamental Theorem of Natural Selection*, and in no way differs from it in substance. θ corresponds with λ of Fisher's (1941) treatment.

2. An attempt to formulate the law of change in gene frequencies due to natural selection has led to a theorem which, for a simple case of random mating with constant fitness of individual genotypes, may be expressed in the following form: For a given short time interval δt , the natural selection causes gene frequency changes, $\delta x_1, \delta x_2, \dots, \delta x_n$, in such a way that the increase of population fitness, $\delta \bar{a}$, shall be maximum under the restriction of

$$\sum_{i=1}^n \frac{(\delta x_i)^2}{x_i} = \frac{1}{2} V_g (\delta t)^2.$$

This theorem is extended to cover a quite general situation. It is remarkable that the set of differential equations describing the law of change in gene frequencies by natural selection can be derived from the theorem. It may be called "a maximum principle in the genetical theory of natural selection" analogous to the principle of least action in physics.

3. The rate of change of the genic variability in fitness has been studied for a simple situation. The result seems to indicate that the genic variance is consumed rather slowly by natural selection.

4. The rate of increase of yield by artificial selection has been given with special reference to the roles of dominance and epistatic components when inbreeding and linkage are involved.

5. The present formulation on the change of population fitness is compared with the results by Fisher (1930) and the effect of population number on fitness has been discussed.

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