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The Genotype × Environment-to-Phenotype Relationship

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Summary. Proceeding from the formal genotype × environment-to-phenotype functional relationship, a few common concepts essentially based upon this relationship have been reviewed and redefined. Particular attention was given to forming unambiguous representations. In summary, these concepts were: the reaction norm and phenotypic range of a genotype, the genetic control of traits, the general representation of genotypic and environmental contributions to a phenotype and the related problem of genotype × environment interaction, the fitness function, selective neutrality and superiority. The role of joint frequency distributions of genotypes and environmental situations for detecting and describing certain properties of the underlying genotype × environment-to-phenotype functional relationship has been demonstrated by means of models for genotype × environment interaction and the fitness function.

Introduction

Presumably the most basic and widely accepted concept underlying the majority of theories, experimental perspectives and interpretations in the fields of population-, ecological- and biometrical genetics is the idea that the phenotype of an individual is completely and uniquely determined by its genotype and the totality of all environmental forces (biotic or abiotic) affecting this individual during its whole life span. Consequently, one of the main objectives in experimental genetics is to detect the functional relationships between genotype combined with environment, on the one hand, and phenotype on the other hand. Conversely, the theoretical population geneticist, for example, has to make assumptions about this functional relationship; for instance he must specify his model. Both the detection and application of such functional relationships involve investigating populations or, more generally, sets of biological organisms, which necessarily are subject to some distributional pattern with respect to the available environment. Thus, what has to be taken into account when analysing or predicting a phenotypic distribution of a population is the fact that this distribution comprises the joint effects of distributional patterns of genotypes over environments, and the functional relationship. In view of this, conclusions based upon results from specific population biological or breeding experiments, in most cases, allow only for extremely cautious generalization beyond the particular situation which has been investigated.

During the last six years or so, this point has been the subject of thorough argument. Stimulated by Jensen's paper "How much can we boost I.Q. and scholastic achievement?" (Jensen 1969), Lewontin (1970) wrote an intense article, in which he tried to prove that Jensen's conclusions are erroneous, since they did not sufficiently account for the fact that "heritability is not a concept that can be applied to a trait in general, but only to a trait in a particular population, in a particular set of environments". In a more general context, the same author (Lewontin 1974) tackled this problem as one of analysis of the causes of variation and - from the standpoint of a human geneticist - arrived at the conclusion that the most frequently applied tool in biological etiology, the analysis of variance, "is not a tool for the elucidation of functional biological relations", as it is frequently considered to be. The negative consequences of such misconceptions for interpreting the significance of heritability induced Feldman and Lewontin (1975) to state that "the simple estimate of heritability" ... "is nearly equivalent to no information at all for any serious problem in human genetics".

The impact of the genotype × environment-to-phenotype functional relationship on the selection theory of biological evolution has been outlined by Waddington (1974) and has been demonstrated in more detail by Cavalli-Sforza (1974), who interpreted

the role of phenotypic plasticity of genotypes in evolution.

The author of the present paper believes that a considerable portion of these well-justified criticisms would have been unnecessary, and modelling of population-, ecological- and biometrical genetic ideas and findings could have been carried out much more effectively in the sense of revealing their true biological relevance, if there were general agreement about an unambiguous and as comprehensive as possible formalization of the genotype × environment-to-phenotype functional relationship and its integration into population biological studies. Such a formalization could be extremely helpful in redefining standard concepts, such as "norm of reaction", "additivity" of genetic and environmental effects and their "interactions", etc., in mathematically precise terms, which at the same time would elucidate their real significance.

It should be mentioned that there already exist several attempts in this direction, for instance within two of the above cited papers (Waddington 1974; Feldman and Lewontin 1975), but unfortunately they are not argued to a sufficient extent. The following statements pursue this object, without claiming completeness but rather with the hope of initiating further discussion.

The concept

In order to make the genotype × environment-to-phenotype relationship a functional one (in the mathematical sense), it is necessary to define what is understood by the units making up an environment. Such a unit is denoted as an "environmental situation" and defined with reference to an individual as the completely ordered set (the order being induced by the time scale used for measuring individuals' ages) of all external forces which are theoretically or actually involved in the phenotypic realization of this individual's genetic information over its entire period of existence. Consequently, these forces are allowed to be of abiotic as well as of biotic nature, as long as they themselves are not part of the individual's genetic information. For example, an individual might be affected during its lifetime by the presence of special competitors, temperature, nutrient concentration in the soil, mating partners, etc.

The idea now is to assign to each pair (g,u), where g is a genotype (with respect to all gene loci) and u is an environmental situation, in a unique manner a value (phenotype) of a trait under consideration. This process of assignment describes a function φ, called the "trait function" or simply "trait", whose range $R(\varphi)$ is given by the set of values $\varphi(g,u)$, g and u varying over a set of genotypes G and a set of environmental situations U under consideration. G and U are referred to as "genotypic state space" and "environmental state space" or "environment", respectively.

If $R(\varphi)$ is a subset of some "phenotypic state space" F, we may write

$$\varphi: G \times U \to F.$$

In the following, $R(\ldots)$ will always denote the range of a function (mapping).

φ reflects the real biological interrelationships between genetic information and external forces which result in the creation of a phenotype.

To account for the practical necessity of investigating populations of genotypes (regarded as subsets of G) which are distributed over an environment (regarded as a subset of U) when trying to reveal the structure of a trait function φ, we include in our considerations a probability measure $P(\ldots)$ over $G \times U$ (assuming specification of appropriate σ-algebras over G and U). Thus the resulting marginal distribution for G is simply the genotypic frequency distribution, i.e. the genetic structure of the population, while the marginal distribution for U is the frequency distribution of the environmental situations. Furthermore, the probability measure over F (again assuming that a σ-algebra over F is specified and that φ is measurable), which gives the phenotypic frequency distribution for φ, can be written as $P(\varphi \in \ldots)$, or $P(\varphi = \ldots)$.

Clearly, changes in a naturally reproducing population can, for instance, be described by a sequence of probability measures $P(\ldots)$ in time, leaving G, U, F and φ unchanged.

The implications of these few basic, conceptual statements for a meaningful redefinition of some frequently used concepts in biometrical and population genetics shall be demonstrated by means of several selected examples in the sequel.

The genotype-to-phenotype relationship (effect of the genotype)

From the preceding formalization, it can be taken at once that the relationship 'genotype-to-phenotype' in general need not be unique, but rather depends on the trait φ and the environment U under consideration. Therefore, the notion of 'genotypic value' in most cases is meaningless - or at least highly artificial - and has to be replaced by a different concept reflecting the mode according to which an environment U modifies the trait values for φ in conjunction with a given genotype g; this is commonly known as the "norm of reaction" of a genotype g, given a trait φ and an environment U. Formally, the norm of reaction thus defined is the function (mapping)

$$\varphi(g,\cdot) : U \to F \quad (\varphi(g,\cdot) \text{ assigns to each } u \in U \text{ the value } \varphi(g,u)),$$

examples for which can be found in Lewontin (1974) and Cavalli-Sforza (1974). In addition we shall denote the range of $\varphi(g,\cdot)$ - i.e. $R(\varphi(g,\cdot)) = \{\varphi(g,u) \mid u \in U\}$ - as the phenotypic range of the genotype g, given a trait φ and an environment U.

Recalling that it is impossible to observe a genotype ab ovo, but rather only from its phenotypic appearance, the question arises as to how to distinguish between different genotypes on the basis of an observable trait φ. Clearly, the highest degree of information about a genotype that may be obtained under these conditions is provided by the reaction norm of this genotype, which suggests treating two genotypes g_1 and g_2 as "phenotypically equivalent" if their reaction norms coincide, i.e. if

$$\varphi(g_1,u) = \varphi(g_2,u) \text{ for all } u \in U.$$

The standard genetic approach to explaining such phenotypic equivalence is based upon models of dominance and epistasy.

Yet, experimental conditions which allow comparisons of reaction norms are hardly attainable, since it is not possible to subject environmental situations to sufficiently precise control. On the other hand, there are opportunities to specify phenotypic ranges of genotypes (e.g. by clonal propagation of forest trees) within acceptable limits of precision. In this case, distinction of genotypes amounts to viewing the

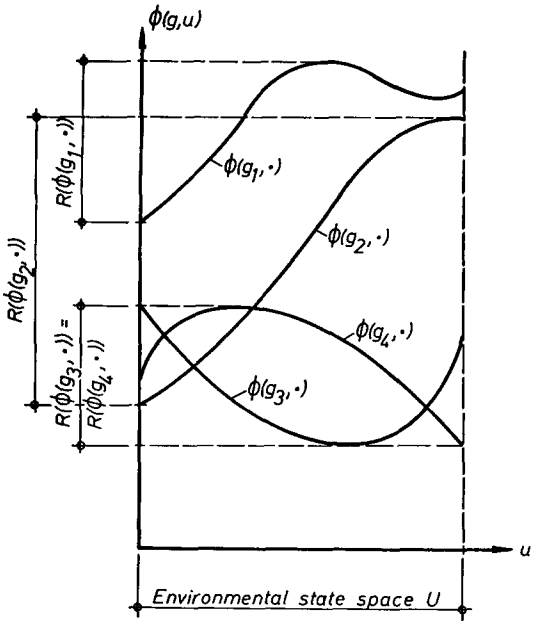

Fig. 1. The norm of reaction $\varphi(g,\cdot)$ of a genotype g with respect to a trait φ. $R(\varphi(g,\cdot))$=phenotypic range of genotype g. Phenotypic ranges of g_3 and g_4 are identical, but reaction norms are not. Phenotypic ranges of g_1 and g_2 are not

degree of overlapping between the appertaining phenotypic ranges, namely the intersection

$$R(\varphi(g_1,\cdot)) \cap R(\varphi(g_2,\cdot)).$$

If this intersection is empty, any value from these two ranges can unambiguously be identified as a phenotypic expression of one of the two genotypes. Otherwise there exist more or less wide-spread regions of ambiguity; at an extreme both ranges are identical, which clearly does not imply that the reaction norms are, although the reverse implication is true (consult Fig. 1).

The question of distinguishing between genotypes based on reaction norms is directly related to the question concerning which gene-loci actually affect the realization of phenotypes, in the usual sense that changes in reaction norm can be explained exclusively by changes of genotypes at these loci (called "controlling" loci), not referring explicitly to biochemical and/or biophysical causal relationships between phenotype and genotype. On the other hand, given a set of gene-loci at which for the moment genotypes are held fixed, the remaining loci are usually called "neutral" if changes of genotypes at these loci do not affect the reaction norm and if this holds for any combination of

genotypes in the initially given set of loci. It is evident that there might exist different sets of controlling loci (e.g. the set of all loci is always controlling if at least two reaction norms are different).

In order to derive a precise formulation of these facts, we refer to the notion of phenotypically equivalent genotypes. According to this concept, G can be decomposed into a number n of mutually disjunct subsets

$$G_i^{\varphi} \quad (i = 1,\ldots,n),$$

each of which contains all those genotypes which give rise to the same reaction norm (thus n is the number of different reaction norms). Additionally, let θ_l be a mapping defined on G, such that

$$\theta_l(g)$$

specifies the genotype at the l-th gene-locus for some genotype $g \in G$. Note that (if m is the number of gene-loci considered within G) each $g \in G$ can be conceived of as - and thus identified with - a vector

$$\theta(g) := (\theta_1(g),\ldots,\theta_m(g))$$

which therefore is an element of the cartesian product

$$\bigtimes_{l=1}^{m} R(\theta_l).$$

Using this representation, G is a part (not necessarily all) of

$$\bigtimes_{l=1}^{m} R(\theta_l).$$

Finally let θ^* be a subvector of θ, that is the components of θ^* are a collection of those contained in θ, preserving the order specified in θ.

Now, if θ^* can be regarded as representing a collection of controlling loci and if

$$\theta^*(G_i^{\varphi}) := \{\theta^*(g) \mid g \in G_i^{\varphi}\},$$

it is clear that two genotypes g_1 and g_2, with different reaction norms, say $g_1 \in G_i^{\varphi}$ and $g_2 \in G_j^{\varphi}$, always obey the relation $\theta^*(g_1) \neq \theta^*(g_2)$; consequently the intersection

$$\theta^*(G_i^{\varphi}) \cap \theta^*(G_j^{\varphi}) \text{ is empty for all } i \neq j \ (i,j = 1,\ldots,n).$$

Conversely, if some collection of gene-loci θ^* has these properties, it is easily seen from the verbal description that θ^* is controlling. Consequently we may define the following:

θ^* represents a vector of controlling loci if,
and only if,
$\theta^*(G_i^{\varphi}) \cap \theta^*(G_j^{\varphi})$ is empty for all $i \neq j$ $(i,j = 1,\ldots,n)$.

Obviously, the only case with no genetic control at all is realized for $n = 1$; i.e. there exists one reaction norm only.

The formal definition of a set of neutral loci requires specification of the mapping $\overline{\theta}^*$, representing the vector of loci, which is complementary to θ^* in the sense that it is composed of those loci which are not contained in θ^*, again preserving the order given in θ. According to the verbal description, θ^* represents a set of neutral loci if they do not change the reaction norm, i.e. for all pairs of genotypes g_1, $g_2 \in G$ with $\overline{\theta}^*(g_1) = \overline{\theta}^*(g_2)$, the reaction norms of g_1 and g_2 are identical, namely $\varphi(g_1,\cdot) = \varphi(g_2,\cdot)$. Equivalently we can state:

$\theta^*(\theta^* \neq \theta)$ represents a vector of neutral loci if, and only if, for each pair of genotypes $g_1, g_2 \in G$ with $\overline{\theta}^*(g_1) = \overline{\theta}^*(g_2)$, this implies $g_1, g_2 \in G_i^{\varphi}$ for some $i = 1,\ldots,n$.

In particular, a set of gene-loci which show only a single genotype is neutral.

The fact that we have not as yet imposed further restrictions on G and φ faces us with the dilemma that, in general, there exist θ^*'s which at the same time represent a set of controlling and neutral loci, as demonstrated by the following example:

Assume $m = 3$; $R(\theta_1) = \{A_1, A_2\}$, $R(\theta_2) = \{B_1, B_2\}$,
$R(\theta_3) = \{C_1,\ldots,C_4\}$;
$g_1 = (A_1,B_1,C_1)$, $g_2 = (A_1,B_1,C_2)$, $g_3 = (A_2,B_2,C_3)$,
$g_4 = (A_2,B_2,C_4)$ and $G = \{g_1,\ldots,g_4\}$; furthermore
$G_1^{\varphi} = \{g_1,g_2\}$, $G_2^{\varphi} = \{g_3,g_4\}$ and $\theta^* = \theta_3$.

It is immediately clear that in this case θ^* is controlling as well as neutral.

This dilemma can be overcome if we further restrict the definition of neutral loci by requiring that within G, genotypes at these loci can be varied over their whole range for fixed genotypes at each of the remaining loci. If

$$\overline{\theta}^{*-1}(S) := \{g \mid g \in G \text{ and } \overline{\theta}^*(g) \in S\} \text{ (the counter-image of } S \text{ under } \overline{\theta}^*)$$

for any subset S from $R(\overline{\theta}^*)$, the above requirement can be given the formulation

$$\theta^*(\overline{\theta}^{*-1}(a)) = R(\theta^*) \text{ for all } a \in R(\overline{\theta}^*).$$

We now can define:

θ^* represents a vector of "effectively neutral" loci, if and only if, θ^* is neutral and $\theta^*(\overline{\theta}^{*-1}(a)) = R(\theta^*)$ for all $a \in R(\overline{\theta}^*)$.

A trivial proof now shows that an effectively neutral θ^* cannot be controlling at the same time, and because of this $\overline{\theta}^*$ is controlling.

It ought to be emphasized that for an arbitrarily given θ^* the classification between "effectively neutral" and "controlling" must not be exhaustive, since it might be none of both but simply not controlling; i.e. for at least one pair of subscripts $i, j\ (i \neq j)$, $\theta^*(G_i^{\varphi}) \cap \theta^*(G_j^{\varphi})$ is not empty.

What remains to be considered in this context is an answer to the question, whether it is possible to specify in a unique way an effectively neutral subvector of θ (called "maximum effectively neutral"), which comprises the components of all effectively neutral vectors, as well as a controlling vector (called "minimum controlling") which is a subvector of all controlling ones.

An affirmative answer can be given for $G = \bigtimes_{l=1}^{m} R(\theta_l)$.

In this case the following assertions are easily proven: The terms "effectively neutral" and "neutral" are synonyms.

The union of two neutral subvectors again is a neutral subvector, whereby the union of two vectors is defined to be the vector whose components are exactly those of the two vectors.

The complementary vector (with respect to θ) of a controlling subvector is neutral.

From these findings we conclude immediately: The union of all neutral subvectors is the only maximum neutral vector, and its complementary vector is the only minimum controlling one, if

$$G = \bigtimes_{l=1}^{m} R(\theta_l).$$

In colloquial usage, when talking about a number of gene-loci controlling a trait, this number is meant to be the number of components represented in the minimum controlling subvector. Therefore, in general, i.e. for any arbitrary set of genotypes G, it might not be feasible to specify such a number at all.

Closing this chapter, it should be pointed out once more that the previous considerations about neutral and controlling gene-loci fundamentally referred to the notion of phenotypic equivalence of genotypes with respect to their reaction norms. However, it is generally possible to base such an equivalence relationship not only on reaction norms but also on phenotypic ranges. If this is done in a meaningful way, the same conclusions can be derived.

Genotype × environment interaction

The term "interaction" is used with a variety of meanings and, even in the special field of biometrical genetics, it is not uniquely defined (see e.g. Mather and Jinks 1971, p. 56 ff). Nevertheless, there is a common basic idea underlying nearly all of the reflections on this subject as far as it is applied to genetics theory. This idea is governed by the wish to distinguish between the contributions to the total phenotype which are due to genotypic and those due to environmental agencies, knowing that complete separation might not always be possible. In other words, the desire is to find two functions, one representing only the genotypic, and the other the environmental agencies, and combine these two functions according to some specified process or model (e.g. additive) so that the trait function under consideration comes out. Thus the first function would characterize the genotypic, and the second the environmental contribution to the trait.

Yet, the possibilities of finding two such functions are restricted by the properties of the model according to which the functions are combined in order to yield the trait function; that is, the model might not allow us to find appropriate functions. It is precisely this situation which is termed "interaction", and since it depends heavily on the model employed, it should be termed "interaction with respect to the model".

These thoughts can be directly transferred into a formal representation using the following notations:

$L_\gamma := \{\gamma \mid \gamma\colon G \to F\}$ is a set of functions (mappings), each of which characterizes a "genotypic contribution". For instance, $\varphi(\cdot, u)$ belongs to L_γ for each $u \in U$.

$L_\varepsilon := \{\varepsilon \mid \varepsilon\colon U \to F\}$ is a set of functions, each of which characterizes an "environmental contribution". For instance, $\varphi(g, \cdot)$ belongs to L_ε for each $g \in G$.

$W := \{\beta \mid \beta\colon G \times U \to F\}$ is a set of functions, each of which characterizes a "hypothetical trait function". For instance the actual trait function φ belongs to W.

$\mu : L_\gamma \times L_\varepsilon \to W$ is a mapping characterizing the model according to which genotypic (γ) and environmental (ε) contributions are combined in order to yield a hypothetical trait function β.

Sometimes in mathematical diction φ is called "separable with respect to μ" or simply "φ-separable" if the equation

$$\mu(\gamma, \varepsilon) = \varphi$$

has a solution $(\gamma^*, \varepsilon^*) \in L_\gamma \times L_\varepsilon$; otherwise φ is not μ-separable. Thus "no μ-separability" of φ is synonymous with "μ-interaction" of genotype and environment with respect to the trait φ; on the other hand, "μ-separability" is synonymous with "no μ-interaction".

Both synonymous terms very well meet our intuitive comprehension of the subject. In fact, on the one side there is the question of whether it is possible to view the influences of genotype and environment on the trait separately, i.e. to separate them, and on the other side, if this cannot be done, to attribute it to a kind of interrelationship, i.e. interaction, between the two influences.

Furthermore, since there is no criterion of global validity imaginable which specifies a priori how to extract the genotypic and environmental contributions from a trait and how to decide upon their separability, it is inevitable that an approach is chosen which explicitly includes the possibility of freely selecting a criterion (μ) for judgement on the interrelationship between the contributions. Above all, it becomes apparent that "interaction" is a relative phenomenon which might be realized with one μ but not with another. It is difficult to answer the question of which μ in the individual case has to be regarded as the most appropriate one.

Doubtless, the most frequently applied representation for μ is the additive model, i.e.

$$\mu(\gamma, \varepsilon) := \gamma + \varepsilon$$

which is meaningful if we assume $F = \mathbb{R}^k$ (k-dimensional real Euclidean space). In particular, for $k = 1$, that is $F = \mathbb{R}^1 = \mathbb{R}$ (set of real numbers), this is the model which enters into the analysis of variance; later we shall return to this model once more.

To avoid producing the impression that the additive model is the only reasonable one, three other examples shall be listed.

The multiplicative model: Assume $F = \mathbb{R}$, then

$$\mu(\gamma, \varepsilon) := \gamma \cdot \varepsilon.$$

The model of complete genetic control:

$$\mu(\gamma, \varepsilon) := \gamma.$$

If the equation $\mu(\gamma, \varepsilon) = \varphi$ has a solution, this means that the reaction norm $\varphi(g, \cdot)$ is constant on U for each $g \in G$; i.e. environment has no modifying influence on trait expression.

The model of genetic neutrality:

$$\mu(\gamma, \varepsilon) := \varepsilon;$$

again, if the equation $\mu(\gamma, \varepsilon) = \varphi$ has a solution, the trait φ is not heritable and is therefore exclusively environmentally dependent.

The last two models are particularly interesting in so far as they reflect the two extremes of absence of interaction (separability), distinguished by the fact that either environmental or genetic effects on the trait are totally eliminated; this corresponds to heri-

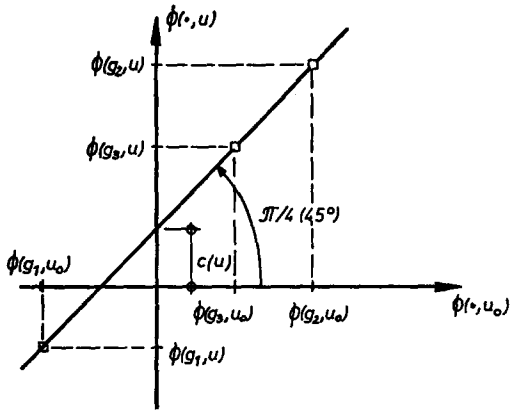

Fig.2. Additivity of the genotypic and environmental contributions to the trait φ: genotypes in two different environmental situations u_0 and u plotted against each other

tabilities of 1 and 0, respectively. In terms of reaction norms, this states that either each reaction norm is constant (in the sense that the corresponding phenotypic range contains one element only) but not all are identical, or that all reaction norms are identical.

Evidently, the above definition of φ showing no μ-interaction of genotype and environment is equivalent to $\varphi \in R(\mu)$, using the already-introduced notion of the range $R(\ldots)$ of a function. In reality, we therefore need reasonable methods which enable effective investigation as to whether $\varphi \in R(\mu)$ or not.

Referring to the additive and multiplicative model this problem shall be tackled briefly by setting up equivalent conditions under which $\varphi \in R(\mu)$, without giving the trivial proofs.

The additive model μ^+

Condition (a^+). $\varphi \in R(\mu^+)$ if and only if for any $u_0 \in U$, $\varphi(g,u)-\varphi(g,u_0)$ is a function of u only.

Condition (b^+). $\varphi \in R(\mu^+)$ if and only if for any $g_0 \in G$, $\varphi(g,u)-\varphi(g_0,u)$ is a function of g only.

Conditions (a^+) and (b^+) simply state that the functions $\varphi(g,\cdot)$ are parallels for all $g \in G$ as well as that the functions $\varphi(\cdot,u)$ are parallels for all $u \in U$, which reflects merely the usual testing basis in practical application.

Since many environmental variables are continuous, and since traits investigated are often controlled by a finite, and perhaps comparatively small, number of gene-loci (and thus a few genotypes) - or at least a small number of genotypes is taken into consideration - condition (a^+) may be regarded as the most effective one in the majority of cases.

For $F = \mathbb{R}$, the direct geometric interpretation of condition (a^+) proceeds as follows:

Consider a two-dimensional cartesian system of coordinates. On one axis the values of the function $\varphi(\cdot,u_0)$ for all $g \in G$ are distributed and on the other those of the function $\varphi(\cdot,u)$.

According to condition (a^+) put

$$\varphi(g,u)-\varphi(g,u_0) =: c(u), \text{ i.e. } \varphi(g,u) = c(u)+\varphi(g,u_0),$$

then clearly for fixed u this equation tells us that for each $g \in G$, the respective pair of coordinates is placed on a straight line with displacement $c(u)$ from the origin and slope 1. This holds for each $u \in U$ (see Fig.2).

Interchanging the significance of g and u, we arrive at an analogous interpretation of condition (b^+).

These considerations are easily transferred to the multiplicative model $\mu^\times$:

Condition $(a^\times)$. If $u_0 \in U$ with $\varphi(g,u_0) \neq 0$ for all $g \in G$, then $\varphi \in R(\mu^\times)$ if and only if $\varphi(g,u)/\varphi(g,u_0)$ is a function of u only.

Condition $(b^\times)$. If $g_0 \in G$ with $\varphi(g_0,u) \neq 0$ for all $u \in U$, then $\varphi \in R(\mu^\times)$ if and only if $\varphi(g,u)/\varphi(g_0,u)$ is a function of g only.

A generalization of these two conditions is derived in the appendix.

The direct geometric interpretation of condition $(a^\times)$ follows the same line as within the additive model, considering the same two-dimensional cartesian system of coordinates. But now put

$$\varphi(g,u)/\varphi(g,u_0) =: c(u), \text{ i.e. } \varphi(g,u) = c(u)\cdot\varphi(g,u_0),$$

then again for fixed u this equation tells us that for each $g \in G$, the respective pair of coordinates is placed on a straight line passing through the origin and having slope $c(u)$. This holds for each $u \in U$ (see Fig.3), and, as before, interchanging the significance of g and u results in an analogous interpretation of condition $(b^\times)$. For further applications and discussions of the multiplicative model see e.g. Mather (1975).

Finally, it should be emphasized again that just as for $\varphi \in R(\mu)$, a solution $(\gamma,\varepsilon) \in L_\gamma \times L_\varepsilon$ of $\mu(\gamma,\varepsilon) = \varphi$

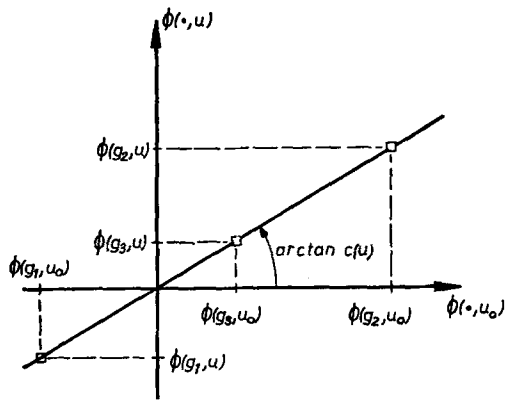

Fig. 3. Multiplicativity of genotypic and environmental contributions to the trait φ: genotypes in two different environmental situations u_0 and u plotted against each other

in general must not be unique, therefore, the 'strength' of interaction (i.e. deviation from μ-separability) for $\varphi \notin R(\mu)$ cannot be properly defined in the frame of this concept because of obvious reasons. Therefore any statement about an 'amount of interaction' should be examined very carefully.

Frequency distributions over G × U and additivity or multiplicativity of genotypic and environmental contributions

In the sequel, the usual and mostly self-evident conventions about notations and the meaning of multiplication and addition of functions or random variables as well as their expectations, conditional expectations, etc. (always assuming they exist) are applied without further definition or explanation. Expectations and variances of random variables X will be denoted E(X) and V(X) and conditional expectations and variances of X given some other variable Y will be denoted E(X|Y) and V(X|Y), respectively. Remember that expectations and variances of variables used in this paper ($\varphi, \varphi(g,\cdot), \varphi(\cdot,u), \varepsilon, \gamma$, etc.) are based upon a probability measure (frequency distributions) P(...) over G × U.

The following propositions and notations will turn out to be useful for the further considerations:
If $\varphi \in R(\mu^+)$ and $(\gamma^*, \varepsilon^*)$ is a particular solution of $\mu^+(\gamma,\varepsilon) = \varphi$, then all solutions (γ,ε) of this equation (i.e. $\gamma + \varepsilon = \varphi$) take the form $\gamma = \gamma^* + s$, $\varepsilon = \varepsilon^* - s$ with $s \in \mathbb{R}^k$; γ determines ε uniquely, since $\varepsilon = \varphi - \gamma$ (and vice versa).

Similarly for the multiplicative model $\mu^\times$, the set of all solutions of the equation $\gamma \cdot \varepsilon = \varphi$ is given by $\gamma = s \cdot \gamma^*$, $\varepsilon = \frac{1}{s} \cdot \varepsilon^*$ with $s \in \mathbb{R}$, $s \neq 0$; in the non-trivial case $\varphi \not\equiv 0$, there always exists $g \in G$ with $\gamma(g) \neq 0$, which allows determination of ε by $\varepsilon(u) = \varphi(g,u)/\gamma(g)$.

These facts suggest that we reduce studies of the set of solutions (γ,ε) of $\mu(\gamma,\varepsilon) = \varphi$, for instance, to the set

$$\Gamma_\varphi^\mu := \{\gamma \mid \gamma \in L_\gamma \text{ and there exists } \varepsilon \in L_\varepsilon \text{ with } \mu(\gamma,\varepsilon)=\varphi\};$$

clearly this set is empty for $\varphi \notin R(\mu)$. Consequently, if

$$\gamma^* \in \Gamma_\varphi^{\mu^+}, \text{ then } \Gamma_\varphi^{\mu^+} = \{\gamma^* + s \mid s \in \mathbb{R}^k\};$$

and if $\gamma^* \in \Gamma_\varphi^{\mu^\times}$, then $\Gamma_\varphi^{\mu^\times} = \{s \cdot \gamma^* \mid s \in \mathbb{R}, s \neq 0\}$.

An advantage of this formulation is that for separability of φ with respect to the additive or multiplicative model, it vividly gives prominence to the simple kind of relationship between the different genotypic contributions γ which can be chosen to represent the genetic influence on the same trait φ; viz. the genotypic contributions simply differ by an additive or a multiplicative constant.

Furthermore, if $\varphi \in R(\mu^+)$, we conclude from condition (a^+) that $\varphi(\cdot,u_0) \in \Gamma_\varphi^{\mu^+}$, since $\varphi(g,u) - \varphi(g,u_0)$ is a function of u only, and this holds for any $u_0 \in U$. Likewise, if $\varphi \in R(\mu^\times)$, $\varphi(\cdot,u_0) \in \Gamma_\varphi^{\mu^\times}$ for any $u_0 \in U$ with $\varphi(\cdot,u_0) \not\equiv 0$ (see condition $(a^\times)$ in the appendix). Theoretically, these statements provide a satisfactory method of finding all possible genotypic contributions for separability with respect to the additive or multiplicative model. Yet, in practical application, this way of proceeding often leads to unresolvable difficulties, mainly because single genotypes or environmental situations cannot be subject to sufficient experimental control. An alternative is offered by the so-called 'quantitative' methods of mathematical statistics resulting from the findings of probability theory. Still the most powerful tool within this frame as applied to genotype × environment interrelationships is the analysis of variance, which essentially involves estimations of certain kinds of expectations and variances

of trait functions φ. The following demonstrations contribute to these aspects, concentrating on genotypic contributions in connection with separable trait functions.

It was mentioned at the beginning of this chapter that we assume a probability measure $P(\ldots)$ over $G \times U$ to be given and that the distributions of random variables refer to this probability measure. In particular, variables such as γ or $\varphi(\cdot, u_0)$ are not explicitly defined on $G \times U$, but rather on G; nevertheless we regard them as functions defined on $G \times U$, assuming they are functionally independent of $u \in U$, which consequently implies that they are distributed according to the marginal or conditional marginal (given u_0) distribution on G with respect to $P(\ldots)$. A similar statement can be made for ε and $\varphi(g_0, \cdot)$ referring to the respective marginal distributions on U.

Dealing with expectations of random variables, the phenotypic state space F has to be real, i.e. $F = \mathbb{R}$.

The additive model: Suppose $\varphi \in R(\mu^+)$, $\gamma \in \Gamma_\varphi^{\mu^+}$ and therefore

$\varepsilon = \varphi - \gamma$. We immediately obtain

$$E(\varphi|u) = \varepsilon(u) + E(\gamma|u),\ E(\varphi|g) = \gamma(g) + E(\varepsilon|g),$$
$$V(\varphi|u) = V(\gamma|u),\ V(\varphi|g) = V(\varepsilon|g).$$

The notation $\varphi|g$ includes two aspects, a functional and a probabilistical one. The functional aspect of $\varphi|g$ refers to the function $\varphi(g, \cdot)$ (the reaction norm of g), while the probabilistical aspect refers to the distribution of $\varphi(g, \cdot)$ which is governed by the conditional probabilities $P(\ldots|g)$. Comprehensively but roughly speaking, $P(u|g)$ is the proportion of individuals among those having genotype g which exist in the environmental situation u. Obviously, the conditional probabilities in general might change with $g \in G$, and so might $E(\varepsilon|g)$, since it also depends on this conditional distribution. The respective arguments for $\varphi|u$ follow the same line.

For the case of stochastic independence between genotypes and environment, the conditional distributions are all identical to the appertaining marginal distribution, and in particular, $E(\varepsilon|g) = E(\varepsilon)$ for all $g \in G$, $E(\gamma|u) = E(\gamma)$ for all $u \in U$. Applying the preceding findings to this situation, we can now state that the two functions of g given by $E(\varphi|g)$ and $\varphi(g,u) - E(\varphi|u)$ belong to $\Gamma_\varphi^{\mu^\times}$ (are genotypic contributions). Note that these two representations of genotypic contributions can be easily estimated in most practical applications and, last but not least, because of this, play a central role in the analysis of variance.

The interpretation of the results for the variances need not be discussed in more detail, since the essential considerations again are based upon the respective underlying conditional distributions. Just for completeness, it shall be pointed out that, in the case of stochastic independence between genotypes and environment, the conditional variances are functionally independent of g and v ($V(\varphi|g) = V(\varepsilon)$ for all $g \in G$ and $V(\varphi|u) = V(\gamma)$ for all $u \in U$), which of course does not mean that they are equal to the total phenotypic variance $V(\varphi)$ of the trait φ.

The multiplicative model: As before, suppose $\varphi \in R(\mu^\times)$, $\gamma \in \Gamma_\varphi^{\mu^\times}$. Now

$$E(\varphi|g) = \gamma(g) \cdot E(\varepsilon|g),\ E(\varphi|u) = \varepsilon(u) \cdot E(\gamma|u),$$
$$V(\varphi|g) = \gamma(g)^2 \cdot V(\varepsilon|g), V(\varphi|u) = \mu(u)^2 \cdot V(\gamma|u).$$

Obviously, with respect to the expectations, there is complete analogy to the implications verified for the additive model. This is quite different for the variances. The standard deviation of the reaction norm as a function of g yields a genotypic contribution, that is,

$$V(\varphi|g)^{\frac{1}{2}} \text{ as a function of g belongs to } \Gamma_\varphi^{\mu^\times}$$

in the case of stochastic independence between genotypes and environment. Another significant distinction between the two models, as brought out by the variances, involves certain invariance properties of genotypic and environmental contributions. That is to say, the conditional variances of genotypic (γ), as well as environmental (ε) contributions, remain unchanged for each permissible choice of γ and ε in the additive model (i.e. $\gamma \in \Gamma_\varphi^{\mu^+}$, $\varepsilon = \varphi - \gamma$), which is not so in the multiplicative model.

At this point, let us briefly go back to the general treatment of the genotype × environment interrelationship, having in mind a more thorough description of trait variability caused by genotypic agencies. The problem has been touched on before, together with the concept of phenotypic equivalence of genotypes and the model of genetic neutrality, focusing attention on reaction norms $\varphi(g, \cdot)$. Now we concentrate on the functions $\varphi(\cdot, u)$. Evidently, genotypes do not affect

trait expression in environmental situation u, if the function $\varphi(\cdot,u)$ is constant on G, and, on the other hand, the degree of genotypic affection on trait expression increases with the number of different values $\varphi(\cdot,u)$ adopts, as well as with the magnitude of the differences between these values. Thus, evaluation of the degree of genotypic affection would require the construction of an appropriate measure of variability within the range $R(\varphi(\cdot,u))$ of $\varphi(\cdot,u)$. Beyond this, variabilities within ranges $R(\varphi(\cdot,u))$ in turn might vary with $u \in U$, an aspect which can be accounted for by taking the mean over all variabilities, but which nevertheless is still worth discussing critically.

It is immediately clear that the statistical analoga to these heuristically described quantities are the conditional variance $V(\varphi|u)$ (measuring the variability within $R(\varphi(\cdot,u))$ and the expectation $E(V(\varphi|\mathring{u}))$ measuring the mean over all variabilities); we used the notation $\mathring{u}$ for u to indicate that $\mathring{u}$ now is regarded as a variable taking values u, which consequently implies that $V(\varphi|\mathring{u})$ is a random variable whose distribution is governed by the marginal distribution over U. In other words, $E(V(\varphi|\mathring{u}))$ in the statistical sense is taken to measure the amount of genotypically-caused trait variability. Furthermore, the generally valid formula

$$V(\varphi) = E(V(\varphi|\mathring{u})) + V(E(\varphi|\mathring{u}))$$

allows us to characterize $E(V(\varphi|\mathring{u}))$ as a contribution to the total phenotypic variance $V(\varphi)$, and because of this suggests the normalized version $E(V(\varphi|\mathring{u}))/V(\varphi)$ - which is not the (broad sense-) heritability - to represent the genotypically-caused part of trait variability.

Unfortunately, there are several inadequacies in this statistical measurement of variability, as can be taken from the above description of the term. Variability within the set $R(\varphi(\cdot,u))$ combines two facets, the abundance (power) of the set (i.e. the number of genotypes differing in trait expression for u) and the spread width among the elements of the set, whereby possible frequency distributions over the set are completely irrelevant. Explicitly, the variance accounts only for the second facet, that is the spread width, and even this can be arbitrarily modified by respective choices of frequency distributions. It is not feasible to penetrate the problem more extensively, because there does not yet exist an adequate analytical representation of variability in the above sense.

Returning to the cases $\varphi \in R(\mu^+)$ or $\varphi \in R(\mu^\times)$, the intrinsic significance of the genotypic contribution γ now becomes evident when looking at the conditional variances. Apart from the just mentioned inadequacies, γ directly and exclusively determines $E(V(\varphi|\mathring{u}))$ for the additive model, since $V(\varphi|u) = V(\gamma|u)$, which does not hold for the multiplicative model in general. This illustrative property of the additive model partially justifies its prominence.

In colloquial technical language, $E(\varphi|g)$ is called the 'genotypic value' of g, and therefore $V(E(\varphi|\mathring{g}))$ is conceived of as the 'genotypic variance', which gives rise to the definition of heritability in the form $V(E(\varphi|\mathring{g}))/V(\varphi)$. As is well known, this definition of heritability is claimed to make the same statement we derived for $E(V(\varphi|\mathring{u}))/V(\varphi)$ proceeding from elementary reflections about genotypic effects on trait expression only. We shall not enter into a lengthy discussion on the priority of one over the other, but restrict ourselves to the remark that both quantities are identical for $\varphi \in R(\mu^+)$ and stochastic independence between genotype and environment, since in this case

$$E(V(\varphi|\mathring{u})) = V(\gamma) = V(E(\varphi|\mathring{g})).$$

The fitness function

This chapter will not be concerned with definition, to say nothing of justifications of fitness concepts like 'darwinian', 'wrightian', 'reproductive value', etc., but rather will again be restricted to the representation of some fundamental and - hopefully - generally acceptable ideas connected with the term fitness.

Pursuing this goal, we principally refer to the papers of Cavalli-Sforza (1974) and Waddington (1974). Both authors agree that fitness has to be regarded as resulting from the joint operation of phenotype and environment, the latter author additionally subdividing the environmental agencies into what he calls 'epigenetic' and 'selective'. Since phenotype in turn is the product of genotype and environment, and recalling the very extensive definition of environmental situations, which naturally includes epigenetic and selective components, the joint operation of phenotype and environment in order to produce fitness val-

ues can, in the last analysis, be traced back to a process of assigning fitness values to pairs of genotypes and environmental situations. This brings us back to our original concept of the trait function, now called the 'fitness function', and consequently allows us to apply all the preceding findings to the trait 'fitness'.

In particular (accounting for its topicality), the notions of 'selectively neutral gene-loci' and 'selectively equivalent genotypes' are mere specifications of the previously introduced terms 'neutral gene-loci' and 'phenotypically equivalent genotypes', when considering the trait 'fitness'.

A further aspect of selective equivalence refers to the gene as the unit of hereditary transmission at a given gene-locus. More concretely, this concerns the idea of selective equivalence of allelomorphs, i.e. alleles at a gene-locus under study. Two alleles are recognized as selectively equivalent if, for any given $g \in G$ containing at least one of the two alleles, substitution of one such allele by the other does not change the fitness (reaction) norm. Notice that this can only be conducted if the respectively required genotypes belong to G. Usually, when talking about newly occurring, selectively neutral mutations, these are understood to be new alleles which are selectively equivalent to pre-existing ones, that is, they do not alter the established fitness pattern. At a selectively neutral gene-locus, clearly all alleles are selectively equivalent.

One of the central concerns of population genetics is the analysis and prediction of genetic structures of populations, a task which essentially involves inferences or assumptions about selective advantage of some genotypes over others. It is common knowledge that the selective superiority of a genotype can be understood only in the context of the circumstances to which it owes its superiority. Despite the great complexity of the subject, it is possible to perform a simple demonstration of the modes according to which selective superiority of genotypes is most often viewed. For this purpose, the fitness (phenotypic) state space F is assumed to be a completely ordered set, and for simplicity we choose $F = \mathbb{R}$ with the ordering relation '$\leqslant$' ('$\geqslant$').

In principle, qualitative comparisons of magnitude of fitness values for genotypes can be divided into three different categories, termed 'single', 'norm dependent' and 'global' comparisons. The meanings of the terms are as follows, using φ as the fitness function:

Single comparison: Elements from $G \times U$ are compared. A genotype g existing in an environmental situation u is said to be superior to a genotype g' existing in u' if $\varphi(g,u) > \varphi(g',u')$.

Norm dependent comparison: Fitness norms $\varphi(g,\cdot)$ are compared. A genotype g is said to be superior with respect to fitness norm to a genotype g', if $\varphi(g,\cdot) \geqslant \varphi(g',\cdot)$, i.e. $\varphi(g,u) \geqslant \varphi(g',u)$ for all $u \in U$.

Global comparison: Fitness (phenotypic) ranges $R(\varphi(g,\cdot))$ are compared. g is globally superior to g' if $\min R(\varphi(g,\cdot)) \geqslant \max R(\varphi(g',\cdot))$, i.e. the smallest fitness value of g in U is greater than or equal to the greatest one of g'.

Examples of these kinds of superiority can be taken from Fig. 1, where g_1 is superior to g_2 with respect to fitness norm, and g_1 is globally superior to g_3.

As a rule, single comparisons (besides genetic drift, migration, etc.) serve to explain the formation of locally differentiated subpopulations, and of genetic clines along environmental pathways, since different genotypes might be favoured within different environmental situations.

On the other hand, considering a single, non-subdivided population, the fitness of a genotype is made up of the fitness values of all individuals in the population having this genotype and the proportions according to which they are exposed to the environmental situations constituting the environment of the population; consequently, the fitness of the genotype is equal to the mean over all these individuals. This in turn requires accounting for the probability measure over $G \times U$, or in other words, the joint distribution of genotypes and environmental situations for the population. Thus the fitness of a genotype is given by $E(\varphi|g)$, and population specific superiority of one genotype over another has to be evaluated with respect to this conditional expectation of the fitness norm $\varphi(g,\cdot)$. Applying elementary properties of the expectation function, the intrinsic significance of norm dependent and global superiority for the population specific superiority of genotypes shows up immediately. If two groups of individuals having genotype g and g', respectively, are distributed over the environment in like manner (i.e. if the conditional probability-distributions $P(\ldots|g)$ and $P(\ldots|g')$ are identical), then

norm dependent superiority of g over g' implies population specific superiority of g over g', that is, $\varphi(g,\cdot) \geqslant \varphi(g',\cdot)$ implies $E(\varphi|g) \geqslant E(\varphi|g')$, an implication which, of course, need not hold in the case of non-identical conditional distributions. In particular, stochastic independence between genotypes and environment always guarantees identity of $P(\ldots|g)$ and $P(\ldots|g')$. On the other hand, irrespective of the underlying conditional distributions, global superiority of g over g' (i.e. $\min R(\varphi(g,\cdot)) \geqslant \max R(\varphi(g',\cdot))$) ensures population specific superiority of g over g'.

Therefore, it should be emphasized that, in general, functional and stochastic (statistical) superiority in fitness should not be confused.

Appendix

In favour of brevity, we use the symbols $A \Rightarrow B$ (read: A implies B) and $A \Leftrightarrow B$ (read: A is equivalent to B).

Since we consider a multiplicative model $\mu^{\times}$ for genotype × environment interaction, the following implications are meaningful:

$\varphi \in R(\mu^{+}) \Rightarrow [\varphi(g,u) = 0 \Rightarrow \varphi(g,\cdot) \equiv 0$ or $\varphi(\cdot,u) \equiv 0]$;
$\varphi(g,\cdot) \equiv 0$ for example, means $\varphi(g,u) = 0$ for all $u \in U$.

Define: $G_o := \{g | g \in G$ and $\varphi(g,\cdot) \neq 0\}$, $U_o := \{u | u \in U$ and $\varphi(\cdot,u) \neq 0\}$,

Clearly, $\varphi \in R(\mu^{\times})$ and $g_o \in G_o \Rightarrow \varphi(g_o,u) \neq 0$ for all $u \in U_o$; similarly, $\varphi \in R(\mu^{+})$ and $u_o \in U_o \Rightarrow \varphi(g,u_o) \neq 0$ for all $g \in G_o$. Furthermore, to avoid triviality assume $\varphi \not\equiv 0$. Then

$\varphi \in R(\mu^{\times}) \Rightarrow$ (a) if $u_o \in U_o$, then for all $(g,u) \in G_o \times U$ $\varphi(g,u)/\varphi(g,u)$ is functionally dependent on u only;
(b) if $g_o \in G_o$, then for all $(g,u) \in G \times U_o$ $\varphi(g,u)/\varphi(g_o,u)$ is functionally dependent on g only.

To invert these implications, assume the right-hand sides to be true; consequently, using (a) for example, allows us to put

$\varphi(g,u)/\varphi(g,u_o) =: \varepsilon(u)$ for $(g,u) \in G_o \times U$ (thus $\varepsilon(u) = 0$ for $u \notin U_o$) and
$\varphi(g,u_o) =: \gamma(g)$ for all $g \in G$ (thus $\gamma(g) = 0$ for $g \notin G_o$),
which implies $\varphi(g,u) = \gamma(g) \cdot \varepsilon(u)$ for all $(g,u) \in G \times U$.

Because of this, we are allowed to state for $\varphi \not\equiv 0$:

Condition $(a^{\times})$. $\varphi \in R(\mu^{\times}) \Leftrightarrow [\varphi(g,u) = 0 \Rightarrow \varphi(g,\cdot) \equiv 0$ or $\varphi(\cdot,u) \equiv 0]$ and if $u_o \in U_o$, then for all $(g,u) \in G_o \times U$, $\varphi(g,u)/\varphi(g,u_o)$ is functionally dependent on u only.

Condition $(b^{\times})$. $\varphi \in R(\mu^{\times}) \Leftrightarrow [\varphi(g,u) = 0 \Rightarrow \varphi(g,\cdot) \equiv 0$ or $\varphi(\cdot,u) \equiv 0]$ and if $g_o \in G_o$, then for all $(g,u) \in G \times U_o$, $\varphi(g,u)/\varphi(g_o,u)$ is functionally dependent on g only.

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