Multiplicative *vs.* Arbitrary Gene Action in Heterosis

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ABSTRACT

In this article we investigate multiplicative effects between genes in relation to heterosis. The extensive literature on heterosis due to multiplicative effects between characters is reviewed, as is earlier work on the genetic description of heterosis. A two-locus diallelic model of arbitrary gene action is used to derive linear parameters for two multiplicative models. With multiplicative action between loci, epistatic effects are nonlinear functions of one-locus effects and the mean. With completely multiplicative action, the mean and additive effects form similar restrictions for all the rest of the effects. Extensions to more than two loci are indicated. The linear parameters of various models are then used to describe heterosis, which is taken as the difference between respective averages of a cross (F_1) and its two parent populations ($\bar{P}$). The difference ($F_2 - \bar{P}$) is also discussed. Two parts of heterosis are distinguished: part I arising from dominance, and part II due to additive × additive ($a \times a$)-epistasis. Heterosis with multiplicative action between loci implies multiplicative accumulation of heterosis present at individual loci in part I, in addition to multiplicative ($a \times a$)-interaction in part II. Heterosis with completely multiplicative action can only be negative (*i.e.*, the F_1 values must be less than the midparent), but the difference ($F_2 - \bar{P}$) can be positive under certain conditions. Heterosis without dominance can arise from multiplicative as well as any other nonadditive action between loci, as is exemplified by diminishing return interaction. The discussion enlarges the scope in various directions: the genetic significance of multiplicative models is considered. The description of heterosis is extended to three loci to show that multiplicative action between loci can make part I very large, but not part II. The genetic role of part II is explained. Finally, we compare multiplicative to arbitrary gene action in general, suggesting that the former may serve to measure nonadditivity of gene interactions in the latter.

IN a recent article MINVIELLE (1987) presented a two-locus diallelic model for which there were no dominance effects but with multiplicative effects that could lead to heterosis. As was shown by COCKERHAM (1959), multiplicative effects between non-alleles which otherwise act additively give rise to epistatic effects of the additive by additive ($a \times a$)-type. The objective of the present paper is to clarify the role multiplicative gene action can play in producing heterosis. The influences exerted on heterosis by multiplicative effects between genes cannot properly be discussed without referring to multiplicative effects between characters. As effects of the latter kind have been dealt with by various authors who sometimes were partly unaware of each other, we shall first recapitulate the main lines of research done in that area. Some earlier work on the genetic description of heterosis will also be reviewed.

REVIEW OF LITERATURE

Multiplicative interaction as a source of heterosis is widely known in complex characters which are products of two or more subcharacters. Plant height, for example, is the product of internode length and number. RICHEY (1942) was the first to realize that the relations between the product of means and the mean of products can lead to heterosis which is not due to dominance. Let the respective levels of two component traits be X' and Y' in parent P', X'' and Y'' in parent P'', and $\bar{X} = (X' + X'')/2$ and $\bar{Y} = (Y' + Y'')/2$ in the midparent as well as in the F_1, assuming heterosis in the components to be absent. In the complex trait, then, the F_1 will differ from the midparent ($\bar{P}$) by

$$F_1 - \bar{P} = \overline{XY} - (X'Y' + X''Y'')/2 = -(X' - X'')(Y' - Y'')/4. \quad (1)$$

The positive effect resulting from (1) when $X' > X''$ but $Y' < Y''$, or vice versa, was called "mock dominance" by RICHEY. He estimated such effects would be too small to account for any substantial part of the heterosis observed in corn, for example. DEMPSTER (1942) doubted whether an interaction like that defined in (1) should be described as "mock" because its leading to heterosis cannot be removed by transformation of scale. POWERS (1944) reported yield heterosis in tomato crosses some of which were closer to

the respective lower parent in both subcharacters, fruit number and weight. This allowed him to illustrate that the explanation of heterosis by at least partial dominance of favorable genes is not necessary when non-allelic genes interact multiplicatively. WILLIAMS (1959), apparently independently, also demonstrated the inevitability of multiplicative interaction, using a constructed numerical example. But he wanted a distinction to be made ". . . between gene interaction and the interrelations of the component parts of the phenotype." This view gave rise to a controversy (HAYMAN 1960; WILLIAMS 1960). MOAV (1966) distinguished several classes of heterosis of sire-dam combinations. His class termed "nonlinearity heterosis" actually includes multiplicative interaction as a special case. GRIFFING (1990) tested a tomato cross and its parents under field and controlled nutrient conditions to compare various hypotheses of heterosis including "somatic multiplication of additive component traits."

Multiplicative accumulation of component heterosis in complex characters is another multiplicative effect which came into view early. WRIGHT (1922) had noted that relative improvements of crossbred matings over both parent stocks in guinea pigs were much greater for total performance than for its component characters. Similar observations in farm animals were later reported by a number of authors. DICKERSON (1955) ascribed the phenomenon emerging from such observations ". . . to the fact that total performance tends to behave as a multiple of its components. . . . A small amount of heterosis in each component becomes relatively very large for the total product." In plants, an early account of multiplicative accumulation of component heterosis is found in a study with six barley crosses reported by IMMER (1941). The F_1 average exceeded the midparent average by 8.3% in number of heads per plant, 11.1% in number of seeds per head, and 4.9% in weight per seed. As the product of these three traits specifies yield, IMMER expected the F_1/midparent ratio of yield per plant to be $1.083 \times 1.111 \times 1.049 = 1.262$. The ratio calculated directly was 1.273. GRAFIUS (1959) studied the same yield components in applying his "geometrical model for yield" to 15 barley crosses. The F_1/midparent ratio for yield, averaging 136.36%, was interpreted as "heterosis due to epistasis." GRAFIUS (1960) postulated that overdominance for yield may have a "geometric explanation." This view was disputed by MOLL, KOJIMA and ROBINSON (1962). There is no disagreement, however, that multiplicative effects between component traits each having little heterosis can produce large amounts of heterosis in the complex trait (GRAFIUS 1961; SINHA and KHANNA 1975; GEIGER and WAHLE 1978; NITTER 1978; and others).

The distinction between the two multiplicative effects discussed above has been hampered by their simultaneous occurrence. In most reported examples (*cf.* SINHA and KHANNA 1975; JAKUBEC and HYÁNEK 1982), the effect of multiplicative interaction is not readily apparent, because the F_1 components are not on their midparent levels, but exhibit heterosis themselves. As component heterosis is usually small, many cases could be interpreted as "merely showing dominance" by those who define heterosis from the better parent. Such authors have used terms such as "combination heterosis" (HAGBERG 1952), "complementary gene action" (WILLIAMS and GILBERT 1960), or "component interaction" (ADAMS and DUARTE 1961), which actually include both kinds of multiplicative effects. GEIGER and WAHLE (1978) separated the two effects in complex traits made up of two or three components. The approach extends the situation considered in (1). Let the respective F_1 levels in the two component traits be $X^* = \bar{X}f_X$ and $Y^* = \bar{Y}f_Y$, where f_X and f_Y are F_1/midparent ratios for the components. In the complex trait, then, one can write $F_1 = X^*Y^* = \overline{XY}f_Xf_Y$ and, as before, $\bar{P} = (X'Y' + X''Y'')/2 = \overline{XY} + (X' - X'')(Y' - Y'')/4$, so that heterosis takes the form

$$F_1 - \bar{P} = \overline{XY}(f_Xf_Y - 1) - (X' - X'')(Y' - Y'')/4. \quad (2)$$

Formula (2) splits the heterosis of the complex trait into two parts: part I, $\overline{XY}(f_Xf_Y - 1)$, combines component heterosis in a multiplicative way, while part II is due to multiplicative interaction between component differences in the parents. GEIGER and WAHLE, analyzing several traits in hybrids of rye, found part II to be of negligible size and as often negative as positive. This result and similar findings in maize (SODENFRAUNHOFEN 1981) corroborate RICHEY's (1942) estimate. BECKER (1984) compiled data from various plants to illustrate that multiplicative interaction may be of greater importance in inbreeders than in outbreeders because of the smaller total heterosis in the former.

The quantitative-genetic description of heterosis by means of a linear model allowing for epistasis was first undertaken by JINKS and JONES (1958). Considering a cross between two inbred lines, they expressed the superiority of the F_1 over the better parent in terms of "components of means" which sum up various genetic effects including two-factor interactions. MATHER and JINKS (1971) used a slightly modified parameter system to give similar expressions, which include terms due to three-factor interactions. COCKERHAM's (1954) factorial model of gene effects and interactions was used by SCHNELL and GEIGER (1970) to identify those types of epistasis up to n-factor interactions which in a cross of two homozygous lines contribute to heterosis measured from the midparent.

TABLE 1

Genotypic values of a two-locus diallelic model specifying multiplicative action between loci

	B_1B_1	B_1B_2 or B_2B_1	B_2B_2
A_1A_1	$a_{11}b_{11}$	$a_{11}b_{12}$	$a_{11}b_{22}$
A_1A_2 or A_2A_1	$a_{12}b_{11}$	$a_{12}b_{12}$	$a_{12}b_{22}$
A_2A_2	$a_{22}b_{11}$	$a_{22}b_{12}$	$a_{22}b_{22}$

Two classes of contributing interactions were identified. Class I comprises all interactions the nomenclature of which involves no "additive" term, but includes "dominance" an odd number of times. Class II comprises all interactions involving "additive" an even number of times, whether "dominance" is involved or not. Class II interactions contribute to the midparent, but not to the F_1. Further, each such interaction as often increases as decreases heterosis in the 2^n completely heterozygous hybrids that can be formed with n diallelic loci. The importance of $(a \times a)$-interactions was emphasized because they would reflect multiplicative gene effects in the linear model. ARUNACHALAM (1977) inferred from the study of a cross between arbitrarily inbred parents that heterosis can result from $(a \times a)$-epistasis without the presence of dominance. HILL (1982) derived formulae for predicting generation means and heterosis of crosses among populations in terms of "composite effects" defined from contrasts in the F_2-population. Extensions to multiple alleles and to more than two loci were also given. WILLHAM and POLLAK (1985) derived similar predictions including linkage in terms of effects defined for the two-locus multiallelic model of KEMPTHORNE (1957).

RESULTS

Linear parameters for various models

The representation of multiplicative gene action is often given in a form similar to the two-locus diallelic model shown in Table 1. There the genotypes, $A_iA_jB_kB_l$ (with $i, j, k, l = 1, 2$), have genotypic values equal to products $a_{ij}b_{kl}$, where a_{ij} and b_{kl} are numerical values assigned to phases A_iA_j and B_kB_l, respectively. Obviously, multiplicative action is only between loci, not within them. To make the model completely multiplicative, we may replace the products of $a_{ij}b_{kl}$ by corresponding products, $A_iA_jB_kB_l$ say, where each factor like A_i now represents a numerical value assigned to that allele. On the other hand, gene action is completely arbitrary when only the genotypic value as a whole is given a numerical value, Y_{ijkl} say. It is for the latter gene action that genotypic values have been decomposed into linear partitions such as the mean, additive and dominance effects, and epistatic effects of various kinds. We wish to apply this linear description to the two multiplicative models considered above. For the sake of simplicity, we shall confine the derivations to the two-locus diallelic case, though extensions to multiple alleles and to any number of loci would be possible throughout. The genotypes listed in the Table form the reference population in which the partitioning of genotypic values is to be made. Let the frequencies of genes A_1, A_2, B_1, B_2 be p_1, p_2, q_1, q_2, respectively, with $p_2 = 1 - p_1$ and $q_2 = 1 - q_1$. Genotypic frequencies are assumed to be in Hardy-Weinberg and linkage phase equilibrium. The convention to be adopted is that numerical values assigned to phases or alleles are positive numbers with $a_{11} \geqslant a_{22}$ and $b_{11} \geqslant b_{22}$, or $A_1 \geqslant A_2$ and $B_1 \geqslant B_2$, respectively.

The linear partitioning of a genotypic value can be done by various methods. It meets our purpose to employ KEMPTHORNE's (1957) approach, which starts from algebraic identities such as

$$A_i = (\sum_m p_m A_m) + (A_i - \sum_m p_m A_m).$$

With only two alleles ($i, m = 1, 2$) this reduces to

$$A_i = (p_1A_1 + p_2A_2) + r_i(A_1 - A_2),$$

where $r_1 = p_2$ and $r_2 = -p_1$. Similarly,

$$B_k = (q_1B_1 + q_2B_2) + s_k(B_1 - B_2),$$

where $s_1 = q_2$ and $s_2 = -q_1$. Corresponding expressions are for A_j and B_l. Then we can write as an algebraic identity,

$$\begin{aligned} A_iA_jB_kB_l = {} & (M_A + r_i\Delta_A)(M_A + r_j\Delta_A) \\ & \cdot(M_B + s_k\Delta_B)(M_B + s_l\Delta_B), \end{aligned} \tag{3}$$

where $M_A = p_1A_1 + p_2A_2$; $\Delta_A = A_1 + A_2$; $M_B = q_1B_1 + q_2B_2$; $\Delta_B = B_1 - B_2$. We may interpret the left side of (3) as the genotypic value for whatever model we are studying. The right side of (3) then makes sense only after being developed into functions of genotypic values of the model under study. We shall do that in two steps. For the present, we expand the right side of (3) without resolving individual terms like M_A or Δ_A. This supplies the linear partitioning of the genotypic values,

$$\begin{aligned} A_iA_jB_kB_l = {} & \mu + (r_i + r_j)\alpha_A + r_ir_j\delta_A + (s_k + s_l)\alpha_B \\ & + s_ks_l\delta_B + (r_i + r_j)(s_k + s_l)\alpha\alpha_{AB} \\ & + (r_i + r_j)s_ks_l\alpha\delta_{AB} + r_ir_j(s_k + s_l)\delta\alpha_{AB} \\ & + r_ir_js_ks_l\delta\delta_{AB}, \end{aligned} \tag{4}$$

where the mean (μ) and the genetic effects (α_A, δ_A, . . ., $\delta\delta_{AB}$) have the formal definitions given in the second column of Table 2. The nomenclature of the effects should be apparent because α and δ read "additive" and "dominance," respectively, and subscripts (A, B) denote the loci referred to. Actually, the genetic

TABLE 2

Linear parameters of the two-locus diallelic model, formal definitions, and values for two models of multiplicative gene action (for explanation see text)

Linear parameter	Formal definition	Definition and value for multiplicative action between loci[a]	Value for completely multiplicative action
μ	$M_A \times M_A \times M_B \times M_B$	$\mu_a\mu_b = \mu$	μ
α_A	$\Delta_A \times M_A \times M_B \times M_B$	$\alpha_a\mu_b = \alpha_A$	α_A
δ_A	$\Delta_A \times \Delta_A \times M_B \times M_B$	$\delta_a\mu_b = \delta_A$	α_A^2/μ
α_B	$M_A \times M_A \times \Delta_B \times M_B$	$\mu_a\alpha_b = \alpha_B$	α_B
δ_B	$M_A \times M_A \times \Delta_B \times \Delta_B$	$\mu_a\delta_b = \delta_B$	α_B^2/μ
$\alpha\alpha_{AB}$	$\Delta_A \times M_A \times \Delta_B \times M_B$	$\alpha_a\alpha_b = \alpha_A\alpha_B/\mu$	$\alpha_A\alpha_B/\mu$
$\alpha\delta_{AB}$	$\Delta_A \times M_A \times \Delta_B \times \Delta_B$	$\alpha_a\delta_b = \alpha_A\delta_B/\mu$	$\alpha_A\alpha_B^2/\mu^2$
$\delta\alpha_{AB}$	$\Delta_A \times \Delta_A \times \Delta_B \times M_B$	$\delta_a\alpha_b = \delta_A\alpha_B/\mu$	$\alpha_A^2\alpha_B/\mu^2$
$\delta\delta_{AB}$	$\Delta_A \times \Delta_A \times \Delta_B \times \Delta_B$	$\delta_a\delta_b = \delta_A\delta_B/\mu$	$\alpha_A^2\alpha_B^2/\mu^3$

[a]
$\mu_a = p_1^2a_{11} + 2p_1p_2a_{12} + p_2^2a_{22}$
$\alpha_a = p_1(a_{11} - a_{12}) + p_2(a_{12} - a_{22})$
$\delta_a = a_{11} - 2a_{12} + a_{22}$
$\mu_b = q_1^2b_{11} + 2q_1q_2b_{12} + q_2^2b_{22}$
$\alpha_b = q_1(b_{11} - b_{12}) + q_2(b_{12} - b_{22})$
$\delta_b = b_{11} - 2b_{12} + b_{22}$.

effects are contrasts which in the diallelic case determine respective effects or interactions of individual genes. For example, the additive effect of the gene A_i is $r_i\alpha_A$, which specifies $p_2\alpha_A$ and $-p_1\alpha_A$ as respective additive effects of the alleles A_1 and A_2. Note that dominance effects (δ_A, δ_B) bear the relation $\delta = -2d$ to the customary dominance parameter d which measures the heterozygote deviation from homozygote average.

Linear parameters for multiplicative action between loci are obtained by further expanding the formal definitions listed in Table 2. Each of the nine definitions is the product of two A terms like $(p_1A_1 + p_2A_2)$ or $(A_1 - A_2)$, and two similar B terms. Expanding such a product and replacing genotypic symbols by genotypic values of the model under study results in the quantitative definition of the respective parameter. For example, replacement by arbitrary genotypic values, Y_{ijkl}, yields the definitions implied in the linear descriptive model. In our case, genotypic values themselves are products $a_{ij}b_{kl}$, where a_{ij} and b_{kl} are uncorrelated in occurrence. The formal definitions, therefore, need expanding only separately with respect to A-term products and B-term products. This amounts to computing a mean, additive and dominance effect for each locus singly. For example, expanding the product $(M_A \times M_A) = (p_1A_1 + p_2A_2)^2$ and replacing phase symbols, A_iA_j, by a_{ij} values gives the mean of the latter, $\mu_a = p_1^2a_{11} + 2p_1p_2a_{12} + p_2^2a_{22}$. The various single-locus parameters, shown in the footnote of Table 2, are designated by usual symbols with small letter subscripts denoting the locus, to distinguish such parameters from one-factor effects (α_A, δ_A, α_B, δ_B) and the general mean (μ). Multiplication of two appropriate single-locus parameters then provides the quantitative definitions of the linear parameters for this model. The various definitions are interrelated in such a way that all epistatic effects are in fact restricted to nonlinear function of one-factor effects and the mean. We shall use these functions as values of respective effects to bring out the existing restrictions. The resulting parameter values are presented together with their definitions in the third column of Table 2.

Linear parameters for completely multiplicative action could be derived from the foregoing model by treating the special case in which $a_{12} = \sqrt{a_{11}a_{22}}$ and $b_{12} = \sqrt{b_{11}b_{22}}$. The direct derivation from the model $A_iA_jB_kB_l$ is simpler, however. As the factors like A_i are uncorrelated in occurrence, no expansion of the formal definitions is necessary. They themselves, written in full, represent the desired quantitative definitions,

$$\left.\begin{aligned} \mu &= (p_1A_1 + p_2A_2)^2(q_1B_1 + q_2B_2)^2, \\ \alpha_A &= (A_1 - A_2)(p_1A_1 + p_2A_2)(q_1B_1 + q_2B_2)^2, \\ \delta_A &= (A_1 - A_2)^2(q_1B_1 + q_2B_2)^2, \\ &\cdots\ \cdots\ \cdots\ \cdots\ \cdots\ \cdots\ \cdots \\ \delta\delta_{AB} &= (A_1 - A_2)^2(B_1 - B_2)^2 \end{aligned}\right\} \quad (5)$$

The interrelations between the various definitions in (5) are of such a kind that epistatic effects as well as dominance effects are restricted to non-linear functions of additive effects and the mean. For example, $\delta_A = \alpha_A^2/\mu$. The full set of restrictions existing within a completely multiplicative model can be seen from the parameter values given in the last column of Table 2. Note that none of the parameters can be negative. Any dominance must therefore be in the direction of the smaller homozygote (*cf.* CHARLES and SMITH 1939). Let $(d/a)_A$ be the degree of dominance at the A-locus and define it in the usual way. In terms of factors A_i we find

$$\begin{aligned} (d/a)_A &= \frac{(2A_1A_2 - A_1A_1 - A_2A_2)(q_1B_1 + q_2B_2)^2/2}{(A_1A_1 - A_2A_2)(q_1B_1 + q_2B_2)^2/2} \\ &= -(A_1 - A_2)/(A_1 + A_2). \end{aligned} \quad (6)$$

We thus expect $(d/a)_A$ between the limits -1 (for A_2 tending to zero) and 0 (for $A_2 = A_1$).

Extensions to more than two loci are straightforward. With multiplicative action between n loci, the quantitative definition of a given linear parameter is a product of n single-locus parameters. These are additive or dominance effects from those loci for which the parameter in question involves such effects by nomenclature, and single locus means from all other loci (*cf.* COCKERHAM 1959). The resulting definition leads to a restricted parameter value which is the product of corresponding one-factor effects, di-

vided by μ^{m-1}, where m is the number of multiplied effects. We shall exemplify the above rules, assuming the inclusion of a third locus, C, say. In each instance, we give the parameter, the quantitative definition, and the restricted parameter value: $\alpha\alpha_{AB} = \alpha_a\alpha_b\mu_c = \alpha_A\alpha_B/\mu$; $\delta\alpha_{BC} = \mu_a\delta_b\alpha_c = \delta_B\alpha_C/\mu$; $\delta\alpha\delta_{ABC} = \delta_a\alpha_b\delta_c = \delta_A\alpha_B\delta_C/\mu^2$. The restricted parameter values of this model can be converted into those for completely multiplicative action by replacing any dominance effect by the square of the respective additive effect, divided by μ. For example, the value given last, $\delta_A\alpha_B\delta_C/\mu^2$, then becomes $\alpha_A^2\alpha_B\alpha_C^2/\mu^4$. It should be noted that restricted parameter values of both multiplicative models do not change their forms when additional loci are included in the model. Moreover, the insertion of such values into equations (4) permits condensed forms of the partitionings. For multiplicative action between loci we may write

$$a_{ij}b_{kl} = \mu a'_{ij}b'_{kl}, \tag{7}$$

where $a'_{ij} = \{1 + (r_i + r_j)\alpha_A/\mu + r_ir_j\delta_A/\mu\}$, etc. A similar form for completely multiplicative action is

$$A_iA_jB_kB_l = \mu A'_iA'_jB'_kB'_l, \tag{8}$$

where $A'_i = (1 + r_i\alpha_A/\mu)$, etc. The mean enters formulae (7) and (8) as a constant. Models involving a constant factor have also been used for representing multiplicative gene action.

Heterosis expected with various models

The genetic description of generation means of two parents, their F_1 and F_2 (*cf.* WILLHAM and POLLACK 1985) is now to be made in terms of the linear partitions (4). The parents, P' and P'', are random mating populations in Hardy-Weinberg and linkage phase equilibrium. The genes A_1, A_2, B_1, B_2 have respective frequencies $p'_1 = p_1 + u$, $p'_2 = p_2 - u$, $q'_1 = q_1 + v$, $q'_2 = q_2 - v$ in parent P', and $p''_1 = p_1 - u$, $p''_2 = p_2 + u$, $q''_1 = q_1 - v$, $q''_2 = q_2 + v$ in parent P''. So, $2u = p'_1 - p''_1$ and $2v = q'_1 - q''_1$ are the differences in gene frequency between the two parents at the A locus and the B locus, respectively. Maximum differences, $2u = \pm 1$ and $2v = \pm 1$, occur when the parents are homozygous lines. Genotypic frequencies in each generation are products of frequencies of uniting gametes. The latter frequencies are products of respective gene frequencies in P', P'', and F_1, assuming that in F_1-genotype gametes A_iB_k came from P', and gametes A_jB_l came from P''. For the F_2 from random mating F_1's, the F_1-gametes A_1B_1, A_1B_2, A_2B_1, A_2B_2 are determined to have respective frequencies $(p_1q_1 + D)$, $(p_1q_2 - D)$, $(p_2q_1 - D)$, $(p_2q_2 + D)$, where $D = \lambda uv$ is the linkage disequilibrium and $(1 - \lambda)/2$ is the recombination fraction. Genotypic frequencies of a given generation are then used to get the respective generation mean by taking expectations of all linear partitions specified in (4), and summing. For example,

TABLE 3

Linear parameters of the two-locus diallelic model, and their coefficients in generation means indicated

Linear parameter	Generation mean			
	P'	P''	F_1	F_2
μ	1	1	1	1
α_A	$2u$	$-2u$	0	0
δ_A	u^2	u^2	$-u^2$	0
α_B	$2v$	$-2v$	0	0
δ_B	v^2	v^2	$-v^2$	0
$\alpha\alpha_{AB}$	$4uv$	$4uv$	0	$2\lambda uv$
$\alpha\delta_{AB}$	$2uv^2$	$-2uv^2$	0	0
$\delta\alpha_{AB}$	$2u^2v$	$-2u^2v$	0	0
$\delta\delta_{AB}$	u^2v^2	u^2v^2	u^2v^2	$\lambda^2u^2v^2$

averaging the partition $r_i\alpha_A$ with the genotypic frequencies of generation P' yields the expectation,

$$\mathscr{E}\{r_i\alpha_A\} = \sum_i\sum_j\sum_k\sum_l p'_ip'_jq'_kq'_lr_i\alpha_A = u\alpha_A,$$

where p'_i is the gene frequency of the gene A_i in P', etc. We likewise have $\mathscr{E}\{r_j\alpha_A\} = u\alpha_A$, and thus expect the parameter α_A to enter the generation mean P' with coefficient $2u$. The coefficients of all nine parameters for each of the generations means P', P'', F_1, F_2 are presented in Table 3.

Heterosis with arbitrary gene action shall be considered first, because it represents the general case. Taking heterosis as the difference between the respective averages of a cross (F_1) and its two parent populations ($\bar{P}$), we find from Table 3,

$$F_1 - \bar{P} = -2u^2\delta_A - 2v^2\delta_B - 4uv\alpha\alpha_{AB}. \tag{9}$$

On the right side of (9), two parts of heterosis will be distinguished: part I consisting of the components due to dominance, and part II due to $(a \times a)$-epistasis. Part II, other than part I, contributes to $\bar{P}$, but not to F_1. Moreover, only part II depends on the differences in gene frequency in sign, though both parts are influenced by them in size. Apparently, the coefficient of the $(a \times a)$-effect, $-4uv$, is positive or negative according as the "best" alleles, A_1 and B_1, have their highest frequency in different parent populations or not. Nothing can be said about sign and size of the genetic effects involved. But note that dominance components make positive contributions to heterosis when dominance effects are negative, *i.e.*, with dominance going in the direction of the larger homozygote. We shall also include a brief account of the difference $(F_2 - \bar{P})$. Although this difference does not measure heterosis, it serves to exemplify how much F_1 heterosis is retained in later generations. We find

$$\begin{aligned} F_2 - \bar{P} = &-u^2\delta_A - v^2\delta_B - 2(2 - \lambda)uv\alpha\alpha_{AB} \\ &- (1 - \lambda^2)u^2v^2\delta\delta_{AB}. \end{aligned} \tag{10}$$

A more elucidating form is

$$F_2 - \bar{P} = (F_1 - \bar{P})/2 + \{-2(1-\lambda)uv\alpha\alpha_{AB} - (1-\lambda^2)u^2v^2\delta\delta_{AB}\}. \quad (11)$$

It shows the difference $(F_2 - \bar{P})$ to be half the difference $(F_1 - \bar{P})$ plus a quantity known as "recombination loss" (DICKERSON 1969). This quantity is often found negative, but is obviously not necessarily so. Its two components each become largest in absolute value with $\lambda = 0$, but vanish with $\lambda = 1$, *i.e.*, if complete linkage prevents recombination.

Heterosis with multiplicative action between loci can be described in a more specific way by inserting the parameter values of this model into formulas (9) and (11). The new versions are

$$F_1 - \bar{P} = -2u^2\delta_A - 2v^2\delta_B - 4uv\alpha_A\alpha_B/\mu, \quad (12)$$

$$F_2 - \bar{P} = (F_1 - \bar{P})/2 + \{-2(1-\lambda)uv\alpha_A\alpha_B/\mu - (1-\lambda^2)u^2v^2\delta_A\delta_B/\mu\}. \quad (13)$$

While the epistatic effects now have their multiplicative values, no changes appear with the dominance effects. Nevertheless, part I of heterosis is also affected by multiplicativeness. Consider the generation means written in terms of single-locus parameters,

$$\left.\begin{aligned} F_1 &= \mu_a\mu_b - u^2\delta_a\mu_b - v^2\mu_a\delta_b + u^2v^2\delta_a\delta_b \\ &= (\mu_a - u^2\delta_a)(\mu_b - v^2\delta_b), \\ \bar{P} &= (\mu_a + u^2\delta_a)(\mu_b + v^2\delta_b) + 4uv\alpha_a\alpha_b. \end{aligned}\right\} \quad (14)$$

The expressions given in brackets obviously are F_1 or $\bar{P}$ means described with a single-locus model, *i.e.*, in terms of either a_{ij} or b_{kl} values alone. For short we write those F_1 means as $a^* = (\mu_a - u^2\delta_a)$ and $b^* = (\mu_b - v^2\delta_b)$, and the $\bar{P}$ means as $\bar{a} = (\mu_a + u^2\delta_a)$ and $\bar{b} = (\mu_b + v^2\delta_b)$, respectively. Further, $f_a = a^*/\bar{a}$, $f_b = b^*/\bar{b}$ are corresponding F_1/midparent ratios. Such a ratio exceeds unity when the dominance effect involved is negative, *i.e.*, when single-locus heterosis is positive. Then we can write the generation means (14) as $F_1 = a^*b^* = \bar{a}\bar{b}f_af_b$ and $\bar{P} = \bar{a}\bar{b} + 4uv\alpha_a\alpha_b$, and hence,

$$F_1 - \bar{P} = \bar{a}\bar{b}(f_af_b - 1) - 4uv\alpha_a\alpha_b. \quad (15)$$

Formula (15), being analogous with the splitting formula (2), reveals multiplicative specialities in both parts of heterosis, *viz.* multiplicative accumulation of single-locus heterosis in part I, and multiplicative $(a \times a)$-interaction in part II. Both specialities arise because the linear parameters for this model are products of single-locus parameters. Since for example the effect δ_A is equal to $\delta_a\mu_b$, and μ_b in part depends on the dominance measured by δ_b, the two dominance effects clearly influence each other in a multiplicative way. Note that this affects the absolute size of dominance effects, but not corresponding degrees of dominance (*cf.* MOLL, KOJIMA and ROBINSON 1962).

Heterosis with completely multiplicative action must be definitely bounded since the degree of dominance is restricted to negative values. The limits of heterosis are calculable as follows. Insertion of the parameter values of this model into formulas (9) and (11) results in respective versions which can be written in the form

$$F_1 - \bar{P} = -2\mu(U^2 + V^2 + 2UV), \quad (16)$$

$$F_2 - \bar{P} = (F_1 - \bar{P})/2 + \mu\{-2(1-\lambda)UV - (1-\lambda^2)U^2V^2\}, \quad (17)$$

where $U = u\alpha_A/\mu$ and $V = v\alpha_B/\mu$. From the definitions (5) we have $\alpha_A/\mu = (A_1 - A_2)/(p_1A_1 + p_2A_2)$, for example. Given p_1, the value of α_A/μ approaches a maximum, $1/p_1$, when A_2 tends to zero. In that case U goes to $u/p_1 = (p_1' - p_2'')/(p_1' + p_2'')$, which has two extremes, -1 and $+1$. The substitution of these extremes for U and V as well gives the limits of heterosis,

$$-8\mu \leq (F_1 - \bar{P}) \leq 0. \quad (18)$$

So, any heterosis with this type of gene action can only be negative. The lower limit in (18) results for $UV = 1$. This is the hypothetical case when the values A_2 and B_2 both tend to zero with either $p_1' = q_1' = 1$ or $p_2'' = q_2'' = 1$, *i.e.*, with homozygous parents one of which carries both favorable alleles, A_1 and B_1. In this case the difference $(F_2 - \bar{P})$ also goes to a negative extreme, $-\mu(7 - 2\lambda - \lambda^2)$. The upper limit in (18) results from the case $UV = -1$, but is seen to be reached whenever the sum, $(U + V)$, happens to be zero, *i.e.*, with $U = -V$. The difference $(F_2 - \bar{P})$ is positive in such cases, consisting of the recombination loss only. We may write the recombination loss in the form, $-\mu(1-\lambda)UV\{2 + (1+\lambda)UV\}$, to see that it comes to positive values with $\lambda < 1$ whenever U and V differ in sign, *i.e.*, when the highest frequency of A_1 and of B_1 is in different parent populations.

Heterosis without dominance means that a non-zero difference between F_1 and $\bar{P}$ arises from part II alone, part I being absent. This is possible with any model provided all genetic effects involving dominance in the nomenclature are zero. The condition for that in the two-locus diallelic model with otherwise arbitrary gene action is $Y_{12kl} = (Y_{11kl} + Y_{22kl})/2$ and $Y_{ij12} = (Y_{ij11} + Y_{ij22})/2$. The analogous condition with multiplicative action between loci is $a_{12} = (a_{11} + a_{22})/2$ and $b_{12} = (b_{11} + b_{22})/2$. The $(a \times a)$-effect then simplifies to $\alpha\alpha_{AB} = \alpha_a\alpha_b = (a_{11} - a_{22})(b_{11} - b_{22})/4$. So, MINVIELLE's (1987) results follow,

$$F_1 - \bar{P} = -uv(a_{11} - a_{22})(b_{11} - b_{22}), \quad (19)$$

$$F_2 - \bar{P} = (F_1 - \bar{P})(2 - \lambda)/2. \quad (20)$$

The occurrence of heterosis in (19) depends on the $(a \times a)$-effect being non-zero. Now, two substantial additive effects lead to a nonzero $(a \times a)$-effect not

only when interacting multiplicatively, but also under any other type of nonadditive action between them. For an example, we briefly consider diminishing return interaction. Such a type of gene action was first studied by RASMUSSON (1933). He proposed the model,

$$Y = A + a(k^x - 1)/(k - 1), \qquad (0 \leqslant k \leqslant 1)$$

where Y is the genotypic value, A and a are constants, k measures the degree of interaction, and x is the number of favorable factors present in the genotype. We used this model to construct the four double homozygotes, $Y_{1111} = A + a(k^3 + k^2 + k + 1)$; $Y_{1122} = Y_{2211} = A + a(k + 1)$; $Y_{2222} = A$, assuming the number of favorable factors in them to be 4, 2, 2, and 0, respectively. Further, we put all remaining genotypes to intermediate values within rows and columns. Dominance is then absent again, but the $(a \times a)$-effect is found to be $\alpha\alpha_{AB} = a(k + 1)(k^2 - 1)/4$, so that heterosis amounts to

$$F_1 - \bar{P} = -uva(k + 1)(k^2 - 1). \qquad (21)$$
$$(0 \leqslant k \leqslant 1)$$

Note that the $(a \times a)$-effect in (21) can only be negative, whereas it was positive in (19).

DISCUSSION

Multiplicative models for the study of heterosis are worth consideration in their own right. We dealt with multiplicative action between loci and besides, two special cases having restrictions on dominance. In terms of the model $a_{ij}b_{kl}$ the restrictions were of the type $a_{12} = \sqrt{a_{11}a_{22}}$ in the completely multiplicative model, and $a_{12} = (a_{11} + a_{22})/2$ in the study of heterosis without dominance. Both special cases seem less well suited for inquiries into heterosis, because a fixation of the degree of dominance to negative values or zero hardly meets what may be the rule in reality. In spite of that, those cases were occasionally studied out of theoretical interest (CHARLES and SMITH 1939; MINVIELLE 1987), and we included them for the same reason. On the other hand, multiplicative action between loci with arbitrary dominance not only is one of the classical types of nonadditive gene action, but also may come close to many real situations. This mainly concerns the numerous characters which in plants and animals are products of several subcharacters. Provided each subcharacter is controlled by a different set of genes, the genetic system of the complex character will show multiplicative action between genes belonging to different sets, but will be arbitrary within sets. A partial multiplicativeness in this sense may exist approximately even though there is universal pleiotropy, if in each subcharacter different sets of genes exert predominant effects. KACSER and BURNS (1981) estimate that enzyme-dependent characters are influenced far above average by those genes which specify enzymes more directly involved in the respective biosynthetic pathways. For such reasons, multiplicative action between loci seems particularly worth investigating for consequential effects on heterosis.

Multiplicative specialities in the two parts of heterosis were seen to result from the linear parameters being products of single-locus parameters. The two specialities are different, however, and so are their consequences. This becomes clearer when we extend the description of heterosis to include a third locus, C, at which the difference in gene frequency is $2w$. Dealing with arbitrary gene action first, we obtain the extension of (9),

$$\begin{aligned} F_1 - \bar{P} = &-2u^2\delta_A - 2v^2\delta_B - 2w^2\delta_C \\ &- 2u^2v^2w^2\delta\delta\delta_{ABC} - 4uv\alpha\alpha_{AB} \\ &- 4uw\alpha\alpha_{AC} - 4vw\alpha\alpha_{BC} \\ &- 4uvw^2\alpha\alpha\delta_{ABC} - 4uv^2w\alpha\delta\alpha_{ABC} \\ &- 4u^2vw\delta\alpha\alpha_{ABC}. \end{aligned} \qquad (22)$$

Here the three dominance effects together with their three-factor interaction, $\delta\delta\delta_{ABC}$, form part I, while part II consists of the residual terms due to $(a \times a)$- or $(a \times a \times d)$-types of epistasis (*cf.* SCHNELL and GEIGER 1970). For a multiplicative version of (22), we only give the extension of (15). Note that for example the pair of components, $(-4uv\alpha\alpha_{AB} - 4uvw^2\alpha\alpha\delta_{ABC})$, receives the form, $(-4uv\alpha_a\alpha_b\mu_c - 4uvw^2\alpha_a\alpha_b\delta_c) = -4uv\alpha_a\alpha_b\bar{c}$, where $\bar{c} = \mu_c + w^2\delta_c$ is the midparent at locus C. In this way we get the version

$$\begin{aligned} F_1 - \bar{P} = \overline{abc}(f_af_bf_c - 1) - (&4uv\alpha_a\alpha_b\bar{c} \\ &+ 4uw\alpha_a\alpha_c\bar{b} + 4vw\alpha_b\alpha_c\bar{a}), \end{aligned} \qquad (23)$$

which is analogous with GEIGER and WAHLE's (1978) formula for splitting heterosis in a character made up of three subcharacters. In comparison with (22), version (23) displays the two multiplicative specialities in extended forms. Part I shows multiplicative accumulation of the three F_1/midparent ratios which reflect the heterosis present at individual loci. Part II now is a sum of three components, each of which involves a multiplicative $(a \times a)$-interaction. So the number of part II components, which was six in (22), reduced to one for each possible pair of loci in (23). Then what are the consequences of multiplicativeness? Evidently, multiplicative action between a number of loci (or similarly: subcharacters) can produce spectacular amounts of heterosis via part I, provided that the multiplied F_1/midparent ratios each exceed unity. In part II, however, similar dramatic effects are not likely to occur. To see that we must have a closer look at the genetic role of part II in general.

The role and expected size of part II of heterosis emerge from conclusions reached by SCHNELL and

GEIGER (1970). As was visible from the descriptions (9) and (22), any component of heterosis is influenced regarding sign only by those differences in gene frequency which refer to a locus represented by "additive" in the nomenclature of the respective genetic effect. Part I effects do not involve any such "additive" terms, but part II effects do. Now let the differences in gene frequency be modified by changing their signs to all possible combinations. With n loci under consideration, there are 2^n such combinations, each of which leads to the same F_1 mean, but defines a differently composed midparent. Heterosis produced by all possible pairs of parents thus has a constant part I, but varies in part II. In fact, each effect in part II occurs equally often with its coefficient being positive and negative, so canceling in the average. Hence part I measures the heterosis averaged over all midparents which lead to the same F_1 proportions of allelic phases at all loci considered. Part II then measures the balance, *i.e.*, the difference between average and actual midparent. With a given cross, heterosis may be increased by some part II components and decreased by others, depending also on the signs of the genetic effects involved. This applies likewise with multiplicative action between loci. Assume additive effects to be positive, and consider the part II component in (15), $-4uv\alpha_a\alpha_b$. For it to increase heterosis, the coefficient $-4uv$ must be positive, requiring that the highest frequency of A_1 and of B_1 be in different parent populations. Similar requirements can simultaneously be fulfilled only for two out of the three components which form part II in the three-locus case (23). With larger numbers of loci (or similarly: subcharacters) the maximum fraction of positive part II components quickly goes down to one half. Positive and negative components will then mostly cancel out to a large extent. So, part II of heterosis will seldom be large, whether gene action is arbitrary or multiplicative.

The relations of multiplicative to arbitrary gene action, on which this investigation is based, are those of a special case to the general one. This implies, of course, that the linear parameters can have such values as result from multiplicative gene action also with arbitrary gene action. So the very speciality of the former is not those parameter values but being restricted to them. The restrictions with multiplicative models undoubtedly are impediments to practical use for analysis, yet remarkably enough, they can be useful in the theory of the unrestricted model. Consider the $(a \times a)$-effect, $\alpha\alpha_{AB}$. Its multiplicative form, $\alpha_A\alpha_B/\mu$, gives positive values supposing the genes A_1 and B_1 are the most favorable alleles for additive effects. Under the same supposition, however, the diminishing return model produced the negative $(a \times a)$-effect in (21). The two cases can be distinguished as certain degrees of complementary and duplicate gene interactions, respectively (MATHER 1967). Alternatively, one can imagine those cases being placed on a single continuous scale which measures both sign and degree of the non-additive gene action causing the $(a \times a)$-interaction. The fitting of nonlinear gene response curves (GILBERT 1961) is not necessary for that. The desired scale is simply the ratio, $T = \alpha\alpha_{AB}/(\alpha_A\alpha_B/\mu)$, which uses the expected multiplicative value as a yardstick for measuring nonadditivity of the actual value. No assumption is needed about the orienting of $(a \times a)$-effects with additive effects. In fact, T will be negative, zero, or positive when the cooperation of the interacting effects is of the type of diminishing, constant, or increasing return, respectively. The measure T, which is adaptable to multiple alleles, is closely related to TUKEY's (1949) interaction constant in the two-way layout. Similar measures of nonadditivity can be defined for all epistatic effects, and for dominance effects as well if expected values are for completely multiplicative action. So, all allelic and nonallelic interactions in the genotypic value can be interpreted as respective products of an expected multiplicative value and a coefficient measuring non-additivity. Only one application of such interpretation shall be mentioned here. Obviously, the coefficients of nonadditivity are fixed to unity at least with all epistatic effects in multiplicative models, but may vary as to sign and size in the unrestricted linear model.

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