Genet. Res., Camb. (1987), **49**, *pp.* 245–247 *Printed in Great Britain*

Dominance is not necessary for heterosis: a two-locus model

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(Received 1 August 1986 and in revised form 14 November 1986)

Summary

Under a two-locus model with additive genes which combine multiplicatively to determine a quantitative trait, heterosis is generally observed in the F_1. It is positive only if both frequencies of the best allele at each locus are not higher in the same parental population. In the F_2, heterosis depends on the rate of recombination between the two loci. If linkage is tight, F_1 superiority is nearly halved in the F_2. But if the two genes are independent, heterosis is maintained in the F_2 at the same level as in the F_1.

1. Introduction

There are two classical genetic interpretations of heterosis, the one-locus dominance hypothesis and the multilocus epistasis hypothesis (Pirchner, 1983). For the former, described in detail by Falconer (1981), superiority of the crossbred performance over the mean of the parental lines depends directly on the existence of dominance. In the latter – less tractable theoretically because it includes several possible inter-locus interactions – hybrid vigour also results from dominance, but indirectly, through interactions involving dominance effects at the different loci (Pirchner, 1983). Then it seems from existing theory that there is always some underlying dominance when heterosis – or, conversely, inbreeding depression – is observed. This is in general agreement with a review by Sheridan (1981), who described the various models of heterosis and compared the dominance and the parental epistasis models, both theoretically and by using crossbreeding data from several animal species.

Still, could there be heterosis for a trait determined by additive genes? The object of this work is to develop and discuss a simple two-locus genetic model with no dominance which leads to heterosis under cross-breeding.

2. Model

A quantitative trait is determined by the combined multiplicative action of two individually additive genes, A and C, each one with two alleles, in two large populations P_1 and P_2. Homozygotes are assigned genotypic values a and b for the A gene, and k and n for the C gene, so the complete array of genotypic values is:

Genotype	A_1A_1	A_1A_2	A_2A_2
C_1C_1	$ka = Q+\frac{1}{2}k(a-b)$	$\frac{1}{2}k(a+b) = Q$	$kb = Q-\frac{1}{2}k(a-b)$
C_1C_2	$\frac{1}{2}(k+n)a = R+\frac{1}{4}(k+n)(a-b)$	$\frac{1}{4}(k+n)(a+b) = R$	$\frac{1}{2}(k+n)b = R-\frac{1}{4}(k+n)(a-b)$
C_2C_2	$na = S+\frac{1}{2}n(a-b)$	$\frac{1}{2}n(a+b) = S$	$nb = S-\frac{1}{2}n(a-b)$

where $Q = \frac{1}{2}k(a+b)$, $S = \frac{1}{2}n(a+b)$ and $R = \frac{1}{2}(Q+S)$.

For simplicity, populations P_1 and P_2 are assumed to be in Hardy–Weinberg equilibrium with respect to both the A and C genes. Gene frequencies are:

	Allele	A_1	A_2	C_1	C_2
Population	P_1	p	q	v	w
	P_2	$p-y$	$q+y$	$v-z$	$w+z$

with $p+q = v+w = 1$, $y \neq 0$ and $z \neq 0$.

The mean genotypic values, $\overline{P}_1$ and $\overline{P}_2$, of the two populations are as follows:

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$$\begin{aligned}\overline{P}_1 &= v^2Q+2vwR+w^2S+\tfrac{1}{2}(a-b)\,[k(p^2v^2-q^2v^2)\\ &\quad+\tfrac{1}{2}(k+n)\,(2p^2vw-2q^2vw)+n(p^2w^2-q^2w^2)]\\ &= v^2Q+vw(Q+S)+w^2S\\ &\quad+\tfrac{1}{2}(a-b)\,(p-q)\,(kv^2+(k+n)\,vw+nw^2)\\ &= vQ+wS+\tfrac{1}{2}(a-b)\,(p-q)\,(kv+nw).\end{aligned}$$

One obtains $\overline{P}_2$ by replacing p, q, v and w by $p-y, q+y, v-z$ and $w+z$, respectively, in the formula for $\overline{P}_1$.

$$\begin{aligned}\overline{P}_2 &= (v-z)\,Q+(w+z)\,S+\tfrac{1}{2}(a-b)\,(p-q-2y)\\ &\quad\times(k(v-z)+n(w+z))\end{aligned}$$

3. Results

(i) *Heterosis in the F_1 between P_1 and P_2*

Gametic types and frequencies from parental populations P_1 and P_2 are:

Gametic type	A_1C_1	A_1C_2	A_2C_1	A_2C_2
Population P_1	pv	pw	qv	qw
P_2	$(p-y)\,(v-z)$	$(p-y)\,(w+z)$	$(q+y)\,(v-z)$	$(q+y)\,(w+z)$

The F_1 genotypic array is then obtained easily and is given below:

	A_1A_1	A_1A_2	A_2A_2
C_1C_1	$pv(p-y)\,(v-z)$	$pv(q+y)\,(v-z)+(p-y)\,(v-z)\,qv$	$qv(q+y)\,(v-z)$
C_1C_2	$pv(p-y)\,(w+z)$ $+(p-y)\,(v-z)\,pw$	$pv(q+y)\,(w+z)+qw(p-y)\,(v-z)$ $+pw(q+y)\,(v-z)+qv(p-y)\,(w+z)$	$qv(q+y)\,(w+z)$ $+qw(q+y)\,(v-z)$
C_2C_2	$pw(p-y)\,(w+z)$	$pw(q+y)\,(w+z)+(p-y)\,(w+z)\,qw$	$qw(q+y)\,(w+z)$

Next, obtaining the mean value of the F_1 is straightforward but tedious. However, by using genotypic values rescaled in terms of Q, R and S, one needs only to consider the six genotypes homozygous at the A locus in most of the calculations.

$$\begin{aligned}\overline{F}_1 &= v(v-z)\,Q+(v(w+z)+w(v-z))\,R+w(w+z)\,S\\ &\quad+\tfrac{1}{2}k(a-b)\,v(v-z)\,(p-q-y)\\ &\quad+\tfrac{1}{4}(k+n)\,(a-b)+(w(v-z)+v(w+z))\,(p-q-y)\\ &\quad+\tfrac{1}{2}n(a-b)\,w(w+z)\,(p-q-y)\\ &= (v-\tfrac{1}{2}z)\,Q+(w+\tfrac{1}{2}z)\,S+\tfrac{1}{4}(a-b)\,(p-q-y)\\ &\quad\times(k(2v-z)+n(2w+z))\end{aligned}$$

after some rearranging and simplifications.

Finally, heterosis in the F_1 is given by $H_1=\overline{F}_1-\frac{1}{2}(\overline{P}_1+\overline{P}_2)$. Terms with Q or S cancel out directly in the subtraction, so

$$\begin{aligned}H_1 &= \tfrac{1}{4}(a-b)\,(p-q-y)\,(k(2v-z)+n(2w+z))\\ &\quad-\tfrac{1}{4}(a-b)\,(p-q)\,(kv+nw)\\ &\quad-\tfrac{1}{4}(a-b)\,(p-q-2y)\,(k(v-z)+n\,(w+z))\\ &= \tfrac{1}{4}(a-b)\,(p-q)\,[k(2v-z)+n(2w+z)\\ &\quad-kv-nw-k(v-z)-n(w+z)]\\ &\quad-\tfrac{1}{4}y(a-b)\,[k(2v-z)+n(2w+z)\\ &\quad-2k(v-z)-2n(w+z)]\end{aligned}$$

The first term between brackets is null and the second one reduces to $kz-nz$. Therefore,

$$H_1=\tfrac{1}{4}yz(a-b)\,(n-k).$$

There will be heterosis when $y\neq 0$, $z\neq 0$, $a\neq b$ and $n\neq k$, that is for all non-trivial values of the parameters. The F_1 is superior to the mean of the parent populations or, equivalently, H_1 is positive, when none, two or all of factors $y, z, a-b$ and $n-k$ are positive.

(ii) *Heterosis in the F_2*

Let r be the rate of recombination between the two loci. The $A_1A_2C_1C_2$ individuals of the F_1 are made up of coupling heterozygotes in the proportion

$$pv(q+y)\,(w+z)+qw(p-y)\,(v-z)$$

and of repulsion heterozygotes in the proportion

$$pw(q+y)\,(v-z)+qv(p-y)\,(w+z).$$

Then F_1 genotypes yield gametes with the following frequencies, obtained from the array of F_1 genotypic frequencies after lengthy but simple mendelian calculations:

A_1C_1	A_1C_2
$\frac{1}{2}(pv+(p-y)\,(v-z)-ryz)$	$\frac{1}{2}(pw+(p-y)\,(w+z)+ryz)$
A_2C_1	A_2C_2
$\frac{1}{2}(qv+(q+y)\,(v-z)+ryz)$	$\frac{1}{2}(qw+(q+y)\,(w+z)-ryz)$

For example, the frequency of the A_1C_1 gametic type is

$$\begin{aligned}&pv(p-y)\,(v-z)+\tfrac{1}{2}pv(p-y)\,(w+z)+\tfrac{1}{2}(p-y)\,(v-z)\,pw\\ &\quad+\tfrac{1}{2}pv(q+y)\,(v-z)+\tfrac{1}{2}(p-y)\,(v-z)\,qv\\ &\quad+\tfrac{1}{2}pv(q+y)\,(w+z)\,(1-r)+\tfrac{1}{2}qw(p-y)\,(v-z)\,(1-r)\\ &\quad+\tfrac{1}{2}pw(q+y)\,(v-z)\,r+\tfrac{1}{2}qv\,(p-y)\,(w+z)\,r\end{aligned}$$

which eventually yields the value given above.

The F_2 genotypic frequencies are then obtained by multiplying appropriate gametic frequencies. For instance, the frequency of the $A_1A_1C_1C_1$ genotype in the F_2 is $\frac{1}{4}(pv+(p-y)\,(v-z)-ryz)^2$. Next, it is straightforward to calculate the mean genotypic value of the F_2, in the same way as for the F_1. One finds

$$\begin{aligned}\overline{F}_2 &= (v-\tfrac{1}{2}z)\,Q+(w+\tfrac{1}{2}z)\,S+\tfrac{1}{4}k(a-b)\\ &\quad\times[(p-q)\,(2v-z)-\tfrac{1}{2}y(4v-3z)-ryz]\\ &\quad+\tfrac{1}{4}n(a-b)\,[(p-q)\,(2w+z)-\tfrac{1}{2}y(4w+3z)+ryz].\end{aligned}$$

https://doi.org/10.1017/S0016672300027142 Published online by Cambridge University Press

Heterosis in the F_2 is given by $H_2 = \overline{F}_2 - \frac{1}{2}(\overline{P}_1 + \overline{P}_2)$. Terms with Q or S cancel out at once, so, after some simplifications,

$$H_2 = \tfrac{1}{4}k(a-b)(-\tfrac{1}{2}yz - ryz) + \tfrac{1}{4}n(a-b)(\tfrac{1}{2}yz + ryz)$$
$$= \tfrac{1}{4}yz(a-b)(n-k)\tfrac{1}{2}(1+2r)$$

then

$$H_2 = \tfrac{1}{2}(1+2r)H_1.$$

If the two loci are independent, $H_2 = H_1$. Otherwise, H_2 is smaller than H_1, and $\lim(H_2) = \frac{1}{2}H_1$ as $r \to 0$.

4. Discussion

The model studied in this work can be viewed as the representation of a genetic system with some biological significance: for example, the C gene might control the rate of translation of the structural gene A.

The main result is that, for a trait determined by two genes, individually additive but acting together in a multiplicative fashion, heterosis under crossbreeding is the rule rather than the exception: the F_1 genotypic mean differs from the mid-parent value for all non-trivial values of the parameters.

However, there is positive heterosis ($H_1 > 0$) only when both frequencies of the best allele at each locus are not higher in the same parent population. Generally speaking, then, positive heterosis will take place in the cross between populations which each have a somewhat random assortment of poorer and better alleles, while negative heterosis will be expected if better alleles are more frequent in one parental population. One must realize, however, that negative heterosis is not observed frequently in practice. Yet it is difficult to try and validate simple one- or two-locus models of heterosis from observed crossbred superiority, since the trait measured phenotypically results from combined dominance, additive and epistasis effects.

Under the model, heterosis in the F_2 depends on the rate of recombination. If the two loci are tightly linked, as might be expected for a structural gene and its corresponding control gene, genotypic superiority of the F_1 will be nearly halved in the F_2. This prediction is close to the one of the dominance model. Yet F_2 data generally do not fit any existing model well, although performance usually is much lower in the F_2 than in the F_1 (Sheridan, 1981). But with this model, if the two genes are independent, heterosis observed in the F_1 is expected to be maintained at the same level in the F_2.

Obviously, this model cannot explain fully the usual values of heterosis obtained from real F_1, F_2, P_1 and P_2 performances, but no existing model does, certainly because of the complex genetic nature of the quantitative traits (e.g. milk production, egg number) most studied.

The main interest of this model is to point to a possible, and so far overlooked, cause of heterosis – and conversely of inbreeding depression – which bears no relation to dominance effects: the non-additive interaction between additive genes.

I thank Professor Yukio Yamada and the Faculty of Agriculture of Kyoto University for their hospitality. The very helpful comments of an anonymous reviewer are gratefully acknowledged.

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