Journal of Animal and Veterinary Advances 8 (6): 1212-1218, 2009
ISSN: 1680-5593

Comparative Estimation on Three-Way Heterosis in Pigs Reveals Genetic Bias of the Widely Used Empirical Formula

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Abstract: The objective of this study is to explore the genetic bias of the empirical formula which was widely used to estimate the magnitude of 3-way heterosis in the pig industry of China. Additive and dominance genetic components partitioned from the Cockerham's model were used to derive the expectation of the heterosis effect from the 3-way crossbreds, which witnessed that the theoretical genetic bias of the expectation between the empirical formula and the Cockerham's model is half of the magnitude of heterosis of F_1 single-cross. Following this research, we made a case analysis to reveal the difference of 3-way heterosis between the empirical formula and the Cockerham's model by using the field performance test data of economically important traits involving in growth, carcass and meat quality traits in pigs. The results indicated that the veracity of the empirical formula for 3-way heterosis estimation is conditional and for those traits with remarkable heterosis effects in F_1 single-cross generation, other alternative estimation methods should be taken into account.

Key words: Pigs, 3-way heterosis, empirical formula, Cockerham's model, genetic component, genetic bias

INTRODUCTION

Heterosis (hybrid vigor), mainly involving in the non-additive genetic effect, is an economically, evolutionarily, ecologically or even biomedically important phenomenon (Tsukahara *et al*., 2008; Baack and Rieseberg, 2007; Riginos and Cunningham, 2007; Lee *et al*., 2002), which has been observed for centuries. The term "heterosis" was firstly proposed by Shull in 1908 to designate the "blending" character like vigour of first-generation (Crow, 1987). Subsequently, the meaning of heterosis evolved to refer to the superiority from any types of hybrid progenies towards their parents on aspects as productivity, viability, adaptability or other concrete traits. To date, heterosis in animals and plants has been utilized on large scale for many years. In livestock production systems, cross between breeds or strains was the most popular production pattern. It has been estimated that over 90% of livestock products, particularly in swine and chicken industries, were produced through hybrid programs in China. Although, a growing number of researches have been conducted to address the accuracy and efficiency of the heterosis prediction based on bio-mathematical models and/or molecular techniques (Gavora *et al*., 1996; Sun *et al*., 2000; Atzmon *et al*., 2002; Barker *et al*., 1997; Stuber *et al*., 1992; Xiao *et al*., 1995; Xu and Zhu, 1999), under the current hybrid programs, comparative evaluation of the magnitude of heterosis or combining ability among breeds and strains is still unavoidable for the selection of optimal cross combination and the utilization of maximum heterosis.

China has the largest yield of hog and pork among nations in the world, most of which were also produced through hybrid production system. Up to date, there have been established several commonly-used cross patterns to meet specific production and marketing objectives, in which the 3-way terminal cross, denoted as A× (B×C), were widely applied in the hog production system in China (Liu *et al*., 1999; Shi *et al*., 2002; Tang *et al*., 2000; Wang *et al*., 2002; Wu *et al*., 2006). The prevalence of 3-way cross pattern instead of single-cross one owes partly to a more efficient use of genetic effects as much as possible for both complementarity of additive genetic effects and the non-additive genetic effects. In the

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utilizations of 3-way cross programs, an empirical formula (Eq. 1) for estimating the magnitude of 3-way heterosis was widely used to rank different 3-way cross combinations. As mentioned above, because the evaluation of heterosis effects is a precondition to sort the optimal hybrid combinations, the veracity of methods for estimating the heterosis effects should be carefully examined. Nevertheless, the veracity and applicable condition of the widely-used empirical formula for 3-way heterosis estimation were never formally evaluated. For instance, how much the potential departure of 3-way heterosis estimated through the empirical formula is? What is the applicable condition of the empirical formula? Are there alternative methods for evaluating 3-way heterosis? Due to the wide uses of the empirical formula in China, by some measures, it necessitates to provide solution to these problems.

In the heterosis studies, the Cockerham's model (Cockerham, 1954) has been widely reported to deal with heterosis as well as to partition the heterosis-related genetic components (Gao and Zhu, 2007; Melchinger *et al.*, 2007; Tang *et al.*, 2007). Given this, in this study we considered the Cockerham's model as a standard control to assess the empirical formula. Concretely, the purposes of this study were: to partition the genetic components under 3-way cross pattern through using the Cockerham's model and explore the theoretical departure between the empirical formula and the expectation inferred from the Cockerham's model and to make a case analysis based on the field performance test data of economic traits involving in growth, carcass and meat quality traits in pigs.

MATERIALS AND METHODS

Two approaches for heterosis estimation on 3-way cross: The first approach for calculating the 3-way heterosis is directly using the widely-used empirical formula. The widely-used empirical formula for 3-way heterosis estimation in the Chinese pig industry, denoted as A× (B×C), is generally described as follow:

$$H\% = \frac{\overline{F} - (0.5\overline{A} + 0.25\overline{B} + 0.25\overline{C})}{0.5\overline{A} + 0.25\overline{B} + 0.25\overline{C}} \times 100 \qquad (1)$$

where, H, % is the value of heterosis ratio (the numerator is heterosis), $\overline{F}$ is the phenotypic mean of triple cross A× (B × C) and $\overline{A}$, $\overline{B}$ and $\overline{C}$ are the phenotypic means of parental lines A, B and C or breeds A, B and C, respectively.

The second approach is the Cockerham's model-based estimation approach. Considering the widely-reported use of Cockerham's model in heterosis studies (Yang, 2004; Kao and Zeng, 2002; Xu and Zhu, 1999; Cockerham and Zeng, 1996), we here use the Cockerham's model to conduct the comparative estimation. For an arbitrary animal, the phenotype can be partitioned as follow:

$$y = \mu + G + e \qquad (2)$$

where:

y = The phenotype

μ = The mean value of population

G = The genetic effect (hereinto, G = A + D + I in which A is the additive effect, D is the dominant effect and I is the epistatic effect)

e = Comprises systematical effect E under multi-environmental conditions

For simplification, we ignored the epistatic effect and assumed the inheritance of trait is followed an additive-dominance model, as done in other researches (Xu and Zhu, 1999) and the component G can be partitioned according to the Cockerham's model as follow:

$$G = \sum_i \alpha_i Ai + \sum_i \sum_j \delta_{ij} Dij \qquad (3)$$

where, α_i is the coefficient of additive genetic effect and $\Sigma_i \alpha_i = 2$ and δ_{ij} is the coefficient of dominance genetic effect and $\Sigma_i \Sigma_j \delta_{ij} = 1$. Thus, for the 3-way hybrid, A× (B×C), the genetic components of straightbred A, B, C and their crossbreds can be partitioned as follows:

$$G_A = 2A_A + D_{AA} \qquad (4)$$

$$G_B = 2A_B + D_{BB} \qquad (5)$$

$$G_C = 2A_C + D_{CC} \qquad (6)$$

$$G_{BC} = A_B + A_C + D_{BC} \qquad (7)$$

$$G_{A(BC)} = A_A + \frac{1}{2}A_B + \frac{1}{2}A_C + \frac{1}{2}D_{AB} + \frac{1}{2}D_{AC} \qquad (8)$$

On the biological meaning of heterosis that is biologically determined by the gap between the performance of hybrid progenies and the average performance of their parents, the genetic components of heterosis of triple-cross population can be estimated as follow:

$$\begin{aligned} H_M &= G_{A(BC)} - \frac{1}{2}(G_A + G_{BC}) \\ &= A_A + \frac{1}{2} A_B + \frac{1}{2}A_C + \frac{1}{2}D_{AB} + \frac{1}{2}D_{AC} - A_A - \\ &\quad \frac{1}{2} D_{AA} - \frac{1}{2}A_B - \frac{1}{2}A_C - \frac{1}{2} D_{BC} \\ &= \frac{1}{2}D_{AB} + \frac{1}{2}D_{AC} - \frac{1}{2}D_{AA} - \frac{1}{2}D_{BC} \end{aligned} \qquad (9)$$

where, H_M is the heterosis of triple-cross progeny according to the biological definition of heterosis.

Let's consider the bias of the empirical formula from the Cockerham's model-based approach. Following the equational structure of the empirical formula, the genetic components of the empirical formula-based 3-way heterosis (1) can be partitioned as follow:

$$H = \frac{1}{2} D_{AB} + \frac{1}{2} D_{AC} - \frac{1}{2} D_{AA} - \frac{1}{4} D_{BB} - \frac{1}{4} D_{CC} \tag{10}$$

Here, it is clear that the expectation of the between H_M and H is 1/2 D_{BC} -1/4 D_{BB} -1/4 D_{CC}, which is just the half of the value of heterosis in F_1 single-cross generation, namely the theoretical genetic bias of the empirical formula is the half of the heterosis effects of F_1 single-cross.

Experiment: The study was conducted at State Tongcheng Pig Conservation Farm in Tongcheng County of Hubei Province. In this trial, the sample for slaughter comprised 32 individuals of Large White pigs (16 castrated boars and 16 gilts), 30 individuals of Landrace pigs (10 castrated boars and 20 gilts), 33 individuals of Chinese indigenous Tongcheng pigs (17 castrated boars and 16 gilts), 33 crossbred individuals of Landrace x (Large White x Tongcheng) pigs (16 castrated boars and 17 gilts) and 34 crossbred individuals of Large White x (Landrace x Tongcheng) pigs (15 castrated boars and 19 gilts). Totally, 5 independent combinations of 162 animals were involved in this investigation. Pigs were given *ad libitum* access to feed and were fed on a 2-phase dietary program and drinking water was available constantly. Diets were based on corn and soybean meal.

When the body weight of pig reached 90 kg, all individuals were slaughtered for carcass and meat quality traits test. The performance test was conducted in the farm laboratory that is supported by financing from Agriculture Ministry. Carcass measurements were obtained from the left side of each carcass and the muscle was measured on a longissimus sample taken at the level of the 10th rib. In this investigation, a total of 20 traits included average daily gain, the weight and length of carcass and carcass components (backfat thickness, dressing percent, leaf percentage, average backfat thickness, carcass length, skin thickness, rib numbers, loin muscle area), pH, subjective scores for longissimus muscle color and marbling based on 5 point scales, shear force, drip loss, water holding capacity, internal fat percentage and content of intramuscular fat. The detailed procedures for performance test can be consulted in our previous research (Zhang, 2004).

Statistical analyses: The genetic components of each combination under 3-way cross pattern were evaluated using the additive-dominance model. The model was written in a matrix form as:

$$y = X\beta + Za + Wd + e \tag{11}$$

where:

y = The observation vector

β = The vector of fixed effects including population mean, sex and batch

a = The vector of additive components

d = The vector of dominance components

e = The vector of residuals. Matrices

X, Z and W = The corresponding incidence matrices, hereinto the elements of the matrices

Z and W = Contained additive coefficients α_i dominance coefficients δ_{ij} and zeroes, respectively

In the model, the environmental influences were assumed to be consistent over all breeds and combinations and the epistatic effects were neglectable. Heterosis ratios were further evaluated according to the estimated genetic components. Simultaneously, heterosis ratios were comparatively calculated through the empirical Eq. (1). The t-test method was employed to assess the statistical significance, in which the standard errors were obtained via the standard error propagation rules (Zhu *et al*., 2008).

RESULTS

Genetic components: Table 1 showed the estimated genetic components of each trait partitioned from the Cockerham's model. In Tongcheng pigs, additive genetic components were negative in the traits of average daily gain, dressing percent, carcass length, ham meat percentage and drip loss and the same as slaughtering age, backfat thickness, dressing percent, leaf percentage, skin thickness, color score, marbling score and internal fat percentage in Landrace pigs and slaughtering age, average daily gain, ham meat percentage, color score, marbling score and intramuscular fat content in Yorkshire pigs, which were in approximate accordance with the actual performance levels of the traits in each breed. Most of the dominance components of pure breeds were lower than that of crossbreds, which seemed to inosculate the dominance theory, firstly proposed by Bruce (1910) and to reveal the genetic mechanism of heterosis at some

Table 1: Genetic components of 20 traits partitioned from Cockerham genetic model[a]

GC	SA	ADG	BFT	DP	LP	IFP	CL	RN	ABFT	ST
A_T	18.7644	-89.3937	11.1064	-1.7127	2.1401	1.0000	-5.6482	1.0000	0.9291	0.0984
A_L	-0.1779	6.6379	-0.3496	-0.5538	-0.0434	-0.4180	1.0646	0.9031	0.6073	-0.0480
A_Y	-0.0386	-0.6863	2.1254	1.0000	0.3968	0.4241	1.0000	0.9730	0.4590	0.0145
D_{TT}	1.0000	1.0000	-0.0239	1.0000	0.0871	7.5311	-1.1824	1.0000	-1.5692	1.0000
D_{LL}	1.0000	0.3478	-6.2289	1.0000	1.0000	-0.2611	-0.1388	0.1686	0.9035	1.0000
D_{YY}	0.2135	-14.5011	1.0000	1.0000	0.4916	-0.6208	0.9920	0.7145	3.8778	0.1921
D_{YT}	-39.3941	81.6421	5.6750	0.0932	0.3854	3.3320	3.7703	0.0828	0.3863	-0.0753
D_{LT}	-29.8227	73.6520	4.5829	1.2432	0.1158	3.1115	2.9298	0.1830	0.5301	-0.0209
D_{YL}	1.0000	0.3542	1.0000	-0.1964	1.0000	0.2946	-0.0467	-0.1891	1.0000	1.0000

GC	LA	HP	HMP	pH	CS	MS	WHC	DL	SF	IMF
A_T	1.0000	1.4866	-9.2179	0.1372	1.3489	1.0000	1.0646	-0.2117	2.8797	0.5676
A_L	10.4917	2.3387	2.2462	0.0611	-0.1753	-0.1810	0.2020	0.1272	1.0000	0.1510
A_Y	7.7479	1.6974	-0.6174	1.0000	-0.1305	-0.3424	1.0000	0.0978	3.4184	-0.0694
D_{TT}	1.0000	-0.4992	1.0598	1.0000	-0.9696	1.0000	0.0717	-0.3683	1.0000	1.0000
D_{LL}	0.9777	1.4314	0.0638	1.0000	-0.1321	1.0000	1.0000	0.0547	1.0000	1.0000
D_{YY}	1.0000	1.0000	-1.1055	1.0000	-0.0277	1.0000	-0.6043	-0.0938	1.0000	1.0000
D_{YT}	-2.6877	-0.2172	-4.4375	-0.0775	-0.1325	0.0731	-0.6502	0.1931	-5.1171	0.0767
D_{LT}	-1.1866	-0.8211	-1.2519	-0.3371	-0.1421	-0.3383	1.0030	0.1915	-7.9315	0.4077
D_{YL}	-0.7560	1.0000	1.0000	1.0000	1.0000	1.0000	0.0602	1.0000	1.0000	0.1616

[a] A_T, A_L and A_Y stand for additive genetic components of T, L and Y; D_{TT}, D_{LL}, D_{YY}, D_{YL} and D_{YT} stand for dominance genetic components of T, L, Y, Y×L, Y×T, L×Y. Abbreviation key: Y = Yorkshire, L = Landrace, T = Tongcheng, YT = Yorkshire x Tongcheng, LT = Landrace x Tongcheng, YL = Yorkshire x Landrace, GC = Genetic Components, SA = Slaughtering Age, ADG = Average Daily Gain, BFT = Backfat Thickness, DP = Dressing Percent, LP = Leaf Percentage, IFP = Internal Fat Percentage, RN = Rib Numbers, CL = Carcass Length, ABFT = Average Backfat Thickness, ST = Skin Thickness, LA = Loin Muscle Area, HP = Ham Percentage, HMP = Ham Meat Percentage, CS = Color Score, MS = Marbling Score, WHC = Water Holding Capacity, DL = Drip Loss, SF = Shear Force, IMF = Content of Intramuscular Fat

Table 2: Comparison of heterosis ratios of twenty traits between empirical formula and Cockerham's model in two triple-cross combinations

Method	Combination	SA	ADG	BFT	DP	LP	IFP	CL	RN	ABFT	ST
Empirical formula	LYT[a]	-0.045	0.046	-0.038	0.018	-0.174	-0.296	0.010	0.037	0.053*	-0.131
	YLT	-0.101	0.082	0.542*	0.197*	-0.138	2.590	0.002	-0.163*	0.068*	-0.370
Cockerham's model	LYT	-0.478	-0.246*	0.512*	0.064	-0.070	0.092	-0.673*	-0.064	0.062*	0.058
	YLT	0.791*[b]	0.333*	0.053	-1.187*	0.222	0.290	-0.148*	-0.211*	-0.440**	3.007

Method	Combination	LA	HP	HMP	pH	CS	MS	WHC	DL	SF	IMF
Empirical formula	LYT	0.058	0.005	0.029	-0.014	-0.011	0.132	-0.067	-0.371	-0.040	-0.177
	YLT	0.037	0.362*	-0.177*	-0.162	-0.073*	-1.115*	-0.371*	-0.042	-0.561*	0.247**
Cockerham's model	LYT	-0.008	-0.114*	-0.424*	-0.119	1.861*	-0.301	0.253*	2.430*	-0.673*	-0.270*
	YLT	-0.122*	0.082	0.102*	0.091	1.396*	0.517*	-0.270*	5.246*	0.744*	-0.588**[a]

LYT = Landrace x (Yorkshire x Tongcheng), YLT = Yorkshire x (Landrace x Tongcheng). [b] Single asterisk (*) means significant at the level of $p<0.05$ and double asterisk (**) means significant at the level of $p<0.01$

extent. Additionally, there was another trend in the results that the magnitude of each genetic component seemed proportional to the dimension of the raw data records of each trait.

Heterosis ratios: Comparisons of heterosis ratio of each trait between the empirical formula and the Cockerham's model in 2 triple-cross combinations, including statistics test, were shown in Table 2. Between 2 methods, the positive and negative signs of heterosis ratios of average daily gain, backfat thickness, internal fat percentage, rib numbers, carcass length, skin thickness, loin muscle area, ham percentage, ham meat percentage, water holding capacity, drip loss color score and marbling score were inverse in Landrace x (Yorkshire x Tongcheng) combination and the positive and negative signs of heterosis ratios of slaughtering age, leaf percentage, carcass length, skin thickness, loin muscle area, ham meat percentage, color score, drip loss, dressing percent, average backfat thickness, pH, marbling score, content of intramuscular fat and shear force were also inverse in Yorkshire x (Landrace x Tongcheng) combination. In addition, the positive and negative signs of heterosis ratios of skin thickness, loin muscle area, ham meat percentage, drip loss, carcass length, color score and marbling score were simultaneously inverse in both combinations. In addition, there seemed overdominance in heterosis for dressing percent, skin thickness, color score and drip loss in the estimation based on the Cockerham's model, as well as for internal fat percentage and marbling score in the estimation based on the empirical formula. The results indicated there were detectable differences between 2 estimation methods.

DISCUSSION

Because of the high cost of performance test, many farms or companies often had difficulties to perform large-scale testing. In utilization of the crossbreeding programs, in order to decrease the testing cost, more convenient efforts were selectively applied in the actual selection of optimal cross combination. The application of the widely-used empirical formula for 3-way heterosis estimation has embodied this point because the slaughter of singlecross parental animals (B×C) can be avoided. It is undoubted that the empirical formula has a special practicability in economic underdeveloped regions. Many research articles have documented that, in the pig industry of China, almost all trials for ranking the optimal 3-way cross combinations had followed the testing route that the empirical formula provided (Liu *et al*., 1999; Shi *et al*., 2002; Tang *et al*., 2000; Wang *et al*., 2002; Wu *et al*., 2006). Obviously, there is an importance for unveiling the potential departure and applicable condition of the widely-used empirical formula, for both genetic research and productive practice.

Our study had primarily demonstrated the widely used empirical formula only provides an approximate evaluation of 3-way heterosis. In theory, the biases of estimated parameters could be conformed through their expectations, based on which the expectation of the difference between H_M and H was proved to be equal to the half of the heterosis effects of F_1 single-cross. In the case analysis, compared with the expectation derived from the Cockerham's model, the departure of the empirical formula could be very large especially when the heterosis of the F_1 single-cross was not negligible. As shown in Table 2, in skin thickness, loin muscle area, ham meat percentage, drip loss, carcass length, color score and marbling score, the departure can arrive at an extreme situation, in which the value of heterosis could change from positive (or negative) value to negative (or positive) value. It should avoid the unlimited application of the empirical equation if the heterosis effect of F_1 single-cross population is significant.

Up to date, a series of hypotheses have been proposed to clarify the genetic essence of heterosis (Bruce, 1910; Jones, 1917; Crow, 1948; Comings and Macmurray, 2000). It has now been known that the genetic base of hybrid performance is mainly or partly due to the complementarity of additive genetic effects and the non-additive genetic effects, in our opinion, from which the genetic mechanism resulting in the departure of the empirical formula can be legitimately interpreted. As we know, the heterosis can be defined that the performance of crossbred progeny exceeds the average of their parents. The essence of 3-way heterosis directly is the difference between the performance of triple-cross progeny (A× (B×C)) and the average performance of the straightbred genitor (A) and the other single-cross genitor (B ×C) (the single-cross progeny of the straightbred B and C) (McDonald and Turner, 1972). But the equation structure of the empirical formula does not accord with this essence. In the empirical formula, only the information of the straightbred genitor is used and there is a lack of the information of the other direct single-cross genitor, which is replaced by the average performance of the indirect genitors B and C at the higher generation. The proportion of blood of the indirect parents included into the empirical formula only reflects the parental complementarity of additive genetic effects, but does not reveal the variability of magnitude of non-additive genetic effects across generations. Obviously, the empirical formula makes a mistake that total genetic effect was substituted by the equally-weighed additive genetic effect. It is thus, easy to understand why the estimation of the empirical formula is biased.

CONCLUSION

In a primitive conclusion, the expected genetic bias of the widely-used empirical formula is half of the heterosis effects of F_1 single-cross. We should restrict the arbitrary applications of the empirical formula for 3-way heterosis estimation and pay attention to the tendency of wrong estimation in production practice. The applicable condition, that the empirical formula is suitable for those traits with low non-additive genetic effect in F_1 single-cross hybrid performance, suggests that when significant heterosis exists in F_1 single-cross genitor, other alternative methods should be under consideration.

ACKNOWLEDGEMENT

This research was supported by Key Project of National Basic Research and Developmental Plan (2006CB102105) of China, the National High Technology Research and Development Program of China (2007AA10Z148) and the National Key Technology R and D Program (2008BADB2B01). The authors thank Y.Q. Du and S.H. Xu for their valuable technical assistance in the performance test work.

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