Evaluation of Reciprocal Cross Design on Detection and Characterization of Mendelian QTL in F_2 Outbred Populations

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ABSTRACT : A simulation study was conducted to evaluate the effect of reciprocal cross on the detection and characterization of Mendelian QTL in F_2 QTL swine populations. Data were simulated under two different mating designs. In the one-way cross design, six F_0 grand sires of one breed and 30 F_0 grand dams of another breed generated 10 F_1 offspring per dam. Sixteen F_1 sires and 64 F_1 dams were randomly chosen to produce a total of 640 F_2 offspring. In the reciprocal design, three F_0 grand sires of A breed and 15 F_0 grand dams of B breed were mated to generate 10 F_1 offspring per dam. Eight F_1 sires and 32 F_1 dams were randomly chosen to produce 10 F_2 offspring per F_1 dam, for a total of 320 F_2 offspring. Another mating set comprised three F_C grand sires of B breed and 15 F_0 grand dams of A breed to produce the same number of F_1 and F_2 offspring. A chromosome of 100 cM was simulated with large, medium or small QTL with fixed, similar, or different allele frequencies in parental breeds. Tests between Mendelian models allowed QTL to be characterized as fixed (LC QTL), or segregating at similar (HS QTL) or different (CB QTL) frequencies in parental breeds. When alternate breed alleles segregated in parental breeds, a greater proportion of QTL were classified as CB QTL and estimates of QTL effects for the CB QTL were more unbiased and precise in the reciprocal cross than in the one-way cross. This result suggests that reciprocal cross design allows better characterization of Mendelian QTL in terms of allele frequencies in parental breeds. (**Key Words :** Quantitative Trait Loci, Swine, Detection Power, Reciprocal Cross)

INTRODUCTION

Quantitative trait loci (QTL) studies on economically important traits in swine have routinely been performed by generating F_2 populations using two breeds (Bidanel and Rothschild, 2002; Choi et al., 2006; Kim et al., 2007). The two models that have been most extensively applied to QTL detection are the line-cross (Haley et al., 1994) and half-sib (Knott et al., 1996) least squares interval mapping methods. The former is used for three-generation breed crosses to detect QTL that differ between breeds. This model is the most powerful when QTL are fixed for alternate alleles in the parental breeds, and power to detect QTL decreases as allele frequencies in the parental breeds become similar (Alfonso and Haley, 1998). If F_1 sire families of adequate size exist, half-sib designs can also be applied to F_2 populations, utilizing the paternal half-sib family structure (de Koning et al., 2001). Unlike line-cross analyses, half-sib analyses can detect QTL for which the parental breeds have similar frequencies (de Koning et al., 2001; Quintanilla et

al., 2003).

Recently, a combined line-cross and half-sib model was developed that exploits information of linkage disequilibrium between breeds and within families. This model was the most powerful when alternate allele frequencies differed in the parental breeds (Kim et al., 2005a). Use of all three models increased power to detect QTL and to allow characterization of QTL in terms of allele segregation within parental breeds (Kim et al., 2005a).

Most of F_2 mating designs in porcine QTL populations are based on the one-way cross, i.e. all grandsires are from one breed, and all grand-dams are from another breed. The one-way mating design can generate progeny with phenotype difference due to breed-specific maternal environmental effects, mitochondrial inheritance, genomic imprinting, or sex-chromosome linked effects (Thallman et al., 1992). Recently, reciprocal cross designs were used for QTL detection in swine, for which individuals of both two breeds were used as grand-sires and grand-dams (Rohrer et al., 2006; Liu et al., 2007).

The purpose of this study was to evaluate the effect of reciprocal mating designs on detection and characterization of QTL using the three Mendelian QTL mapping models.

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MATERIALS AND METHODS

QTL analysis models

Derivation of a combined model for QTL mapping in an F_2 cross between two outbred breeds (1 and 2) was described in detail in Kim et al. (2005a). The following models were defined and fitted at each 1 cM position:

Line-cross model (LC)
$$y_{ij} = X_{ij}b_{ij}+s_i+aP_{aij}+dP_{dij}+e_{ij} \tag{1}$$

Half-sib model (HS)
$$y_{ij} = X_{ij}b_{ij}+s_i+\alpha_{HSi}P_{Sij}+e_{ij} \tag{2}$$

Combined model (CB)
$$y_{ij} = X_{ij}b_{ij}+s_i+aP_{aij}+dP_{dij}+\alpha_{CBi}P_{Sij}+e_{ij} \tag{3}$$

where y_{ij} is the phenotype of F_2 progeny j of F_1 sire i, X_{ij} and b_{ij} are the design matrix and solution vector for fixed effects and covariates. s_i is the effect of the ith F_1 sire, and e_{ij} is a residual. In models 1 and 3, coefficients a and d are the additive and dominance effects of breed-origin alleles at a putative QTL at the fitted position. Coefficient a was defined as half of the difference between effects of the two homozygotes for breed-origin alleles (11 and 22) and d as the difference of the average effect of the two heterozygotes (12 and 21) from the two homozygotes. Following Haley et al. (1994), coefficients P_{aij} and P_{dij} are the corresponding breed-origin coefficients for each animal at the putative QTL position conditional on flanking marker genotypes, such that $P_a = P_{11}-P_{22}$ and $P_d = P_{12}+P_{21}$, where P_{kl} is the probability of inheriting an allele from breed k (l) from the F_1 sire (dam). In models 2 and 3, following Knott et al. (1996), α_{HSi} and α_{CBi} represent the substitution effect for the two putative QTL alleles carried by the ith F_1 sire and P_{Sij} the probability that the F_2 offspring inherited one versus the other QTL allele from its F_1 sire.

All three models were fitted across a chromosome to detect QTL. For chromosomal regions where at least one of the three models was significant at the 5% chromosome-wise level, a series of tests was applied to distinguish the following types of QTL: (1) the QTL is fixed for alternate alleles in the F_0 parents from breeds 1 and 2 (LC QTL), (2) the QTL segregates in F_0 parents from the two breeds at similar frequency (HS QTL), or (3) the QTL segregates in F_0 parents from the two breeds but at different frequencies (CB QTL). The three types of QTL were identified using the following lack-of-fit tests between the three models, with tests conducted at the 5% comparison-wise level:

i) LC QTL: The QTL is detected under the LC model, but the lack-of-fit test of the CB over the LC model is not significant. The lack-of-fit test was based on the following

test statistic at the most likely position under the LC model.

$$LOF_{LC} = ((RSS_{LC}-RSS_{CB})/(df_{LC}-df_{CB}))/(RSS_{CB}/df_{CB}).$$

where RSS_K and df_K are the residual sum of squares and residual degrees of freedom for model K.

ii) HS QTL: The QTL is detected under the HS model, not significant under the LC model, and the lack-of-fit test of the CB over the HS model is not significant. This test was based on the following test statistic at the most likely position under the HS model:

$$LOF_{HS} = ((RSS_{HS}-RSS_{CB})/(df_{HS}-df_{CB}))/(RSS_{CB}/df_{CB})$$

iii) CB QTL: The QTL is detected with the CB model but cannot be defined as LC or HS QTL based on tests 1 and 2.

For QTL detection, empirically derived 5% chromosome-wise significance thresholds were used for each model. Lack-of-fit tests were performed at a 5% comparison-wise level using standard F statistic thresholds.

Simulation

To compare the power and ability to distinguish alternative QTL types, F_2 populations were simulated based on two designs: one-way cross and reciprocal cross designs. The one-way cross design comprised six F_0 grandsires of one breed and 30 F_0 grand-dams of another breed to generate 10 F_1 offspring per dam. Sixteen F_1 sires and 64 F_1 dams were randomly chosen to produce a total of 640 progeny. In the reciprocal cross design, three F_0 grand sires of breed A were mated to 15 F_0 grand-dams of breed B to generate 10 F_1 offspring per dam. Eight F_1 sires and 32 F_1 dams were randomly chosen to produce 10 F_2 offspring per dam, for a total of 320 F_2 offspring. Also, three F_0 grand sires of breed B and 15 F_0 grand-dams of breed A were used to generate the same numbers of F_1s, which were subsequently chosen to produce a total of 320 F_2 offspring.

A chromosome of 100 cM was simulated with 11 markers at 10 cM intervals. Markers were simulated with four frequencies of 0.5, 0.3, 0.1, 0.1 in one breed and 0.1, 0.1, 0.3, 0.5 in the other breed. This simulation was based on the marker information content in an experimental QTL population using F_0s of Korean Native Pig and Yorkshire (data not shown). An additive biallelic QTL with an additive effect (a) of 0.8, 0.5 or 0.32 phenotypic standard deviations was simulated at position 75 cM on the chromosome. At equal frequencies of QTL alleles in the F_2 generation, the QTL explained 32, 12.5 or 5.1% of the phenotypic variance, respectively, for the quantitative trait that was simulated. A QTL with dominance effect ($a = d$) was also simulated with equal error variances as that for

Table 1. Overall power to detect QTL under different Mendelian models, and proportion of detected QTL declared as line-cross, half-sib, or combined QTL in different QTL modes, sizes, and mating designs

QTL size (allele frequency)[b]	One way cross[a]				Reciprocal cross[a]			
	Detection power (%)[c]	CB QTL[d]	LC QTL[d]	HS QTL[d]	Detection power (%)[c]	CB QTL[d]	LC QTL[d]	HS QTL[d]
Additive								
Large (1.0/0.0)	100	5.7	94.3	0.0	100	4.0	96.0	0.0
Large (0.8/0.2)	100	84.0	15.7	0.3	100	92.3	7.7	0.0
Large (0.5/0.5)	99.7	42.0	1.0	56.7	99.7	46.3	0.7	52.7
Medium (1.0/0.0)	100	6.0	94.0	0.0	100	4.3	95.7	0.0
Medium (0.8/0.2)	99.7	48.7	44.7	6.3	98.0	56.0	38.7	3.3
Medium (0.5/0.5)	85.7	15.3	5.7	64.7	85.0	22.7	4.7	57.7
Small (1.0/0.0)	99.3	5.3	94.0	0.0	99.7	5.0	94.7	0.0
Small (0.8/0.2)	79.7	12.0	58.0	9.7	72.7	22.7	43.7	6.3
Small (0.5/0.5)	42.3	4.0	6.7	31.7	44.0	5.3	7.3	31.3
Dominance								
Large (1.0/0.0)	100	3.3	96.7	0.0	100	4.0	96.0	0.0
Large (0.8/0.2)	100	71.3	27.7	1.0	100	89.0	10.3	0.7
Large (0.5/0.5)	97.7	41.3	2.3	54.0	99.3	43.7	2.3	53.3
Medium (1.0/0.0)	100	4.7	95.3	0.0	100	5.7	94.3	0.0
Medium (0.8/0.2)	99.7	44.3	49.7	5.7	97.7	57.7	37.0	3.0
Medium (0.5/0.5)	83.3	19.3	6.0	58.0	83.7	21.7	5.3	56.7
Small (1.0/0.0)	100	5.7	94.3	0.0	100	5.0	95.0	0.0
Small (0.8/0.2)	80	19.7	49.0	11.3	76.3	18.7	52.0	5.7
Small (0.5/0.5)	45.3	7.3	7.3	30.7	48.3	6.3	7.3	34.7

[a] In the one-way cross design, six F_0 grand sires of one breed and 30 F_0 grand dams of another breed generate 10 F_1 offspring per dam. Sixteen F_1 sires and 64 F_1 dams are randomly chosen to produce 10 F_2 offspring per F_1 dam, for a total of 640 F_2 offspring. In the reciprocal design, one mating set comprised three F_0 grand sires of A breed and 15 F_0 grand dams of B breed to generate 10 F_1 offspring per dam. Eight F_1 sires and 32 F_1 dams are randomly chosen to produce 10 F_2 offspring per F_1 dam, for a total of 320 F_2 offspring. Another mating set used three F_0 grand sires of B breed and 15 F_0 grand dams of A breed to produce the same number of F_1 and F_2 offspring.

[b] Large, medium and small indicate QTL effects, such that additive (dominance) QTL effects are a ($a = d$) = 0.8, 0.5 and 0.32 p, explaining 32% (41.4%), 12.5% (17.7%) and 5.1% (7.5%) of phenotypic variance, respectively. QTL allele frequency differences are between F_0 grandparents from the two breeds.

[c] Proportion of replicates in which QTL were detected at 5% chromosome-wise level in at least one of the line-cross (LC), half-sib (HS), and combined line-cross and half-sib (CB) models.

[d] Relative proportion of declared QTL type for the detected QTL. LC QTL: alternate breed alleles are fixed in their respective breeds. HS (CB) QTL: alternate breed alleles are evenly (differently) distributed within F_0 parental breeds.

additive QTL, and it explained 41.4, 17.6, or 7.5% of the phenotypic variance, respectively. The QTL genotypes for the F_0 parents were drawn from three alternative sets of frequencies of the favorable QTL allele in the two parental breeds: 1.0:0.0, 0.8:0.2, and 0.5:0.5. Three hundred replicate data sets were simulated for each set. Thresholds at the 5% chromosome-wise level for QTL detection for the three models were derived from three thousand replicates with QTL effects set to zero.

RESULTS

Power to detect QTL and their characterization

Table 1 presents the power to detect additive and dominant QTL and proportions of declared QTL types in the one-way and the reciprocal mating designs. The power to detect QTL was greatest for large QTL but decreased with QTL size. Power to detect QTL also decreased as allele frequency difference (FD) became similar, which was more pronounced for small QTL. Generally, the overall

detection powers were similar in the two mating designs across all levels of QTL mode, size, and FD. However, when QTL effect was small with FD = 0.6, the powers to detect QTL were greater in the one way cross than in the reciprocal cross, e.g. 80% vs. 73% and 80% vs. 76% for additive and dominance QTL, respectively (Table 1). The proportion of LC QTL was greatest when alternate QTL alleles were fixed in F_0 parents (FD = 1.0), the proportion of CB QTL was greatest when frequencies of alternate alleles were different (FD = 0.8-0.2 = 0.6) for large or medium QTL, and the proportion of HS QTL was greatest when FD = 0.0 (Table 1). These results were consistent with our previous report, in which 512 F_2 offspring were produced by crossing eight F_1 sires and 32 F_1 dams in one-way mating design from two F_0 grandsires and 10 F_0 grand-dams (Kim et al., 2005a).

The proportions of LC QTL and HS QTL were similar between the two mating designs when FDs were 1.0 and 0.0, respectively, across all levels of QTL effects and sizes. However, the proportion of CB QTL was greater in the

Table 2. Mean and standard deviation (in parenthesis) of estimates of QTL effects by additive and dominance QTL declared as line-cross (LC), half-sib (HS), and combined (CB) type, depending on the difference in QTL modes, sizes, and mating designs in simulated data for an F_2 breed cross under two alternate mating designs

QTL size (allele frequency)[b]	One way cross[a]				Reciprocal cross[a]			
	CB QTL[c]		LC QTL[c]		CB QTL[c]		LC QTL[c]	
	Additive	Dominant	Additive	Dominant	Additive	Dominant	Additive	Dominant
Additive								
Large (1.0/0.0)	0.77 (0.067)	0.01 (0.062)	0.80 (0.050)	0.00 (0.074)	0.84 (0.054)	-0.02 (0.087)	0.80 (0.050)	0.00 (0.078)
Large (0.8/0.2)	0.46 (0.140)	0.00 (0.084)	0.59 (0.087)	0.00 (0.093)	0.48 (0.108)	0.00 (0.080)	0.62 (0.085)	-0.02 (0.069)
Large (0.5/0.5)	0.01 (0.228)	0.00 (0.104)	-0.31 (0.055)	0.03 (0.027)	-0.01 (0.190)	0.01 (0.108)	-0.12 (0.260)	-0.07 (0.104)
Medium (1.0/0.0)	0.49 (0.102)	0.01 (0.057)	0.50 (0.060)	0.00 (0.087)	0.49 (0.053)	0.01 (0.072)	0.50 (0.054)	0.00 (0.080)
Medium (0.8/0.2)	0.30 (0.115)	-0.01 (0.097)	0.34 (0.072)	0.00 (0.094)	0.30 (0.084)	0.01 (0.087)	0.33 (0.080)	0.00 (0.095)
Medium (0.5/0.5)	0.05 (0.202)	-0.02 (0.118)	-0.06 (0.201)	-0.03 (0.177)	0.00 (0.161)	-0.03 (0.139)	0.07 (0.194)	0.06 (0.136)
Small (1.0/0.0)	0.32 (0.083)	0.03 (0.075)	0.33 (0.059)	-0.01 (0.097)	0.31 (0.053)	0.01 (0.072)	0.32 (0.056)	0.00 (0.088)
Small (0.8/0.2)	0.23 (0.094)	-0.02 (0.115)	0.24 (0.053)	-0.01 (0.109)	0.22 (0.066)	0.01 (0.102)	0.24 (0.055)	-0.01 (0.108)
Small (0.5/0.5)	-0.08 (0.185)	0.00 (0.154)	0.00 (0.174)	0.00 (0.166)	0.01 (0.149)	-0.03 (0.147)	-0.04 (0.172)	-0.01 (0.202)
Dominance								
Large (1.0/0.0)	0.79 (0.107)	0.81 (0.062)	0.80 (0.053)	0.80 (0.074)	0.79 (0.046)	0.79 (0.085)	0.80 (0.050)	0.80 (0.071)
Large (0.8/0.2)	0.46 (0.157)	0.26 (0.155)	0.49 (0.112)	0.43 (0.140)	0.47 (0.124)	0.29 (0.146)	0.55 (0.158)	0.44 (0.153)
Large (0.5/0.5)	-0.06 (0.255)	0.06 (0.131)	0.11 (0.218)	0.15 (0.118)	-0.01 (0.206)	0.06 (0.145)	0.02 (0.240)	0.10 (0.184)
Medium (1.0/0.0)	0.48 (0.107)	0.51 (0.062)	0.50 (0.058)	0.50 (0.084)	0.49 (0.051)	0.48 (0.086)	0.50 (0.055)	0.50 (0.080)
Medium (0.8/0.2)	0.30 (0.129)	0.15 (0.119)	0.31 (0.081)	0.24 (0.125)	0.30 (0.097)	0.17 (0.112)	0.32 (0.091)	0.23 (0.127)
Medium (0.5/0.5)	-0.06 (0.192)	0.03 (0.139)	-0.02 (0.227)	0.07 (0.153)	-0.03 (0.161)	0.05 (0.160)	0.02 (0.198)	0.09 (0.192)
Small (1.0/0.0)	0.31 (0.103)	0.33 (0.062)	0.32 (0.062)	0.32 (0.090)	0.31 (0.053)	0.31 (0.078)	0.32 (0.058)	0.32 (0.083)
Small (0.8/0.2)	0.21 (0.999)	0.14 (0.102)	0.22 (0.063)	0.15 (0.124)	0.22 (0.074)	0.12 (0.139)	0.24 (0.056)	0.15 (0.115)
Small (0.5/0.5)	-0.09 (0.154)	0.04 (0.149)	-0.06 (0.172)	0.02 (0.165)	0.00 (0.149)	-0.03 (0.174)	0.00 (0.173)	0.06 (0.203)

[a, b] Described in Table 1.

[c] For additive QTL ($d = 0$), expected additive QTL effects (a) are 0.8, 0.5, and 0.32, with allele frequency (1.0/0.0), 0.48, 0.30, and 0.19 with allele frequency (0.8/0.2), and 0.0, 0.0, and 0.0 with allele frequency (0.5/0.5), for large, medium and small QTL, respectively. For dominance QTL ($a = d$), expected additive (dominant) QTL effects are 0.8 (0.8), 0.5 (0.5), and 0.32 (0.32) with allele frequency (1.0/0.0), 0.48 (0.29), 0.30 (0.18), and 0.19 (0.12) with allele frequency (0.8/0.2), and 0.0 (0.0), 0.0 (0.0), and 0.0 (0.0) with allele frequency (0.5/0.5), for large, medium and small QTL, respectively.

reciprocal design than in the one-way design when FD was 0.6, e.g. 92% vs. 84%, 56% vs. 49%, and 23% vs. 12% for large, medium, and small additive QTL, respectively (Table 1).

Estimates of QTL effects

Means of estimates of additive and dominance effects of declared LC and CB QTL are shown in Table 2. Expectations of QTL effects decreased proportional to FD. For example, the expectation of additive effect is Δf^*a, where Δf is FD of alternate QTL alleles in grand-parental breeds. e.g. for large additive QTL with FD = 0.6, $\Delta f^*a = 0.6*0.8 = 0.48$, and expectation of dominant effect is Δf^2*d (de Koning et al., 2002). Mean estimates were generally similar to their expectation, but estimates were less biased for large QTL and for expected QTL type with the corresponding FD. For example, for the large additive QTL with FD = 1.0 in the one-way cross design, the average estimate of the LC QTL was 0.80, while that of the CB QTL was 0.77. For the same QTL with FD = 0.6 in the reciprocal cross design, the average estimate of the CB QTL was 0.48, while that of the LC QTL was 0.62 (Table 2).

When allele frequencies differ between the grand parental breeds (FD = 0.6), the estimates of additive or dominant effects for CB QTL were less biased than those for LC QTL. e.g. 0.47 and 0.29 for the large dominant CB QTL vs. 0.55 an 0.44 for the LC dominant QTL in the

reciprocal cross (expected values of additive and dominant effects are 0.48 and 0.29, respectively). For CB QTL with FD = 0.6, estimates of QTL effects were less biased in the reciprocal cross than in the one-way cross, which was more pronounced for the estimates of dominant effect, e.g. 0.26 vs. 0.29, and 0.15 vs. 0.17, for the large and medium QTL, (expected values are 0.29 and 0.18, respectively), and estimates in the reciprocal cross were consistently more precise (small standard deviation) than those in the one-way cross, across all levels of QTL mode and size. When allele frequencies were similar between the grand parental breeds (FD = 0), estimates of additive effect for CB QTL were less biased, or close to zero, in the reciprocal cross than in the one-way cross. e.g. for the small additive QTL that were declared CB QTL, the estimates of additive effects were -0.08 and 0.01 in the one-way and in the reciprocal crosses, respectively (Table 2).

Some estimates of additive and/or dominant effects were biased downward for FD = 0. This bias resulted from negative estimates of QTL effects offsetting positive estimates (results not shown).

Estimates of QTL position

Mean estimates of QTL position for replicates with significant QTL are shown in Table 3. Position estimates for LC QTL were nearly unbiased and had high precision (low standard deviation) when the power to detect LC QTL was

Table 3. Mean and standard deviation (in parentheses) of estimates of position QTL declared as line-cross (LC), half-sib (HS), and combined (CB) type, depending on the difference in QTL modes, sizes, and mating designs in simulated data for an F_2 breed cross under two alternate mating designs at 75 cM

QTL size (allele frequency)[b]	One way cross[a]			Reciprocal cross[a]		
	CB QTL[c]	LC QTL[c]	HS QTL[c]	CB QTL[c]	LC QTL[c]	HS QTL[c]
Additive						
Large (1.0/0.0)	75.2 (1.54)	74.9 (1.16)	-	74.9 (1.26)	75.0 (1.18)	-
Large (0.8/0.2)	74.8 (3.13)	75.0 (3.07)	76.0 (0.00)	75.2 (3.43)	74.9 (1.30)	-
Large (0.5/0.5)	69.6 (17.4)	64.3 (8.18)	68.7 (21.6)	71.0 (18.9)	47.0 (27.0)	68.8 (21.8)
Medium (1.0/0.0)	74.2 (3.25)	75.0 (3.06)	-	75.5 (4.14)	75.0 (3.04)	-
Medium (0.8/0.2)	73.8 (9.47)	75.4 (8.03)	63.2 (28.4)	73.8 (10.8)	74.6 (6.68)	65.4 (34.1)
Medium (0.5/0.5)	70.2 (22.2)	55.4 (21.3)	63.1 (26.8)	64.2 (25.3)	57.4 (25.5)	64.9 (27.8)
Small (1.0/0.0)	72.9 (6.52)	74.5 (8.20)	-	77.3 (5.98)	74.8 (6.05)	-
Small (0.8/0.2)	68.6 (18.4)	73.4 (13.5)	59.4 (31.3)	72.5 (18.0)	72.6 (13.6)	56.4 (31.3)
Small (0.5/0.5)	66.1 (22.5)	64.8 (26.0)	65.4 (27.4)	64.9 (31.8)	53.5 (32.0)	58.1 (31.9)
Dominance						
Large (1.0/0.0)	75.1 (1.30)	75.0 (1.10)	-	75.3 (1.31)	75.0 (1.12)	-
Large (0.8/0.2)	74.6 (4.78)	74.5 (4.20)	64.0 (13.4)	75.3 (3.61)	74.2 (1.92)	40.0 (40.0)
Large (0.5/0.5)	71.3 (15.1)	70.0 (12.4)	66.7 (24.3)	68.9 (21.4)	53.6 (28.3)	66.9 (24.4)
Medium (1.0/0.0)	74.5 (2.06)	75.1 (1.94)	-	75.3 (2.67)	75.0 (1.91)	-
Medium (0.8/0.2)	73.4 (9.84)	74.2 (9.29)	59.0 (30.6)	75.0 (7.92)	74.6 (8.81)	56.6 (38.6)
Medium (0.5/0.5)	70.3 (18.2)	70.3 (18.2)	60.9 (28.1)	64.1 (27.0)	51.2 (28.9)	64.6 (27.9)
Small (1.0/0.0)	73.4 (3.63)	73.4 (3.63)	-	76.1 (3.92)	74.8 (4.47)	-
Small (0.8/0.2)	70.2 (19.6)	70.2 (19.6)	54.0 (30.3)	67.2 (25.4)	74.8 (9.46)	65.9 (29.5)
Small (0.5/0.5)	58.5 (26.1)	58.5 (26.1)	63.4 (27.5)	65.3 (30.9)	46.0 (31.0)	63.0 (30.5)

[a, b, c] Described in Table 1.

high, i.e. FD = 1.0. For CB QTL with FD = 0.6, position estimates were generally unbiased for large or medium QTL, but tended to be biased when QTL effects were small. Point estimates for HS QTL were least unbiased, i.e. biased toward the central position of the test chromosome, across all levels of QTL mode, size and FD. Generally, there were no significant differences in position estimates between the two mating designs for a given level of QTL mode, size and FD. However, for the large or medium dominance QTL with FD = 0.6, position estimates for dominant CB QTL tended to be less biased in the reciprocal cross than in the one-way cross, and vice versa for the small QTL (Table 3).

DISCUSSION

Our simulation results showed that the combined model had the greatest power to detect QTL when QTL segregated in the parental breeds with different allele frequencies in both one-way and reciprocal cross designs. Also, the complementary information that is exploited in the line-cross, half-sib and combined models can be used to obtain greater power to detect QTL and allows characterization of detected QTL in terms of their segregation within the parental breeds. These results are consistent with our previous simulation study, in which greater power of the CB model over the LC and HS models was observed when QTL alleles segregated within the grandparental breeds at different frequencies (Kim et al., 2005a). This provides valuable information for subsequent QTL analyses and marker-assisted breeding programs.

In this study, however, we used different simulation approaches from those used previously (Kim et al., 2005a), in that a reciprocal cross scheme was considered to evaluate detection and characterization of QTL. Our simulation results can be summarized as follows: when QTL are segregating within parental breeds with different allele frequencies, 1) a greater proportion of detected QTL were classified as CB QTL in the reciprocal mating design, and 2) more accurate and precise estimates of CB QTL effects were found in the reciprocal cross, especially for dominance QTL.

In contrast, under the one-way cross design, a lower proportion of detected QTL was classified as CB QTL when QTL have segregating alleles within parental breeds (Tables 1 and 2). Most QTL studies in swine have been performed with two breeds, i.e. individuals of one breed as grandsires and those of another breed as grand-dams are crossed to generate F_1 and F_2 offspring (Bidanel and Rothschild, 2002; Kim et al., 2005b; Yang et al., 2005). Also, a small number of F_1 sires have been used in porcine QTL mapping populations, which may bias the selection of F_1 sires, i.e. genetic materials of parental breeds are not randomly transmitted to F_2 progeny due to sampling effects of F_1 sires. This would render distribution of QTL alternate alleles in unexpected patterns (e.g. close to allele fixation or evenly distributed) in F_2 progeny, causing a smaller proportion of detected QTL to be classified as CB QTL, when QTL alleles segregate with different frequencies in parental

breeds. However, the reciprocal cross, in which F_1s are sired or dammed by both breeds, could offset non-random transmissions of alternate alleles to F_2 offspring, resulting in a greater proportion of QTL that are declared CB QTL under the different allele frequencies in the parental breeds.

Our simulation results suggest that implementation of reciprocal cross designs better characterizes QTL (as CB QTL) in terms of allele frequencies in parental breeds, and allows more accurate and precise estimates of QTL effects for the CB QTL when QTL alleles are segregating within the parental breeds.

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