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Combined line-cross and half-sib QTL analysis of crosses between outbred lines

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Summary

Data from an F_2 cross between breeds of livestock are typically analysed by least squares line-cross or half-sib models to detect quantitative trait loci (QTL) that differ between or segregate within breeds. These models can also be combined to increase power to detect QTL, while maintaining the computational efficiency of least squares. Tests between models allow QTL to be characterized into those that are fixed (LC QTL), or segregating at similar (HS QTL) or different (CB QTL) frequencies in parental breeds. To evaluate power of the combined model, data wih various differences in QTL allele frequencies (FD) between parental breeds were simulated. Use of all models increased power to detect QTL. The line-cross model was the most powerful model to detect QTL for FD > 0·6. The combined and half-sib models had similar power for FD < 0·4. The proportion of detected QTL declared as LC QTL decreased with FD. The opposite was observed for HS QTL. The proportion of CB QTL decreased as FD deviated from 0·5. Accuracy of map position tended to be greatest for CB QTL. Models were applied to a cross of Berkshire and Yorkshire pig breeds and revealed 160 (40) QTL at the 5% chromosome (genome)-wise level for the 39 growth, carcass composition and quality traits, of which 72, 54, and 34 were declared as LC, HS and CB QTL. Fourteen CB QTL were detected only by the combined model. Thus, the combined model can increase power to detect QTL and mapping accuracy and enable characterization of QTL that segregate within breeds.

1. Introduction

Quantitative trait loci (QTL) mapping by exploiting linkage disequilibrium between breeds or within families is routinely practised in experimental or structured populations of livestock species (Andersson, 2001). The two models that have been most extensively applied for 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 generally used for three-generation breed crosses to detect QTL that differ between breeds. Half-sib designs are used to detect QTL that segregate within a commercial breed, utilizing the paternal half-sib family structure that often exists in such breeds, e.g. Holstein dairy cattle (Kim & Park, 2001). The line-cross model is most powerful when the QTL are fixed for alternate alleles in the parental breeds and power decreases as allele frequencies in the parental breeds become similar (Alfonso & Haley, 1998). Half-sib QTL analysis can also be applied to three-generation line-cross populations if F_1 sire families of adequate size are present in the F_2 generation, as suggested by de Koning *et al.* (2001). Unlike line-cross analyses, half-sib analysis can detect QTL for which the parental breeds have similar frequencies (de Koning *et al.*, 2001; Kim *et al.*, 2003; Quintanilla *et al.*, 2003).

Perez-Enciso & Varona (2000) presented a mixed model approach for QTL detection in breed crosses. Such models consider both between-breed differences in QTL frequencies and segregation of QTL within parental breeds, utilizing segregation of QTL within half-sib and full-sib families in the hierarchical mating

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designs that are often the basis of F_2 populations. These methods are, however, computationally demanding.

The first objective of this study was to develop and implement a least-squares regression interval mapping method that combines the main sources of information for QTL detection in an F_2 cross between outbred breeds, i.e. the line-cross and half-sib model. The second objective was to use the combined model, along with the half-sib and line-cross models, to develop and evaluate tests to determine the extent to which frequencies of detected QTL differ between the parental breeds. This information is important for the use of detected QTL in follow-up studies and in marker-assisted selection or introgression programmes. Our final objective was to apply the developed methods to detect and characterize QTL for growth, carcass composition and meat quality in a cross between two commercial breeds of pigs.

2. Materials and methods

(i) *QTL analysis models*

Derivation of a combined model for QTL mapping in an F_2 cross between two outbred breeds (1 and 2) was based on the framework of line-cross and half-sib least-squares regression interval mapping models (Haley *et al*., 1994; Knott *et al*., 1996). The following models were defined and fitted at each 1 cM position:

Line-cross model (LC):

$$y_{ij} = \mathbf{X}_{ij}\mathbf{b} + s_i + aP_{aij} + dP_{dij} + e_{ij}$$

Half-sib model (HS): $y_{ij} = \mathbf{X}_{ij}\mathbf{b} + s_i + \alpha_{HSi}P_{Sij} + e_{ij}$

Combined model (CB):

$$y_{ij} = \mathbf{X}_{ij}\mathbf{b} + s_i + aP_{aij} + dP_{dij} + \alpha_{CBi}P_{Sij} + e_{ij}$$

where y_{ij} is the phenotype on F_2 progeny j of F_1 sire i, $\mathbf{X}_{ij}$ and $\mathbf{b}$ are the design vector 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 the LC and CB models, following Haley *et al*. (1994), coefficients a and d are the additive and dominance effects of breed-origin alleles at a putative QTL at the fitted position and P_{aij} and P_{dij} are the corresponding breed-origin coefficients. In the HS and CB models, 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 the one versus the other QTL allele from its F_1 sire, following Knott *et al*. (1996). In the CB model, a and d account for the average effects of alleles obtained from the parental breeds through the sire and the dam, which depend on the difference in QTL allele frequencies between the parental breeds, similar to the LC model (Alfonso & Haley, 1998). In contrast, substitution effects α_{CBi} model the difference between the two QTL alleles that a given F_1 sire received from the two parental breeds as a deviation from their average additive effect, thereby allowing QTL alleles received from the parental breeds to differ between sires. Compared with the HS model, effects a and d in the CB model account for average effects of breed-origin alleles through both the F_1 sire and the F_1 dam. Expectations of QTL effects under the three models and their dependence on differences in QTL allele frequencies in the parental breeds are derived in the Appendix.

All three models were fitted across the genome 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 is segregating in F_0 parents from the two breeds at similar frequency (HS QTL), or (3) the QTL is segregating in F_0 parents from the two breeds but at different frequency (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:

(1) LC QTL: the QTL is detected under the LC model, but the CB is not significant over the LC model. This test was based on the following test statistic at the most likely position under the LC model,

$$LOF_{LC} = [(RSS_{LC} - RSS_{CB})/(df_{LC} - df_{CB})]/ \times [RSS_{CB}/df_{CB}],$$

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

(2) HS QTL: the QTL is detected under the HS model, not significant under the LC model, and the CB model is not significant over the HS model based on the following test statistic at the most likely position under the HS model:

$$LOF_{HS} = [(RSS_{HS} - RSS_{CB})/(df_{HS} - df_{CB})]/ \times [RSS_{CB}/df_{CB}].$$

(3) CB QTL: the QTL is detected with the CB model but cannot be defined as a 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.

(ii) *Simulation*

To validate the models and tests, and to evaluate their power and ability to distinguish alternative QTL types, F_2 populations were simulated based on two designs that are relevant to experimental pig QTL mapping populations (Bidanel & Rothschild, 2002). Design I mimicked the Berkshire and Yorkshire F_2 cross described in Malek *et al.* (2001*a*) as part of the current study (see later). The simulated design comprised 2 F_0 grandsires of one breed and 10 F_0 grand-dams of another breed, to generate 10 F_1 offspring per dam. Eight F_1 sires and 32 F_1 dams were randomly chosen to produce 16 F_2 offspring per F_1 dam, for a total of 512 F_2 offspring. The second design was based on a larger number of parents, with 20 F_0 sires and 80 F_0 dams with 5 offspring per dam. A total of 19 F_1 sires and 57 F_1 dams were randomly chosen to produce 513 F_2 progeny (9 per full-sib family). A chromosome of 100 cM was simulated with 11 markers at 10 cM intervals. Markers were simulated with four alleles with frequencies 0·6, 0·2, 0·1, 0·1 in one breed and 0·1, 0·1, 0·2, 0·6 in the other breed, following previous simulations (Zhao *et al.*, 2003) that were designed to mimic marker information content of the Berkshire and Yorkshire cross (Malek *et al.*, 2001*a*). An additive biallelic QTL with an additive effect (a_Q) 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% (large), 12·5% (medium) or 5·1% (small) of the phenotypic variance for the quantitative trait. A QTL with complete dominance ($a_Q = d_Q$) was also simulated. Using the same residual variances as for the additive QTL, the dominant QTL explained 41·4%, 17·7%, or 7·5% of the phenotypic variance.

The QTL genotypes for the F_0 parents were drawn using six alternative sets of frequencies of the favourable QTL allele in the two parental breeds: 1·0/0·0, 0·9/0·1, 0·8/0·2, 0·7/0·3, 0·6/0·4 and 0·5/0·5. One thousand replicates were generated for each set of QTL allele frequencies. Thresholds at the 5% chromosome-wise level for QTL detection for the three models were derived from 3000 replicates with QTL effects set to zero.

(iii) *Application to mapping QTL for pig growth, composition and meat quality*

The LC, HS and CB models and lack of fit tests were used to detect and characterize QTL for 39 growth, body composition and carcass quality traits in a cross between pigs from two commercial breeds, the Berkshire and Yorkshire breeds. The three-generation resource family structure and traits were described in detail in Malek *et al.* (2001*a*, *b*). Genotypes for 183 genetic markers, mainly microsatellites, were used (Thomsen *et al.*, 2004). Linkage maps were constructed using Crimap version 2.4 (Green *et al.*, 1990), by using the flips and all options to get the best order. In addition to the fixed effects and covariates described by Malek *et al.* (2001*a*, *b*) for a LC analysis, the fixed effect of F_1 sire was included in all models. For QTL detection, empirical chromosome-wise (ChW) significance levels were obtained for each model and trait using 10 000 permutations. Random shuffling of marker genotypes was restricted to within each F_1 sire family for the HS and CB analyses. Genome-wise (GW) significance levels were obtained following de Koning *et al.* (2001) as:

$$P_{GW} = 1 - (1 - P_{ChW})^{1/r}$$

where r is the proportion of total genome length attributed to the chromosome. Multiple QTL were declared on a chromosome if significant effects were separated by at least 40 (30) cM for QTL significant at the 5% ChW (GW) level.

3. Results

(i) *Power to detect QTL*

Fig. 1 presents power to detect an additive QTL, as a function of the absolute difference, FD, of the frequency of alternate alleles between the F_0 grandsires and the F_0 grand-dams for each replicate. Note that FD = 0 if the frequency of Q among the generated F_0 grandsires was the same as its frequency among F_0 grand-dams and FD = 1 if all F_0 grandsires were QQ and all F_0 grand-dams qq (or vice versa). Although data were simulated using six sets of allele frequencies, resulting in distinct expected values for FD, sampling from these populations resulted in a nearly continuous distribution of FD in the simulated F_0 grandparents. This distribution is also summarized in Fig. 1.

The LC model had greater power to detect the QTL than the HS or CB model, when alternate QTL alleles were fixed in F_0 parents (FD = 1), especially for the QTL of medium or small effect (Fig. 1), because it explains all QTL variation with the smallest number of degrees of freedom; the HS model was least powerful for this case because it uses more degrees of freedom and only considers segregation of the QTL through F_1 sires. However, power of the LC model decreased with FD, consistent with results of Alfonso & Haley (1998), because the LC model contrasts the effects of average QTL alleles derived from the two parental breeds. This was confirmed by the decline in the proportion of variance explained by LC QTL as FD declined (Table 1). Nevertheless, power of the LC model remained as high as 70% for the medium-sized QTL (explaining 13% of phenotypic variance) and >35% for the small QTL (explaining 5% of phenotypic variance), even when FD was as low as 0·5.

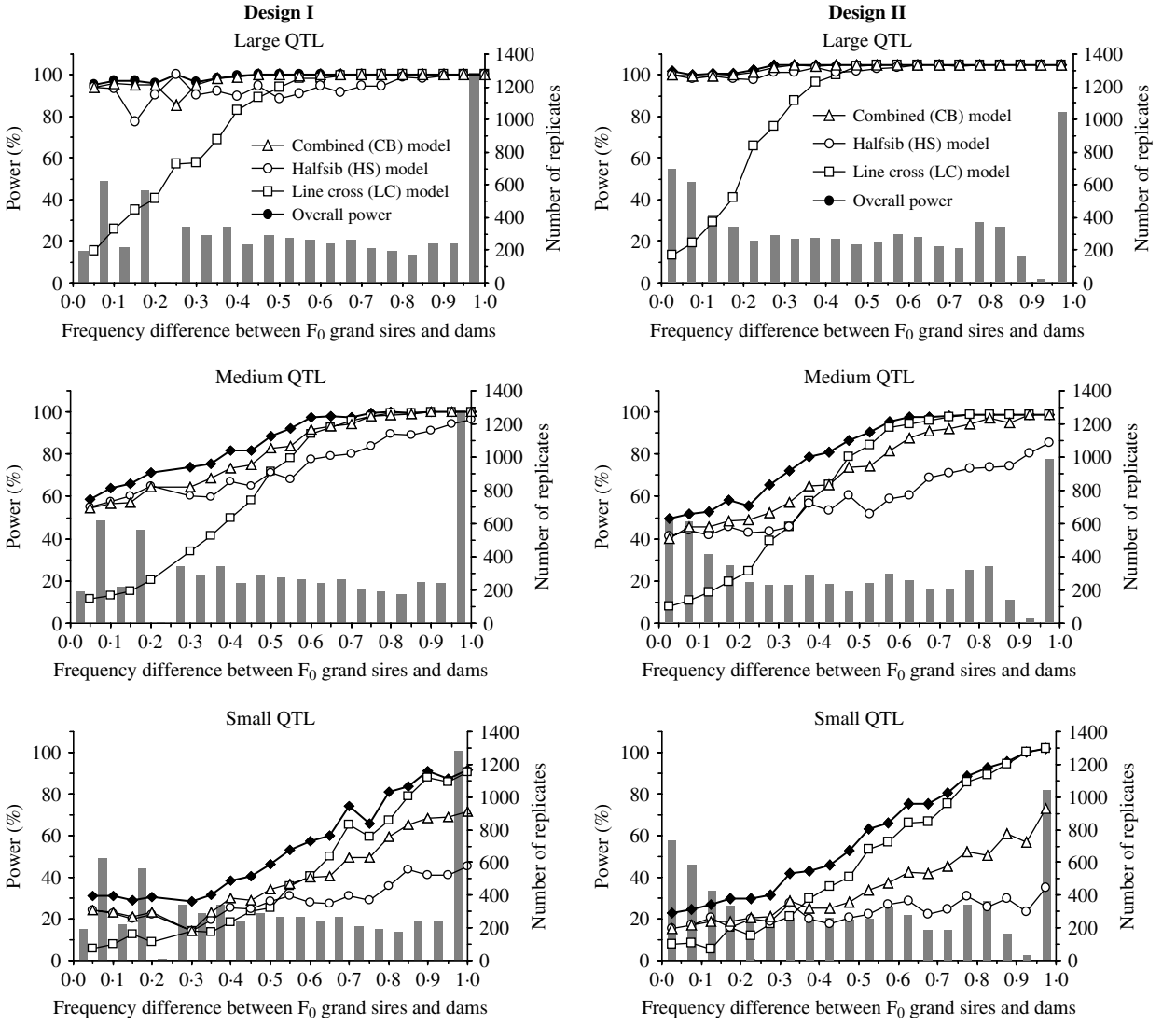

Fig. 1. Power to detect a large, medium or small additive QTL (a = 0·8, 0·5 or 0·32 phenotypic standard deviations) using the line-cross (LC), half-sib (HS) and combined (CB) models, and using all three models (overall power), as a function of the difference in frequency of QTL alleles between F_0 grandsires and grand-dams in the simulated mating designs with a small (design I) and larger (design II) number of F_0 and F_1 parents. Bars indicate the number of replicates that had a given frequency difference.

These results explain why several studies have found QTL detected by LC analysis to be segregating within the parental breeds in subsequent within-breed analyses (Evans *et al*., 2003; Nagamine *et al*., 2003).

The HS model had lower power than the LC model when alternate QTL alleles were fixed in the parental breeds but maintained power to detect the QTL when allele frequencies were similar (FD = 0) in the parental breeds (Fig. 1). This is because, for the simulated allele frequencies, a substantial proportion of the F_1 sires remained heterozygous for the QTL when FD = 0 (Table 1), albeit that the favourable QTL allele may have been derived from alternate breeds from one sire to the next. In general, the CB model had power that was intermediate to power of the LC and HS models for FD > 0·5, greater power for 0·2 < FD < 0·5 (for moderate QTL), and similar or slightly lower power than the HS model for FD < 0·2 (Fig. 1).

In general, power to detect QTL using the LC model was similar for the two designs (Fig. 1). However, for moderate and small QTL, power of the HS model was lower for design II than design I, because of the larger number of F_1 sires and smaller family size. Power to detect a dominant QTL for different allele frequencies showed similar patterns as for an additive QTL (results not shown). However, power was up to 15% (18%) greater for the dominant than additive QTL under the LC and CB models in design I (II) when QTL size was small and alternate alleles were intermediate or fixed (FD > 0·5). Also, the CB and HS models had up to 10% (7%) greater power for dominant QTL of moderate or small size in design

Table 1. *Estimates of QTL effects and proportion of phenotypic variances explained by additive QTL declared as line-cross (LC), half-sib (HS) or combined (CB) QTL, depending on the difference in allele frequencies between F_0 sires and dams in F_2 data simulated based on design I*[a]

Allele frequency difference (FD)[b]	Additive effect[c]				% of F_2 variance explained[d]						Allele substitution effect[e]	
	LC QTL		CB QTL		LC QTL		HS QTL		CB QTL			
	Expectation	Mean estimate	Expectation	Mean estimate	Estimate	Expected	Estimate	Expected	Estimate	Expected	HS QTL	CB QTL
Large QTL ($a=0{\cdot}8\ \sigma_p$[f])												
0·0–0·2	0·11	0·07 (0·19)	0·10	0·03 (0·22)	3·3	0·6	9·2	7·6	11·2	8·3	0·83 (0·11)	0·88 (0·11)
0·2–0·4	0·24	0·15 (0·25)	0·25	0·13 (0·26)	4·9	3·0	9·1	8·1	12·2	10·7	0·82 (0·12)	0·91 (0·12)
0·4–0·6	0·39	0·32 (0·30)	0·38	0·31 (0·25)	9·9	7·9	9·8	9·3	14·9	13·0	0·84 (0·11)	0·98 (0·13)
0·6–0·8	0·55	0·56 (0·22)	0·53	0·50 (0·18)	17·1	16·3	–	–	18·8	17·8	–	1·07 (0·13)
0·8–1·0	0·78	0·78 (0·06)	0·71	0·71 (0·10)	27·0	31·6	–	–	25·6	28·4	–	1·16 (0·16)
Medium QTL ($a=0{\cdot}5\ \sigma_p$)												
0·0–0·2	0·06	0·04 (0·19)	0·06	0·05 (0·20)	2·7	0·2	5·8	3·0	7·1	3·2	0·74 (0·08)	0·76 (0·09)
0·2–0·4	0·16	0·11 (0·21)	0·16	0·11 (0·23)	3·4	1·3	5·8	3·2	7·5	4·2	0·73 (0·08)	0·80 (0·11)
0·4–0·6	0·24	0·22 (0·19)	0·24	0·23 (0·19)	4·3	3·0	5·7	3·6	8·4	5·0	0·74 (0·08)	0·82 (0·11)
0·6–0·8	0·33	0·33 (0·14)	0·33	0·33 (0·16)	6·3	5·7	5·1	4·2	9·8	6·5	0·79 (0·08)	0·87 (0·13)
0·8–1·0	0·48	0·48 (0·07)	0·45	0·46 (0·11)	10·6	11·4	–	–	13·0	10·2	–	0·96 (0·13)
Small QTL ($a=0{\cdot}32\ \sigma_p$)												
0·0–0·2	0·04	0·01 (0·18)	0·03	0·01 (0·19)	2·6	0·1	5·1	1·2	5·7	1·3	0·72 (0·08)	0·72 (0·08)
0·2–0·4	0·10	0·08 (0·20)	0·10	0·09 (0·20)	2·8	0·6	5·0	1·3	6·2	1·8	0·73 (0·08)	0·76 (0·09)
0·4–0·6	0·16	0·20 (0·13)	0·15	0·17 (0·17)	3·1	1·3	4·9	1·5	6·3	2·1	0·71 (0·08)	0·76 (0·09)
0·6–0·8	0·22	0·25 (0·10)	0·22	0·22 (0·14)	3·5	2·3	5·1	1·8	6·8	2·8	0·73 (0·07)	0·79 (0·11)
0·8–1·0	0·31	0·32 (0·06)	0·30	0·31 (0·10)	4·9	4·6	4·6	2·2	8·0	4·4	0·70 (0·04)	0·84 (0·10)

[a] Two F_0 grand sires of one breed and 10 F_0 grand dams of another breed generate 10 F_1 offspring per dam. Eight F_1 sires and 32 F_1 dams are randomly chosen to produce 16 F_2 offspring per F_1 dam, for a total of 512 F_2 offspring.

[b] QTL allele frequency difference between F_0 grandparents from the two breeds.

[c] Mean (and standard deviation) of estimated additive effects for replicates with a declared line-cross (LC) or combined (CB) QTL. Expected values are functions of the observed allele frequency difference and true QTL effects for the corresponding replicates (additive: $\Delta f a = |p_1 - p_2|a$) where p_1 and p_2 are allele frequencies of the Q allele in breeds A and B, respectively). Each estimate is a weighted average of realized replicates with different allele frequencies within the defined allele frequency difference range.

[d] Expected proportion of phenotypic variances due to the QTL were obtained for each type of QTL as described in the Appendix. Estimates were based on reductions in residual sum of squares (*RSS*) from the models with or without fitting QTL in the LC, HS and CB models ($V_{QTL} = (RSS_{noQTL} - RSS_{QTL})/RSS_{noQTL}$). Each estimate is a weighted average of realized replicates within the defined FD range.

[e] Mean (and standard deviation) of absolute value of estimates of allele substitution effects in families with significant QTL evidence at a 5% comparison-wise level for HS or CB QTL. For CB QTL, the effect for each F_1 sire was the sum of estimates of the LC additive and the HS allele substitution effects. Expected allele substitution effects are equal to the additive effect, assuming equal QTL allele frequencies in the F_2.

[f] Standardized QTL effect, such that additive QTL with $a=0{\cdot}8$, 0·5 and 0·32 σ_p explained 32%, 12·5% and 5·1% of phenotypic variance.

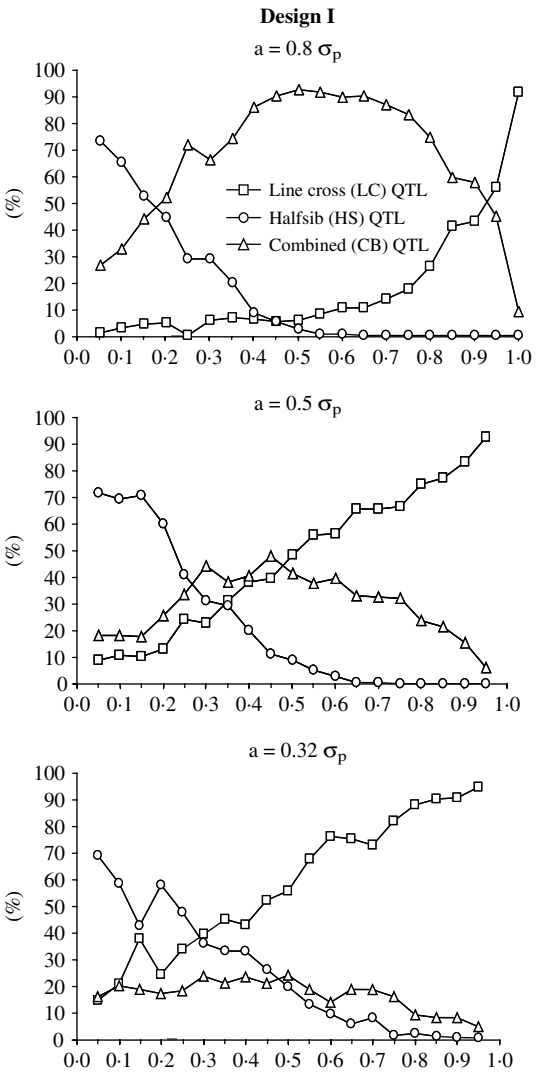

Fig. 2. Proportion (%) of QTL that are declared as line-cross, half-sib or combined QTL for simulated replicates with QTL evidence at the 5% chromosome-wise level as a function of the frequency difference of alternate alleles in F_0 grandparents and for QTL with large, medium and small additive effects (a = 0·8, 0·5 and 0·32 phenotypic standard deviations) for mating design I.

I (II) when allele frequencies were similar (FD < 0·2) than for additive QTL (results not shown).

(ii) *QTL characterization*

The QTL that were declared significant under at least one model were further characterized into LC, HS and CB QTL, using the lack of fit tests described. Fig. 2 shows the results of these tests based on analysis of simulated data for an additive QTL for design I. Results were very similar for design II and for dominant QTL (results not shown). When alternate QTL alleles were fixed in the F_0 parents (FD = 1), most (>90%) of the detected QTL were defined as LC QTL, regardless of QTL size, mode of gene action and design. The proportion of LC QTL decreased nearly linearly with FD and was less than 10%, 10% and 20% for the large, medium and small additive QTL, respectively, when FD = 0. The proportion of QTL that were characterized as HS QTL followed an opposite pattern to LC QTL: the proportion of HS QTL of any effect was high (>70%) when FD = 0 and decreased as FD increased (Fig. 2). The proportion of HS QTL was nearly zero for FD greater than 0·5 and 0·7 for the large and medium additive QTL, respectively. The proportion of detected QTL declared as CB QTL was greatest for intermediate FD and declined as FD moved to 0 or 1 (Fig. 2). The proportion of CB QTL at intermediate FD was greatest for the large QTL (90% at FD = 0·5) and nearly constant across FD for the small QTL (Fig. 2).

(iii) *Estimates of QTL effects*

Expectations and means of estimates of additive effects of QTL that were declared as LC and CB QTL are in Tables 1 and 2 for the two designs. Expectations of breed cross additive effects of the QTL decreased proportional to FD. Mean estimates were generally similar to their expectation for FD > 0·4, but estimates of additive effect were biased downward for small FD (Tables 1, 2). This bias resulted from negative estimates of QTL effects offsetting positive estimates. Estimates of dominance effects for LC and CB QTL generally followed their expected values across designs, QTL sizes and values of FD (results not shown).

For HS QTL, significant estimates of allele substitution effects were nearly unbiased or slightly biased upward for the large additive QTL, for which the HS model had greatest power (Table 1). Estimates became, however, severely biased upward as power decreased with decreasing QTL effects and a reduction in family size (design II compared with design I). For the same FD, estimates of allele substitution effects tended to be slightly larger for CB QTL than for HS QTL of moderate or small magnitude. Also, dominant QTL had slightly larger estimates of allele substitution effects than additive QTL at the same FD (results not shown), although expected substitution effects were equal, assuming QTL allele frequencies in the F_2 were 0·5.

The expectation and mean estimated proportions of phenotypic variance in the F_2 that were explained by significant LC, HS or CB QTL are also shown in Tables 1 and 2. For all models, the expected proportion of phenotypic variance explained by the QTL decreased with FD. However, the decrease was more pronounced for the LC model than for the HS and CB models, which reflects the large decrease of power to detect LC QTL as FD decreased (Fig. 1). When FD

Table 2. *Estimates of QTL effects and proportion of phenotypic variances explained by additive QTL declared as line-cross (LC), half-sib (HS) or combined (CB) QTL, depending on the difference in allele frequencies between F_0 sires and dams in F_2 data simulated for design II*[a]

Allele frequency difference (FD)[b]	Additive effect[c]				% of F_2 variance explained[d]						Allele substitution effect[e]	
	LC QTL		CB QTL		LC QTL		HS QTL		CB QTL			
	Expectation	Mean estimate	Expectation	Mean estimate	Estimate	Expected	Estimate	Expected	Estimate	Expected	HS QTL	CB QTL
Large QTL ($a=0{\cdot}8\ \sigma_p$[f])												
0·0–0·2	0·08	0·04 (0·18)	0·08	0·05 (0·18)	2·7	0·4	11·8	8·0	13·5	8·3	1·09 (0·09)	1·12 (0·10)
0·2–0·4	0·24	0·22 (0·12)	0·24	0·28 (0·12)	4·0	2·7	11·6	8·5	14·9	9·6	1·09 (0·09)	1·14 (0·10)
0·4–0·6	0·41	0·43 (0·08)	0·41	0·40 (0·11)	9·9	8·8	11·4	9·4	17·6	12·6	1·14 (0·05)	1·19 (0·10)
0·6–0·8	0·57	0·60 (0·07)	0·57	0·56 (0·11)	17·5	17·0	–	–	22·5	17·8	–	1·29 (0·11)
0·8–1·0	0·77	0·77 (0·06)	0·69	0·68 (0·09)	27·1	30·0	–	–	27·2	24·2	–	1·42 (0·11)
Medium QTL ($a=0{\cdot}5\ \sigma_p$)												
0·0–0·2	0·05	0·06 (0·17)	0·05	0·06 (0·18)	2·6	0·2	8·9	3·1	9·6	3·3	1·08 (0·09)	1·08 (0·09)
0·2–0·4	0·16	0·23 (0·07)	0·16	0·21 (0·11)	3·2	1·3	8·9	3·4	10·5	3·8	1·09 (0·09)	1·10 (0·09)
0·4–0·6	0·26	0·28 (0·06)	0·26	0·27 (0·10)	4·3	3·3	8·8	3·9	11·4	4·9	1·08 (0·08)	1·13 (0·10)
0·6–0·8	0·35	0·36 (0·07)	0·35	0·37 (0·10)	6·5	6·3	8·4	4·4	13·1	6·9	1·10 (0·08)	1·17 (0·11)
0·8–1·0	0·48	0·48 (0·07)	0·45	0·42 (0·11)	10·5	11·4	–	–	15·8	10·2	–	1·22 (0·10)
Small QTL ($a=0{\cdot}32\ \sigma_p$)												
0·0–0·2	0·03	0·04 (0·15)	0·03	0·00 (0·17)	2·5	0·1	8·4	1·3	8·9	1·3	1·10 (0·10)	1·08 (0·10)
0·2–0·4	0·10	0·20 (0·09)	0·10	0·14 (0·13)	2·8	0·5	8·6	1·4	9·3	1·6	1·09 (0·10)	1·13 (0·09)
0·4–0·6	0·16	0·23 (0·05)	0·16	0·23 (0·10)	3·1	1·4	8·4	1·6	9·6	2·0	1·09 (0·09)	1·11 (0·10)
0·6–0·8	0·23	0·26 (0·06)	0·23	0·23 (0·12)	3·6	2·6	8·3	1·9	10·3	2·9	1·09 (0·08)	1·13 (0·09)
0·8–1·0	0·30	0·32 (0·06)	0·30	0·32 (0·12)	4·9	4·6	8·3	2·2	11·3	4·4	1·19 (0·04)	1·17 (0·11)

[a] Twenty F_0 grandsires of one breed and 80 F_0 grand-dams of another breed generate 5 F_1 offspring per dam. Nineteen F_1 sires and 57 F_1 dams were randomly chosen to produce 9 F_2 offspring per F_1 dam, for a total of 513 F_2 offspring.

[b,c,d,e,f] Described in Table 1.

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 allele frequencies between* F_0 *sires and dams in simulated data for an* F_2 *breed cross under two alternate designs with an additive QTL of different magnitude at 75 cM*

Allele frequency difference (FD)[a]	Design I[b]			Design II[b]		
	LC QTL	HS QTL	CB QTL	LC QTL	HS QTL	CB QTL
Large QTL ($a=0{\cdot}8\ \sigma_p$[c])						
0·0–0·2	55·2 (28·3)	74·5 (9·3)	75·2 (8·2)	42·9 (31·4)	74·4 (8·1)	74·5 (7·2)
0·2–0·4	67·6 (20·4)	74·7 (11·7)	74·7 (5·7)	65·2 (23·3)	74·1 (7·3)	74·6 (5·6)
0·4–0·6	73·3 (9·8)	75·6 (6·9)	75·0 (3·6)	75·6 (8·3)	77·9 (9·1)	75·0 (4·1)
0·6–0·8	74·8 (3·1)	–	74·9 (2·7)	74·7 (2·4)	–	75·2 (2·9)
0·8–1·0	74·9 (1·7)	–	75·2 (2·0)	74·9 (1·6)	–	74·9 (2·1)
Medium QTL ($a=0{\cdot}5\ \sigma_p$)						
0·0–0·2	65·9 (26·3)	73·2 (13·0)	72·5 (16·9)	55·7 (28·3)	70·4 (19·3)	73·6 (17·1)
0·2–0·4	68·2 (20·5)	71·4 (17·2)	74·1 (11·7)	69·7 (19·5)	68·6 (19·2)	73·3 (12·8)
0·4–0·6	72·6 (12·9)	74·5 (11·2)	73·9 (9·7)	72·8 (12·9)	74·6 (11·8)	73·8 (10·6)
0·6–0·8	74·6 (9·5)	72·0 (4·7)	74·8 (6·5)	74·5 (7·6)	72·5 (0·5)	75·9 (6·9)
0·8–1·0	74·9 (4·0)	–	75·6 (5·1)	74·8 (3·8)	–	75·6 (5·0)
Small QTL ($a=0{\cdot}32\ \sigma_p$)						
0·0–0·2	58·8 (25·1)	66·8 (22·9)	65·4 (25·6)	53·9 (30·8)	62·2 (27·5)	60·6 (25·9)
0·2–0·4	65·9 (21·3)	68·1 (22·1)	68·9 (21·3)	64·1 (22·2)	63·0 (27·2)	69·9 (20·1)
0·4–0·6	71·2 (18·3)	71·0 (19·9)	71·3 (15·6)	69·9 (19·4)	63·1 (21·0)	73·7 (14·8)
0·6–0·8	72·6 (14·2)	70·9 (20·1)	72·5 (12·6)	73·4 (13·6)	66·8 (23·1)	73·8 (12·4)
0·8–1·0	74·3 (8·8)	49·1 (19·5)	75·0 (7·9)	74·6 (8·8)	59·0 (3·7)	72·2 (12·5)

[a] QTL allele frequency differences (FD) in F_0 parental breeds (see Table 1).
[b] In design I, 2 F_0 grandsires of one breed and 10 F_0 grand-dams of another breed generate 10 F_1 offspring per dam. Eight F_1 sires and 32 F_1 dams are randomly chosen to produce 16 F_2 offspring per F_1 dam, for a total of 512 F_2 offspring. In design II, 20 F_0 grandsires of one breed and 80 F_0 grand-dams of another breed generate 5 F_1 offspring per dam. Nineteen F_1 sires and 57 F_1 dams were randomly chosen to produce 9 F_2 offspring per F_1 dam, for a total of 513 F_2 offspring.
[c] Standardized QTL effect, such that the additive QTL with $a=0{\cdot}8$, 0·5 and 0·32 σ_p explained 32%, 12·5% and 5·1% of phenotypic variance.

was intermediate, the QTL that were detected in the CB model or that were classified as CB QTL had the largest expected and estimated variance, reflecting the fact that the CB model had greater power than the LC and HS models for intermediate FD (Fig. 1).

In general, mean estimated proportions of variance explained by the QTL obtained from residual sums of squares were biased upward, which was more pronounced for design II (Table 2) than design I (Table 1). Biases increased as power decreased for all models, i.e. with decreasing QTL effect and decreasing FD. These tendencies were the same for dominant QTL (results not shown).

Estimates of variance explained by the QTL can also be obtained by substituting estimates of QTL effects into the equations derived for the expected variance explained by the QTL. This resulted in estimates that were similar to those obtained based on RSS for LC QTL (less than 2 percentage points greater for most cases in Tables 1 and 2), but in overestimates for CB and HS QTL because of the errors in estimates of individual allele substitution effects (results not shown).

(iv) *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 close to being unbiased and had high precision (low standard deviation) when power to detect LC QTL was high, i.e. when FD was high. The QTL that were declared as HS QTL generally had close to unbiased position estimates, except for the small QTL, consistent with the need for sufficient power to obtain unbiased position estimates. Position estimates for CB QTL tended to be least biased across all levels of FD and QTL effects, except for the small QTL when FD was small. The CB QTL also tended to have the greatest mapping accuracy for a given level of FD. Similar results were obtained for the additive and dominant QTL (results not shown).

(v) *QTL results for the swine breed cross*

A total of 160 QTL for the 39 growth, carcass composition and quality traits were detected at the 5% ChW significance level for at least one of the three models. In many cases, QTL for several traits with

similar characteristics were found in the same chromosomal region. These may represent QTL with pleiotropic effects. Of the 160 QTL, 72, 54 and 34 QTL were declared as LC, HS and CB QTL, respectively. Fourteen QTL were detected only by the CB model. Forty QTL that were significant at the 5% GW significance level are summarized in Table 4. Of these, 16, 8, and 16 QTL were declared as LC, HS and CB QTL, respectively. The QTL at the 5% GW level explained from 3·5% to 13·3% of phenotypic variance. More detailed results on all QTL with ChW significance are in Dekkers *et al*. (2003).

4. Discussion

(i) *QTL detection method*

A least squares regression interval mapping model is presented that combines the power of QTL detection based on the line-cross (LC) and half-sib (HS) designs in F_2 crosses between outbred lines. These models can be implemented using existing software (e.g. Haley *et al*., 1994; Knott *et al*., 1996) and provide the flexibility to include alternate effects and genetic models and the computing efficiency that is associated with least squares linear model analyses. Our simulation studies and real data analyses show that the combined model based on least squares regression can increase power to detect QTL when QTL are segregating in the parental breeds. The complementary information that is capitalized on 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. This provides valuable information for subsequent QTL analyses and marker-assisted breeding schemes.

Musani & Jansen (2003) applied a similar combined model to detect QTL in a design where F_1 dams were backcrossed to purebred sires. In their design, the combined model capitalizes on two independent sources of information for QTL detection: linkage disequilibrium information between breeds from F_1 dams and disequilibrium within half-sib families from purebred sires that are heterozygous for the QTL. In an F_2 cross between outbred breeds, as considered in the present study, the line-cross and half-sib models are not independent, because linkage information from F_1 sires is used in both models. However, because the confounding is not complete, the combined model can result in an increase in power. Using simulation, we observed greater power of the CB over the LC or HS models when QTL alleles segregated within the grandparental breeds but at different frequencies, e.g. as high as 11% (10%) for the medium-size QTL in design I (II) (Fig. 1) when the difference in QTL allele frequencies between the F_0 parents from the two breeds (FD) was between 0·30 and 0·55. These results demonstrate that a single model does not provide greatest power for all QTL that can be encountered in a cross between outbred lines, but that all three models must be used to maximize power to detect QTL. The use of multiple models for analysis, as in the present study, does increase type I error rates beyond those set for each model individually. A Bonferroni correction of type I error rates to account for the use multiple models is too stringent, because of dependencies between the models. To maintain a desired type I error rate across the three models, one approach would be to adapt the permutation tests by applying all three models to the permuted data but saving only the test statistic from the most significant model. Significance thresholds for a given model would then be based only on test statistics for which it was the most significant model. This would reduce the overall power to detect QTL that is shown in Fig. 1.

(ii) *QTL type declaration*

A sequence of simple tests was developed and evaluated to characterize the QTL that were detected. In general, the ability to correctly characterize the QTL was limited, except when the QTL was close to being fixed for alternate alleles in the F_0 parents ($FD > 0{\cdot}9$, LC QTL) or segregating at similar frequencies ($FD < 0{\cdot}1$, HS QTL). For intermediate frequency differences ($0{\cdot}4 < FD < 0{\cdot}6$), the ability to correctly classify QTL as CB QTL was substantial only for QTL of large effect. The limited ability to correctly identify CB QTL may be related to the larger number of parameters that are fitted in the CB model and the fact that the lack of fit tests conducted will favour the model with the smaller number of parameters. Other lack of fit tests, such as information criterion tests that do not depend on nested models (Verbeke & Molenberghs, 2000), could be applied to overcome this problem. In general, the ability to characterize QTL was little affected by the number of F_0 and F_1 parents used (designs I and II in Fig. 2) but an increase in sample size did allow better declaration of CB QTL (results not shown). It must be noted, however, that conclusions drawn based on a design with larger numbers of randomly selected F_0 parents will be more reflective of the breed than a design with few parents.

The previous discussion, and results presented in Fig. 2, address the proportion of QTL that are declared as LS, HS or CB QTL for a given level of FD. In practice, however, it is not known what the true level of FD is. This raises the question of what conclusions can be drawn about segregation of QTL among the F_0 parents if a QTL is declared as being LC versus HS versus CB. The answer to this question

Table 4. *Most likely positions, F-statistic values and declared QTL types, estimated additive and dominance effects of QTL for growth, composition and meat quality traits that were detected at 5% genome-wise level*

Chromosome / Trait	QTL Position (cM)[a]	Flanking markers (cM)		*P* value[b]	QTL type[c]	QTL variance[d] (% of F_2)	Breed QTL effects[e] Additive	Dominance
SSC1								
Marbling	52	S0312 (52)	S0331 (65)	0·033*	CB	6·6	−0·11 (0·09)	0·26 (0·09)
Marbling	127	SW373 (105)	SW1301 (128)	0·003**	HS	5·1		
SSC2								
Tenth rib back fat (cm)	0	SW2443 (0)	SWC9 (1)	0·001**	CB	10·8	0·08 (0·09)	−0·05 (0·09)
Lumber back fat (cm)	2	SWC9 (1)	SW2623 (13)	0·001**	CB	11·8	0·15 (0·09)	−0·07 (0·09)
Last rib back fat (cm)	0	SW2443 (0)	SWC9 (1)	0·001**	CB	8·6	0·12 (0·09)	−0·04 (0·09)
Average back fat (cm)	0	SW2443 (0)	SWC9 (1)	0·001**	CB	13·3	0·14 (0·08)	−0·07 (0·09)
Loin eye area (cm^2)	1	SW2443 (0)	SWC9 (1)	0·001**	CB	10·0	0·04 (0·09)	0·10 (0·09)
Drip loss (%)	47	SW2445 (41)	SW1686 (64)	0·030*	CB	7·3	0·08 (0·10)	0·07 (0·12)
Off-flavor score	59	SW2445 (41)	SW1686 (64)	0·016*	LC	3·9	0·29 (0·07)	0·14 (0·11)
SSC4								
Carcass weight (kg)	140	SW58 (127)	SW1461 (147)	0·004**	LC	4·4	0·30 (0·06)	0·17 (0·11)
SSC5								
Lumber back fat (cm)	123	SW995 (118)	SW1954 (129)	0·020*	CB	6·3	0·38 (0·09)	0·21 (0·09)
Last rib back fat (cm)	124	SW995 (118)	SW1954 (129)	0·023*	LC	3·6	0·27 (0·06)	0·13 (0·09)
Average back fat (cm)	126	SW995 (118)	SW1954 (129)	0·045*	CB	5·7	0·36 (0·08)	0·12 (0·09)
SSC6								
Tenth rib back fat (cm)	134	SW322 (129)	SW2052 (152)	0·050*	CB	5·3	−0·30 (0·09)	0·20 (0·09)
24-hr Ham pH	50	SW1302 (44)	SWR1130 (55)	0·014*	LC	3·5	−0·14 (0·07)	0·36 (0·10)
SSC7								
Lumber back fat (cm)	59	S0064 (29)	SWR1928 (65)	0·001**	LC	6·1	0·36 (0·06)	−0·05 (0·09)
Lumber back fat (cm)	104	SW1083 (96)	S0101 (117)	0·001**	LC	4·5	0·33 (0·06)	−0·05 (0·11)
Last rib back fat (cm)	73	SWR1928 (65)	SW2040 (75)	0·021*	CB	6·4	0·36 (0·09)	−0·05 (0·10)
Average back fat (cm)	72	SWR1928 (65)	SW2040 (75)	0·004**	CB	7·3	0·41 (0·08)	−0·07 (0·10)
Average back fat (cm)	105	SW1083 (96)	S0101 (117)	0·001**	LC	5·1	0·32 (0·05)	−0·09 (0·11)
SSC8								
Carcass weight (kg)	48	SW1843 (38)	S0086 (48)	0·007**	CB	7·3	−0·12 (0·08)	0·34 (0·07)
Loin eye area (cm^2)	1	S0098 (0)	SWR1101 (25)	0·034*	HS	4·0		
SSC10								
Last rib back fat (cm)	79	SWR493 (79)	SW1626 (102)	0·045*	CB	5·9	0·31 (0·08)	−0·24 (0·10)
Star Probe Force (kg)	70	SW1991 (68)	SWR493 (79)	0·023*	LC	3·9	−0·29 (0·07)	−0·11 (0·11)
SSC11								
Color score	85	S0071 (44)	SW13 (85)	0·015*	HS	6·0		
Drip loss (%)	69	S0071 (44)	SW13 (85)	0·037*	HS	6·7		
SSC12								
24-hr Ham Minolta	44	SW874 (36)	S0090 (48)	0·026*	HS	6·0		
24-hr Ham Minolta	80	S0147 (63)	SWC23 (85)	0·004**	HS	6·5		
24-hr Ham Hunter	44	SW874 (36)	S0090 (48)	0·044*	HS	5·9		
24-hr Ham Hunter	80	S0147 (63)	SWC23 (85)	0·008**	HS	6·2		
SSC15								
48-hr Loin Minolta	72	SW120 (68)	RN (74)	0·001**	CB	8·2	−0·41 (0·09)	0·11 (0·09)
48-hr Loin Hunter	73	SW120 (68)	RN (74)	0·002**	CB	7·8	−0·40 (0·08)	0·12 (0·09)
24-hr Ham pH	81	SW936 (78)	SW1983 (89)	0·030*	LC	3·5	0·28 (0·07)	−0·09 (0·10)
24-hr Loin pH	84	SW936 (78)	SW1983 (89)	0·001**	LC	4·9	0·34 (0·07)	−0·03 (0·10)
48-hr Loin pH	44	SW964 (38)	SW1263 (53)	0·019*	LC	3·8	0·28 (0·07)	−0·21 (0·10)
48-hr Loin pH	73	SW120 (68)	RN (74)	0·032*	LC	3·5	0·27 (0·07)	−0·08 (0·09)
Glycogen (μmol/g)	71	SW120 (68)	RN (74)	0·033*	LC	3·6	−0·23 (0·07)	0·24 (0·10)
SSC17								
Color score	90	S0359 (67)	S0332 (92)	0·040*	LC	3·6	0·24 (0·07)	−0·20 (0·10)
48-hr Loin Minolta	90	S0359 (67)	S0332 (92)	0·018*	LC	4·2	−0·29 (0·07)	0·12 (0·10)
48-hr Loin Hunter	90	S0359 (67)	S0332 (92)	0·035*	LC	3·8	−0·27 (0·07)	0·11 (0·10)

[a] Position at which the F-statistic value for the QTL model was maximized, for which QTL type was declared.
[b] Genome-wise *P* value for the test statistic (Ho: no QTL model *vs* Ha: the QTL model with declared QTL type). * Significant at the 5% genome-wise level. ** Significant at the 1% genome-wise level.
[c] LC, for QTL declared as line-cross type, HS as half-sib type, CB as combined type.
[d] Proportion (%) of phenotypic variance explained by QTL $[(RSS_{noQTL} - RSS_{QTL}/RSS_{noQTL}]$, where RSS is residual sum of squares for the model with or without QTL.
[e] Estimates of additive and dominance effects with standard errors for LC or CB QTL, expressed in residual standard deviations.

Table 5. *Probability distribution of the difference in QTL allele frequency between F_0 parents (FD) in design I, given the declared QTL type of the detected QTL (LC[a], CB or HS) and the prior probability distribution of FD*

Probability	Prior probability	Large QTL			Medium QTL			Small QTL		
		LC	CB	HS	LC	CB	HS	LC	CB	HS
					Prob(FD = 1) = 0[b]					
FD < 0·25	44	30	26	83	16	27	67	14	31	55
0·25 < FD < 0·50	31	23	40	17	29	38	28	25	36	34
0·50 < FD < 0·75	19	23	27	0	37	28	5	40	25	10
FD > 0·75	6	24	7	0	18	6	0	22	8	1
					Prob(FD = 1) = 0·1					
FD < 0·25	39	14	25	83	12	27	67	9	29	55
0·25 < FD < 0·50	28	11	40	17	21	37	28	17	34	34
0·50 < FD < 0·75	17	11	27	0	27	28	5	27	24	10
FD > 0·75	16	64	8	0	41	9	0	47	13	1
					Prob(FD = 1) = 0·2					
FD < 0·25	35	9	25	83	9	26	67	7	27	55
0·25 < FD < 0·50	25	7	39	17	15	36	28	12	32	34
0·50 < FD < 0·75	15	7	26	0	20	27	5	19	22	10
FD > 0·75	25	78	10	0	56	11	0	63	18	2
					Prob(FD = 1) = 0·3					
FD < 0·25	31	6	24	83	6	25	67	5	25	55
0·25 < FD < 0·50	22	4	38	17	11	35	28	9	30	34
0·50 < FD < 0·75	13	4	26	0	15	26	5	14	21	10
FD > 0·75	34	85	12	0	67	15	0	73	24	2

[a] LC = line-cross QTL; CB = combined QTL; HS = half-sib QTL.
[b] The prior probability distribution of FD was assumed to originate from independent uniformly distributed QTL allele frequencies in the two parental breeds, but with an increase in the frequency of QTL that are fixed for alternate alleles in the two breeds (= Prob(FD = 1)).

depends on the distribution of FD between breeds, along with the power to detect QTL and the probability of declaring a given QTL type for a given level of FD. Specifically, using Bayes theorem, the probability distribution of FD when a QTL is detected and declared to be of type k (k = LC, HS or CB) is equal to:

$$f(\text{FD}|\text{QTL detected and type} = \text{k}) = \frac{f(\text{QTL type} = \text{k}|\text{FD, QTL detected})f(\text{QTL detected}|\text{FD})f(\text{FD})}{\sum_{\text{FD}} \{f(\text{QTL type} = \text{k}|\text{FD, QTL detected})f(\text{QTL detected}|\text{FD})f(\text{FD})\}}$$

where f(QTL type = k | FD, QTL detected) is given in Fig. 2, f(QTL detected | FD) is the overall power to detect a QTL, as given in Fig. 1, and f(FD) is the prior distribution of FD, which is unknown. Using four alternate prior distributions of FD that cover what might be expected in practice, the distribution of FD for QTL declared as LC, HS, or CB QTL in design I is given in Table 5. The first distribution of FD assumed that QTL frequencies were uniformly and independently distributed in the two parental breeds. This resulted in $f(\text{FD}) \sim 1 - \text{FD}$, which is a linearly declining function, with maximum density at FD = 0 and zero density at FD = 1. The other three distributions differed from this distribution only by an increase in the frequency at FD = 1 by 0·1, 0·2 and 0·3, respectively. These distributions of FD also assume a uniform distribution of allele frequencies, except for an increase in the proportion of QTL with frequencies 0 and 1, as would be expected based on random drift or selection (Falconer & Mackay, 1996), and when breeds that are used are divergent for the traits of interest.

Results in Table 5 show that most QTL declared as HS QTL are expected to have very similar QTL frequencies in the F_0 parents; the percentage of HS QTL that have FD < 0·25 was 83% for the large QTL and 55% for the small QTL. These percentages were not affected by the fixation probability of QTL in parental breeds because no HS QTL were declared for FD > 0·8 (Fig. 2). Most of the QTL declared to be LC QTL were indeed close to fixation in alternate breeds

(FD > 0·75), in particular if the prior probability of fixation of QTL was large. With no fixation of QTL in the parental breeds (Prob(FD = 1) = 0), probabilities for LC QTL were very similar for all four FD categories and there was little discriminatory power. Nevertheless, the probability of FD > 0·75 was substantially greater than its prior probability (24% versus 6%). In general, QTL declared to be CB QTL, had the greatest probability of having an FD between 0·25 and 0·75, substantially greater than their prior probabilities. Although probabilities for CB QTL to have FD < 0·25 or FD > 0·75 were lower than their prior probabilities, these probabilities were still substantial, in particular for FD < 0·25, and there was limited discriminatory power. The general conclusion from Table 5 is that classification of QTL into LC, HS and CB QTL conveys most information about breed QTL frequencies for QTL that are declared as HS QTL, some for LC QTL, but limited for CB QTL. Stronger discriminatory power is obviously expected for designs with larger numbers of F_2 progeny.

(iii) *Real data analysis*

Results from re-analysis of the Berkshire–Yorkshire swine breed cross confirm that application of the three models improves the ability to detect and characterize QTL by providing some information on the distribution of QTL alleles across the parental breeds.

Selection for fast growth and correspondingly low backfat thickness has been consistently implemented in the Yorkshire breed for the last several decades (Cameron, 1994). For several of the LC and CB QTL, however, the favourable allele originated from the Berkshire breed (Dekkers *et al*., 2003). Such cryptic QTL were also detected for several meat quality QTL, for which the Berkshire breed is expected to be superior. For example, for marbling, tenth rib backfat and Star probe force, Berkshires are expected to have higher scores (Malek *et al*., 2001*a*, *b*). However, for the three QTL that were detected for these traits on SSC1, SSC6 and SSC10, respectively, Berkshire alleles reduced quality (Table 3). The finding of such cryptic alleles, which has also been reported in other pig studies (de Koning *et al*., 1999; Moser *et al*., 1998; Rohrer & Keele, 1998*a*), indicates opportunities exist to select for increased performance in breed crosses.

Most LC and CB QTL reported in Table 4 were also detected in previous analyses of this population using the LC model (Malek *et al*., 2001*a*, *b*; Thomsen *et al*., 2004) and detailed results are discussed in those reports. Because of the inclusion of the F_1 sire in the LC model and consideration of the CB model, significance levels did change for several of the QTL compared with previous reports. The eight HS QTL that were detected at the 5% GW significance level (Table 3) were not reported in previous analyses of this population using the LC model (Malek *et al*., 2001*a*, *b*; Thomsen *et al*., 2004), or in other populations (Bidanel & Rothschild, 2002). Rohrer & Keele (1998*b*) did detect a QTL for loin eye area on SSC8 in a backcross population of Meishan and Large White crossbreds, but in a different region than the HS QTL for the same trait in this study (Table 4). The lack of the number of QTL in the previous reports that were detected in the chromosomal regions where the HS QTL were identified in this study may be partly due to the limited application of half-sib analyses.

The number (34) of CB QTL detected in this study was smaller than the number (54) of HS QTL, and much smaller than the number (72) of LC QTL detected (Dekkers *et al*., 2003). This limited number of CB QTL may be because of the limited power in declaring CB QTL when QTL effects are not large, even if the QTL allele frequencies may be in the best range (intermediate FD) to be classified as a CB QTL (see simulation results). Nevertheless, the finding of substantial numbers of HS and CB QTL suggests evidence of QTL that provide a source of genetic variation within breeds.

Appendix. Expected QTL effects and variance associated with the line-cross, half-sib and combined models

Let p_1 and p_2 and q_1 and q_2 be the frequencies of QTL alleles Q and q in breeds 1 and 2 that are used to develop the F_2 population and let a_Q and d_Q be the additive and dominance effects at the QTL, following Falconer & Mackay (1996). Under random mating, expected frequencies of Q and q in the F_2 are $p = (p_1 + p_2)/2$ and $q = (q_1 + q_2)/2$, respectively. Then, the additive QTL variance in the F_2 population is $V_A = 2pq\alpha_{Q^2}$, where α_Q is allele substitution effect, which is equal to $a_Q + d_Q(q - p)$, and the dominance QTL variance $V_D = (2pqd_Q)^2$. When the alternate QTL alleles are not fixed in the parental populations, expected estimates of additive and dominance effects under the line-cross (LC) model depend on the difference in QTL frequencies between the breeds ($\Delta f = p_1 - p_2 = q_2 - q_1$) and are $E(a_{LC}) = \Delta f a_Q$ and $E(d_{LC}) = \Delta f^2 d_Q$, respectively (de Koning *et al*., 2002). Then the expected estimate of the allele substitution effect is $E(\alpha_Q) = E(a_{LC}) + E(d_{LC})(q - p)$, and the expected QTL variance explained by the LC model is $V_{LC} = 0{\cdot}5(E(a_{LC}))^2 + 0{\cdot}25(E(d_{LC}))^2$.

For the half-sib (HS) model, only the progeny from heterozygous F_1 sires have an expected allele substitution effect different from zero and equal to $E(\alpha_{HS}) = a_Q + d_Q\,(q - p)$ for Qq F_1 sires (Q allele from breed 1) and $-E(\alpha_{HS})$ for qQ sires. The expected frequency of such sires is $E(f_H) = p_1q_2 + q_1p_2$. The

QTL variance explained by the HS model is $V_{HS} = 0{\cdot}25[E(\alpha_{HS})]^2 E(f_H)$.

For the combined (CB) model, QTL effects and variances for the LC components are the same as given above for the LC model. For F_1 sires, allele substitution effects in HS components are adjusted for effects explained by the LC components of the model. For Qq F_1 sires the adjusted allele substitution effect is $E(\alpha_{CB},Qq) = E(\alpha_{HS}) - [E(a_{LC}) + E(d_{LC})(q-p)]$, and for qQ F_1 sires the adjusted effect is $E(\alpha_{CB},qQ) = -E(\alpha_{HS}) - [E(a_{LC}) + E(d_{LC})(q-p)]$. For QQ and qq F_1 sires, adjusted allele substitution effects in the CB model are $E(\alpha_{CB},QQ) = E(\alpha_{CB},qq) = -[E(a_{LC}) + E(d_{LC})(q-p)]$, such that the sum of the substitution effect based on the LC component and the adjusted substitution effect is zero, and provides no contribution to the variance. Then, the total variance explained by the QTL in the CB model is $V_{CB} = V_{LC} + 0{\cdot}25[E(\alpha_{CB},Qq)^2 p_1 q_2 + E(\alpha_{CB},qQ)^2 q_1 p_2]$.

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