

## Comparison of efficiency in the test of the presence of a QTL between full-sib and half-sib designs

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### SUMMARY

Efficiency of detection of a QTL was compared between full-sib and half-sib designs in terms of the size of substitution effect of a QTL. Efficiency designated as  $t$ -value in full-sib design in compared to in half-sib design has become higher with the increase of size of the effect of a QTL. Efficiency in half-sib design with paternal family size and number of sire being 30 and 10, respectively was nearly the same as that of full-sib design under the number of sire, dam and offspring per dam being 10, 5 and 8, respectively, as long as sire haplotype is fully identified from marker genotype of the offspring and under the condition that 10 % of the genetic variance in a trait whose heritability is 0.3 is explained by the QTL. In full-sib design, increasing the number of offspring per dam results in higher efficiency in detection of a QTL than increasing the number of dam when the product of number of dam and number of daughter is the same.  $T$  values in locating a QTL at position 0.1 treating marker distance as 1.0 are slightly higher than at position 0.5.

**Keywords:** QTL, full-sib and half-sib designs, substitution effect

### INTRODUCTION

Detection of a QTL can be achieved by finding a difference in a trait value of two groups of offspring inheriting alternative marker alleles from a common heterozygous parent. Marker-QTL association analysis based on crosses between genetically very different outbred lines is proposed by Haley et al. (1994) by using full-sib family. On the other hand, large half-sib families are typical in dairy cattle where artificial insemination is widely implemented. Offspring in half-sib design are easily obtained in commercial dairy population. Crosses generated in this way can be used as sires and parents in half-sib and full-sib designs, respectively. Some sires and some parents can be in complete linkage disequilibrium between a QTL and flanking markers with the same known linkage phase indicating that the identification of origin of gamete from a parent is not necessary in full-sib design. Major purpose of this paper is to compare the efficiency in identification of a QTL between half-sib and full-sib designs in terms of the size of substitution effect. In addition,  $t$ -values are compared in terms of the position of a QTL at positions of 0.1 and 0.5 treating the marker distance as 1.0 and in terms of the different combination of number of dam and number of daughter per dam in a constant size of the product of number of dam and number of daughter per dam.

### MATERIALS AND METHODS

Two lines are assumed fixed for alternative alleles at both flanking marker loci and a QTL.

All the sires in half-sib design and all the parents in full-sib design generated from crossing two genetically different lines are assumed to be in complete linkage disequilibrium between a QTL and flanking markers with the same known linkage phase, i.e. M1-Q-M2/m1-q-m2. Marker distance is assumed 20cM and no-double-crossover situation is considered. Only one chromosome segment flanked by two marker loci locating a QTL at positions of 0.1 and 0.5 treating marker distance as 1.0 is considered for the purpose of comparing the efficiency of marker-QTL association analysis in half-sib and full-sib designs. Number of genetic marker allele is assumed 2, then it is often the case that sire haplotype can not be identified from marker genotype of the offspring in half-sib design. Then two situations are considered in half-sib design, i.e. one is the above case and the other one is the case that sire haplotype is fully identified with the assist of the other marker information specific to sire haplotype. Three different size of substitution effects are considered in terms of the proportion to total genetic variance in a trait whose heritability is 0.3, i.e. 10%, 20% and 40%. Number of sires is assumed 10 in both half-sib and full-sib designs. In full-sib design, number of dam is 5 and number of daughter per dam is 3,6,8 or 10. Half-sib family size is 30. In addition, different combination of numbers of dam and daughter per dam is compared in full-sib design with constant size of product of numbers of dam and daughter per dam, i.e. 5-10 vs.10-5. The following model was applied:

$y_{ij} = \mu + bx_{ij} + f_i + e_{ij}$  where  $y_{ij}$  is the phenotypic value of jth progeny from ith sire in half-sib design and ith parent in full-sib design;  $x_{ij}$  is the expected number of Q in jth progeny from ith sire or ith parent;  $b$  is regression coefficient or substitution effect;  $f_i$  is the ith sire or ith parent effect which is assumed fixed effect and  $e_{ij}$  is a normally distributed residual variable with mean 0 and variance  $\sigma^2_e$ . The trait value of an individual is determined by the sum of the effects; real number of Q times substitution effect, fixed effects of overall mean and sire/parent which are given pre-determined value and random residual effect. Expected number of Q is given by Gonzales(1992), Goddard(1992) and Togashi et al.(1997). The contribution of a QTL to the variance of a trait is calculated as the difference in sum square error between the full model and a model that ignored a QTL. Testing the null-hypothesis that a QTL is not within the segment is done by t-statistics by Searle(1982) and Haley et al.(1994). Four hundred replicates are simulated for each class regulated by the above factors.

## RESULTS AND DISCUSSION

Results of t statistics in half-sib and full-sib designs locating a QTL at position 0.1 are shown in Figure 1. T value is taken as an efficiency in detection of a QTL because of a large number of observations. Efficiency in detecting a QTL in full-sib design in compared to in half-sib design has become higher with the increase of the effect of a QTL. On the other hand, as long as sire haplotype is fully identified, efficiency in detecting a QTL in half-sib design with a certain size of effect by which 10 % of total genetic variance is explained was nearly the same as that of a QTL in full-sib design with 8 offspring per dam. In fact, it is difficult to distinguish sire haplotype from marker genotype of the offspring. This means that other marker information that distinguishes sire haplotype from marker genotype of the offspring is of great use in half-sib design. The same trend was seen in another QTL position of 0.5. T values and type I error probabilities in different combination of number of dam and number

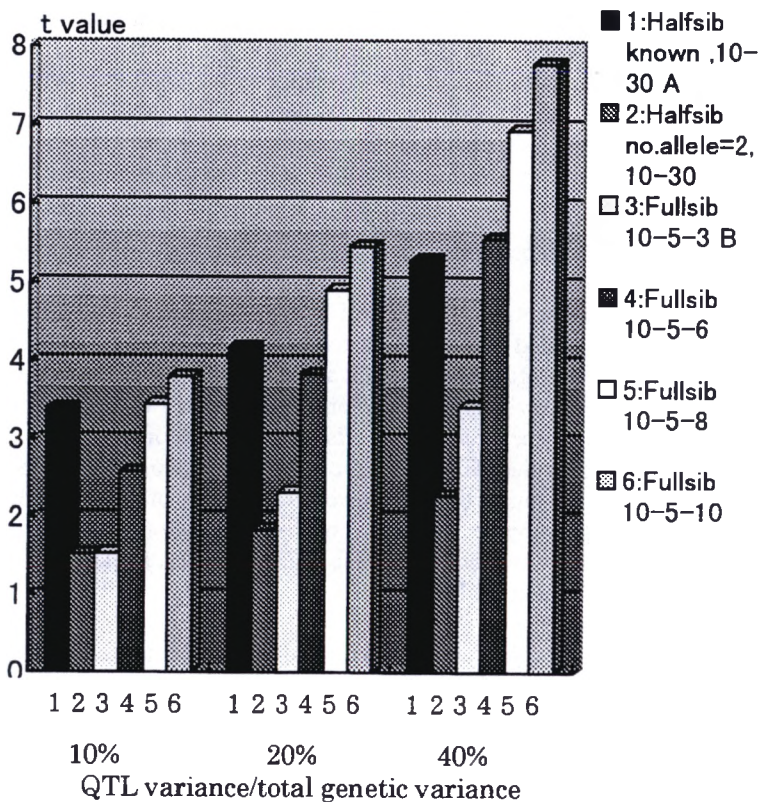
of daughter in full-sib design are shown in Table 1. T values in a combination of 5-10 were slightly higher than those of 10-5. It indicates that increasing the number of offspring per dam results in higher efficiency in detection of a QTL in compared to increasing number of dam. It would be due to more number of segregation in marker genotype of the offspring. Half-sib families are normal population structure and have the advantage of the great ease with which they can be generated. Therefore, a trial to combine crosses between two genetically different lines with the ease of generation of half-sib family structure can pave a new way for the marker-QTL association analysis in dairy cattle population with the assist of other marker

information that distinguishes sire haplotype. In a practical situation with difficulty in identification of sire haplotype, however, full-sib design would have the advantage over half-sib design with the increase of substitution effects. All sires in half-sib design and all the parents in full-sib design were assumed heterozygous for an identical QTL, it may not be realistic. Some of them may be homozygous for the QTL and thus uninformative. In this case, the power to detect a QTL will be increasingly reduced and its effect will be underestimated, since the difference of the value of the trait in the offspring will become smaller due to homozygosity in the QTL. That is, similar QTL allele frequency in the two lines results in the poor power in detecting a QTL. In this article, however, a situation of complete linkage disequilibrium was considered to compare the effect of half-sib and full-sib designs in detecting a QTL. This issue would be overcome by accounting for QTL allele frequency in maximum likelihood analysis by Knott et al.(1996).

Table 1. T values and type I error probabilities in different combinations of numbers of dam and offspring locating a QTL at position of 0.1 treating marker distance as 1

QTL variance/ total genetic variance	10-5-10 <sup>A</sup>		10-10-5	
	t-value	error pro.	t-value	error pro
10%	3.81	1.60D-4	3.39	7.71D-4
20%	5.47	7.41D-8	4.97	9.99D-7
40%	7.79	4.80D-14	7.16	3.77D-12

<sup>A</sup> No. of sire-No. of dam-No. of offspring



A: No. of sire-paternal family size  
 B: No. of sire-No. of dam-No. of daughter per dam

Figure 1. T-value for testing  $H: QTL\ effect=0$

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