

Genetic Evaluation Using Markers Completely Linked to QTLs

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Introduction

- Direct markers that are completely linked to QTLs are valuable information for tracking QTL segregations in marker-assisted selection.
- However, these markers result in linear dependency among QTL effects and singularity of gametic relationship matrix (Tuchscherer et al. 2004).
- This makes the marker information difficult to be integrated in the currently used gametic model BLUP method (Fernando and Grossman 1989).
- Mixed effect mixture model equations (MEMME) developed by Liu and Zeng (2005) were applied to address the above problem in marker-assisted genetic evaluation with direct markers integrated.

Method

Conditional probability of QTL alleles

Let P_k^+ to be vector containing the probabilities for individual k 's two QTL alleles to be A^+ :

$$P_k = \begin{pmatrix} \Pr(Q_k^1 \equiv A^+) \\ \Pr(Q_k^2 \equiv A^+) \end{pmatrix} \quad (1)$$

where k can be individual (i), sire (s) or dam (d). Then, the probability for the QTL alleles of descendant i to be allele A^+ is

$$P_i = T_i' \begin{pmatrix} P_s \\ P_d \end{pmatrix} \quad (2)$$

where,

$$T_i = \begin{pmatrix} P(Q_i^1 \Leftarrow Q_s^1 | M) & P(Q_i^2 \Leftarrow Q_s^1 | M) \\ P(Q_i^1 \Leftarrow Q_s^2 | M) & P(Q_i^2 \Leftarrow Q_s^2 | M) \\ P(Q_i^1 \Leftarrow Q_d^1 | M) & P(Q_i^2 \Leftarrow Q_d^1 | M) \\ P(Q_i^1 \Leftarrow Q_d^2 | M) & P(Q_i^2 \Leftarrow Q_d^2 | M) \end{pmatrix}$$

in which $P(Q_i^2 \Leftarrow Q_s^1 | M)$ is the probability that progeny i 's second QTL allele originated from its sire s 's first allele, conditional on marker information (M) (Liu et al. 2002). The maximum number of possible QTL alleles in a population is taken twice the number of founders of the population and denoted as I in this study. The calculation can be done recursively.

Mixture model approach

Consider a single QTL locus. Each founder i in the population has two QTL alleles, Q_i^1 or Q_i^2 , with respective effects, a_i^1 and a_i^2 . The QTL allelic distribution of an individual in the population can be inferred from pedigree and marker information as described above. Let $\mathbf{a}$ be a vector of QTL allelic effects, *i.e.*

$\mathbf{a} = (a_1^1 \ a_1^2 \ a_2^1 \ a_2^2 \ \dots a_I^1 \ a_I^2)'$ for all I founders of the population. Then, the single locus model for individual j in the population is

$$y_j = \mathbf{x}_j' \boldsymbol{\beta} + \mathbf{z}_j' \mathbf{u} + \sum_{r=1}^{2I} \xi_j^r \mathbf{w}_{jr}' \mathbf{a} + e_j \quad (3)$$

where $\mathbf{x}_j$, $\boldsymbol{\beta}$, $\mathbf{z}_j$ and $\mathbf{u}$ are design matrices; e_j is model residual; $\mathbf{w}_{jr}'$ is the j th row of design matrix $\mathbf{W}$ corresponding to observation y_j ; and ξ_j^r is an indicator variable defined as

$$\xi_j^r = \begin{cases} 1 & \text{if individual inherits QTL allele } r \\ 0 & \text{if individual does not inherit QTL allele } r \end{cases}$$

To estimate the parameters in the above mixture linear model, the following MEMME (Liu and Zeng, 2005) were used:

$$\begin{pmatrix} X'X & X'Z & X'U_a \\ Z'X & Z'Z + \sigma_e^2 \Sigma_u^{-1} & Z'U_a \\ U_a'X & U_a'Z & V_{aa} + \sigma_e^2 \Sigma_a^{-1} \end{pmatrix} \begin{pmatrix} \hat{\beta} \\ \hat{u} \\ \hat{a} \end{pmatrix} = \begin{pmatrix} X'y \\ Z'y \\ U_a'y \end{pmatrix} \quad (4)$$

where,

$$U_a = \sum_{r=1}^{2I} \Pi \mathbf{d}_s * \mathbf{W}_r$$

$$V_{aa} = \sum_{r=1}^{2I} \sum_{r'=1}^{2I} \mathbf{W}_r' [\mathbf{W}_{r'} * \Pi(\mathbf{d}_r \# \mathbf{d}_{r'})].$$

Here, # stands for Hadamard product and * for the element-by-element product of each column in a matrix by a column vector. The breeding values of individuals in the population can be estimated by

$$\mathbf{EBV} = \mathbf{u} + \Pi \mathbf{D} \mathbf{a} \quad (5)$$

where $\mathbf{D}$ is a matrix to denote mixture structure of the model (Liu and Zeng, 2005) and $\mathbf{d}_r$ is its r th row.

Numerical example

To demonstrate the method, the data in Table 1 is used.

Table 1. Example pedigree, marker and phenotypic data

Animal (i)	Sire (s)	Dam (d)	Marker Genotypes	Phenotypic observation
1	0	0	M_1M_1	80
2	0	0	M_2M_2	120
3	0	0	M_1M_2	90
4	1	2	M_1M_2	110
5	3	4	M_1M_1	115
6	1	4	M_1M_2	88
7	5	6	M_1M_2	118

Assume that the marker is a direct marker for the QTL. Since QTL is not observable, it is assumed that founders 1, 2 and 3 carried QTL alleles Q_1^1 , Q_1^2 , Q_2^1 , Q_2^2 , Q_3^1 and Q_3^2 . The QTL transmission probabilities from parents to progeny given marker genotypes are listed in Table 2 and the probabilities for progeny to inherit these QTL alleles of founders were calculated using formula (2) and listed in Table 3.

**Table 2. QTL allelic transmission probabilities, from parents to progeny,
conditional on markers**

Animal	Allele	Probability of descent for marker			
i	1	$Q_i^1 \Leftarrow Q_s^1$	$Q_i^1 \Leftarrow Q_s^2$	$Q_i^1 \Leftarrow Q_d^1$	$Q_i^1 \Leftarrow Q_d^2$
	2	$Q_i^2 \Leftarrow Q_s^1$	$Q_i^2 \Leftarrow Q_s^2$	$Q_i^2 \Leftarrow Q_d^1$	$Q_i^2 \Leftarrow Q_d^2$
1	1	-	-	-	-
	2	-	-	-	-
2	1	-	-	-	-
	2	-	-	-	-
3	1	-	-	-	-
	2	-	-	-	-
4	1	0.5	0.5	0	0
	2	0	0	0.5	0.5
5	1	1	0	0	0
	2	0	0	1	0
6	1	0.5	0.5	0	0
	2	0	0	0	1
7	1	0.5	0.5	0	0
	2	0	0	0	1

Table 3. Conditional probabilities for animal i to inherit QTL alleles of A^1 to A^6

Animal (i)	Allele	Probability of QTL allelic IBD					
		$Q_i^1 \equiv A^1$	$Q_i^1 \equiv A^2$	$Q_i^1 \equiv A^3$	$Q_i^1 \equiv A^4$	$Q_i^1 \equiv A^5$	$Q_i^1 \equiv A^6$
		$Q_i^2 \equiv A^1$	$Q_i^2 \equiv A^2$	$Q_i^2 \equiv A^3$	$Q_i^2 \equiv A^4$	$Q_i^2 \equiv A^5$	$Q_i^2 \equiv A^6$
1	1	1	0	0	0	0	0
	2	0	1	0	0	0	0
2	1	0	0	1	0	0	0
	2	0	0	0	1	0	0
3	1	0	0	0	0	1	0
	2	0	0	0	0	0	1
4	1	0.5	0.5	0	0	0	0
	2	0	0	0.5	0.5	0	0
5	1	0	0	0	0	1	0
	2	0	0	0.5	0.5	0	0
6	1	0.5	0.5	0	0	0	0
	2	0	0	0.5	0.5	0	0
7	1	0	0	0.25	0.25	0.5	0
	2	0	0	0.5	0.5	0	0

An iterative computation was conducted using MEMME. QTL allelic effects were estimated as:

Founder	1		2		3	
Allele	Q_1^1	Q_1^2	Q_2^1	Q_2^2	Q_3^1	Q_3^2
Effect	-1.31	-1.31	1.53	1.53	0.34	-0.78

The estimates of the residual polygenic effects, QTL genotypic effects, EBV and the expectations of observations for each individual are listed as follows:

Animal	Polygene	QTL	EBV	E(Y)
1	-5.48	-2.62	-8.10	93.07
2	6.84	3.07	9.91	111.09
3	-1.36	-0.45	-1.80	99.37
4	3.06	0.22	3.29	104.46
5	4.18	1.87	6.05	107.23
6	-2.54	0.22	-2.32	98.86
7	3.25	2.49	5.74	106.91

Conclusions

- The number of marker alleles at a locus is usually small and the number of animals to be evaluated can be very large. Therefore, the full-rank sub-matrix could be a very small part in a gametic relationship matrix in actual situations, and genetic evaluation using the gametic model BLUP could become quite complicated in comparison with the procedure for linked markers.

- A mixture model approach (Liu and Zeng 2005) is ready to use for marker-assisted genetic evaluation to address the problem, especially in case of complete linkage of markers with QTL.
- Probabilistic analyses of marker-QTL co-segregation can be applied for using the marker information and handling the uncertainty of QTL segregation.
- Numerical example data demonstrates the usefulness of the approach.
- The method is useful for linked markers and especially useful for direct markers.

References

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