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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,

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

in which $P(Q_i^2 \Leftarrow Q_s^1 \mid M)$ 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.* $\mathbf{a} = (a_1^1\ a_1^2\ a_2^1\ a_2^2 \ldots a_I^1\ a_I^2)'$ 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 jth row of design matrix $\mathbf{W}$ corresponding to observation y_j; and ξ_j^r is an indicator variable defined as

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

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

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

where,

$$\mathbf{U}_a = \sum_{r=1}^{2I} \boldsymbol{\Pi}\,\mathbf{d}_s * \mathbf{W}_r$$

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

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

$$\mathbf{EBV} = \mathbf{u} + \boldsymbol{\Pi}\,\mathbf{D}\,\mathbf{a} \qquad (5)$$

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

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