MAXIMUM LIKELIHOOD ALLOWS TESTING THE EFFECT OF QTL ALLELES ON VARIANCE

L. Gomez-Raya[1], L. Varona[1], W.M. Rauw[1], O. Vidal[2] and J.L. Noguera[1]

[1] Àrea de Producció Animal, Centre UdL-IRTA, Alc. Rovira Roure, 177, 25198 Lleida, Spain
[2] Departament of Ciència Animal i dels Aliments. Universidat Autònoma de Barcelona. 08193 Bellaterra. Spain

INTRODUCTION

Detection of quantitative trait loci using regression analysis has been widely used in farm animals (Haley and Knott, 1992; Martinez and Curnow, 1992). The use of regression analysis as the method of choice can be attributed to its simplicity and also to the utilisation of most of the marker information contained in the data. However, standard linear regression methods assume that the variances within each QTL genotype are the same. In practice, epistatic interactions of alleles with the genes at the polygene might result in heterogeneity of polygene variance within QTL genotypes. The objective of this paper is to show that maximum likelihood can be used to test the effect of QTL alleles on variance. The method is developed for analysis within outbred populations that are typed for random anonymous markers such as microsatellites. An example, using 23 microsatellites typed in 5 boars and approx 40 females and 400 piglets, is used to illustrate the method. The trait registered was percentage of lean tissue in carcass.

MAXIMUM LIKELIHOOD ESTIMATION WITHIN SIRE FAMILIES

The testing is carried out within boars and no test is performed for the inheritance of dam alleles. This is done because the small family groups within dam (around 10 piglets) gives little information for detection (Gomez-Raya and Sehested, 1999) and requires a large number of parameters to be estimated (one for each sire and one for each dam).

The likelihood of an individual i from sire j and dam k with performance x_{ij} conditional on marker information is:

$$L_{ij}(x_{ij}| M_{i1}, M_{i2}, M_{j1}, M_{j2}, M_{k1}, M_{k2}) = p(Q_{j1}| M_{i1}, M_{i2}, M_{j1}, M_{j2}, M_{k1}, M_{k2}) z_{j1} + p(Q_{j2}| M_{i1}, M_{i2}, M_{j1}, M_{j2}, M_{k1}, M_{k2}) z_{j2}$$

where M_{i1} and M_{i2} are the marker alleles for individual i; M_{j1} and M_{j2} are the alleles for sire j; M_{k1} and M_{k2} are the alleles for dam k; $p(Q_{j1}| M_{i1}, M_{i2}, M_{j1}, M_{j2}, M_{k1}, M_{k2})$ and $p(Q_{j2}| M_{i1}, M_{i2}, M_{j1}, M_{j2}, M_{k1}, M_{k2})$ are the probabilities of inheriting QTL alleles 1 or 2 from boar j conditional on marker information, respectively. The trait will be assumed to follow a normal distribution. The values of z_{j1} and z_{j2} depend on the test being performed. If the objective is testing for the mean performance of alternative QTL alleles within boar then

$$z_{j1}(x,\mu_{j1},\sigma^2)=\frac{1}{\sigma\sqrt{2\pi}}e^{\frac{-(x-\mu_{j1})^2}{2\sigma^2}} \text{ and } z_{j2}(x,\mu_{j2},\sigma^2)=\frac{1}{\sigma\sqrt{2\pi}}e^{\frac{-(x-\mu_{j2})^2}{2\sigma^2}}$$

where μ_{j1} and μ_{j2} are the means of the subgroups of progeny inheriting alternative alleles from boar j, and σ^2 is the variance of the trait which is assumed to be equal for the two subgroups of progeny.

If the objective is testing for the effect of QTL alleles on the polygene variance then

$$z_{j1}(x,\mu,\sigma^2_{j1})=\frac{1}{\sigma_{j1}\sqrt{2\pi}}e^{\frac{-(x-\mu)^2}{2\sigma^2_{j1}}} \text{ and } z_{j2}(x,\mu,\sigma^2_{j2})=\frac{1}{\sigma_{j2}\sqrt{2\pi}}e^{\frac{-(x-\mu)^2}{2\sigma^2_{j2}}}$$

with σ_{j1} and σ_{j2} being the phenotypic standard deviations of the subgroups of progeny inheriting alternative alleles from boar j, and μ is the mean of the trait assumed equal for the two subgroups.

The likelihood of n offspring from each of nb boars for testing the mean is:

$$L(\mu_{j1},\mu_{j2},\sigma^2)=\prod_{j=1}^{nb}\prod_{i=1}^{n}L_{ij}$$

Similarly, for testing the effect of QTL alleles on variance:

$$L(\mu,\sigma^2_{j1},\sigma^2_{j2})=\prod_{j=1}^{nb}\prod_{i=1}^{n}L_{ij}$$

Hypothesis testing can be carried out using a likelihood ratio test: LRT~ -2 ln(max L_{ho}/ max L_{ha}), where max L_{ho} is the maximum likelihood under the null hypothesis ($\mu_{j1}=\mu_{j2}$ for the test of the means and $\sigma_{j1}=\sigma_{j2}$ for the test of the variance) and max L_{ha} is the maximum likelihood in the unrestricted model. LRT is χ^2 distributed with nb degrees of freedom.

PERCENTAGE OF LEAN MEAT IN AN OUTBRED LANDRACE POPULATION

A total of 23 microsatellites (Table 1) were typed in approx. 400 piglets sired by 5 boars. The trait registered was percentage of lean meat in carcass measured with a FAT-O-METER® in a commercial slaughterhouse of COPAGA at 175 days of age. Molecular information about the microsatellites can be found in the web site **www.genome.iastate.edu/mapsmarcmap.html**. The data were pre-corrected for fixed effects: age, sex and batch. The data was then analysed using the two maximum likelihood models testing the mean and the variance in the two subgroups of progeny within each boar.

RESULTS AND DISCUSSION

Maximum likelihood allows estimation and testing of the effect of QTL alleles on variance. The analysis of lean percentage in pigs using 23 microsatellites revealed 1) markers SW2443 and IGF2 were significant at 5 and 1% when testing for differences in the average performance of offspring inheriting alternative alleles from their boars; and 2) markers SW2618

Table 1. Likelihood ratio test (LRT) for differences in mean and variance for 23 microsatellites. Position is in cM. Chr= chromosome, d.f.= degrees of freedom

Marker	Chr	Position	d.f.	LRT	
				mean	variance
S0313	1	78.7	2	1.06	0.08
SW2185	1	67.6	5	5.88	6.93
SW2443	2	0.0	4	11.46*	7.43
SWC9 (IGF2)	2	0.6	5	15.31**	7.62
SW72	3	17.8	4	3.03	5.71
S0206	3	42.3	4	3.47	11.57*
SW2618	3	50.8	5	6.67	16.22**
SW35	4	55.9	4	2.16	4.24
S0001	4	41.8	4	4.76	2.99
S0214	4	79.3	5	9.51	6.03
S0121	6	116.0	5	5.31	8.51
S0059	6	92.8	4	3.23	5.33
TNFB	7	58.1	5	4.81	4.49
SW1369	7	48.2	5	5.06	3.88
SW905	8	20.8	3	2.07	1.65
SWR1101	8	38.3	3	2.07	3.65
SW21	9	15.1	4	1.82	2.9
SWR1848	9	49.3	4	1.82	8.45
S0070	10	62.3	4	0.12	13.73**
SW173	10	56.1	2	1.22	3.86
SWC19	10	50.5	3	0.51	4.44
SW1056	13	96.1	3	1.57	1.84
SW398	13	79.3	4	1.06	2.16

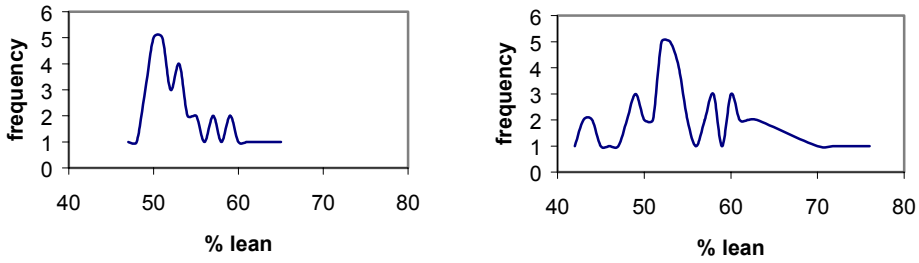
*P<0.05 **P<0.01

S0070 were significant at 1% when testing the effect of QTL alleles on polygene variance. The performance of offspring inheriting both alleles from boar 2 is depicted in Figure 1 to illustrate the different variance in the two subgroups of progeny.

A QTL affecting muscle mass and mapped to IGF2 has been previously reported (Jeon *et al*., 1999). This finding is very consistent with our result of a QTL affecting lean percentage segregating in the neighbourhood of IGF2 within boars.

As far as we know, there are no published reports on the effect of QTL alleles on variance so comparison with the results from literature is not possible. The genetic interpretation of the effect of QTL alleles on variance is the overall interaction of the QTL alleles being tested with other genes (located elsewhere in the genome) or with the environment. This is, a different overall epistatic effect for each of the two alleles from the boar might result in heterogeneity of variances in the two subgroups of progeny. If one of the QTL alleles has an effect on polygene.

Figure 1. Distribution of percentage of lean tissue after pre-correction of fixed effects in the two groups of offspring inheriting alternative alleles from boar 2. The marker was SW2618



variance then a further investigation of the genotypes at the polygene might lead to the identification of high producing individuals with particular combinations of genotypes at the QTL and at the polygene that could be used in marker assisted selection in a non-additive fashion. It could also be carried out by evaluating individuals for the polygene and for the QTL followed by selection of the high-ranking individuals at the polygene within the subgroup of progeny with the QTL allele with higher variance.

Two other practical consequences from this result are: 1) it is desirable for the industry to have lower variation among the animals to be sold for slaughtering, and 2) if the trait is in the selection criteria then there will be a trend to pick up animals as parents for the next generation from the subgroup of progeny with higher variance.

The method for testing QTL alleles on variance could be extended to include testing of both the mean and the variance, simultaneously. In fact, QTL alleles affecting the mean should also be tested for the variance before implementation of marker assisted selection.

ACKNOWLEDGMENTS

We thank Merixell Arqué for excellent technical assistance. We are grateful to the personnel in Nova Genètica S.A. and COPAGA slaughterhouse for their cooperation. This research has been supported by MCYT, Spain (grant nº 2FD97-0916-C02-01).

REFERENCES

Gomez-Raya, L. and Sehested, E. (1999) *Genet. Sel. Evol.* **31** : 351-374.

Jeon, J-T., Carlborg, Ö., Törnsten, A., Giuffra, E., Amarger, V., Chardon, P., Andersson-Eklund, L., Andersson, K., Hansson, I., Lundström, K., and Andersson, L. (1999) *Nature Genet.* **21** : 157-158.

Haley, C. S. and Knott, S. A. (1992) *Heredity* **69** : 315-325.

Martinez, O. and Curnow, R. N. (1992) *Theor. Appl. Genet*. **85** : 480-488.