Mixed models

The mixed model:

$$\mathbf{y} = \mathbf{X}\,\mathbf{b} + \mathbf{Z}\,\mathbf{u} + \mathbf{e}$$

where,

- **y** vector with n observations,
- **b** vector with f fixed effects,
- **u** vector with s random effects,
- **e** vector with error terms ,
- **X** incidence-matrix indicating for each observation the **fixed** effects by which it is influenced,
- **Z** incidence-matrix indicating for each observation the **random** effects by which it is influenced.

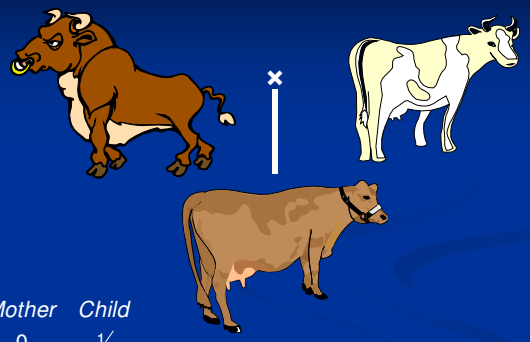
$$\begin{bmatrix} X'X & X'Z \\ Z'X & Z'Z + \alpha A^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'Y \end{bmatrix}$$

$$where\ \alpha = \frac{\sigma_e^2}{\sigma_u^2}$$

Animal or individual model :

$$\sigma_u^2 = \sigma_A^2 \quad \Rightarrow \alpha = \frac{(1-h^2)}{h^2}$$

Animal model



A-matrix

	Father	*Mother*	*Child*
Father	1	0	½
Mother	0	1	½
Child	½	½	1

$\sigma_A^2 \Rightarrow$ Additive genetic variance

$$\mathbf{y} = \mathbf{X\beta} + \mathbf{Zu} + \mathbf{Wv} + \mathbf{e}$$

where:

u is the vector with random additive genetic effects due to loci not linked to the genetic marker,

v is the vector with random gametic effects at the QTL,

W incidence matrix linking alleles to records

$$\begin{bmatrix} X'X & X'Z & X'W \\ Z'X & Z'Z + A_u^{-1}\alpha_u & Z'W \\ W'X & W'Z & W'W + G_{v|\theta}^{-1}\alpha_v \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \\ \hat{v} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \\ W'y \end{bmatrix}$$

A_u = numerator relationshipmatrix

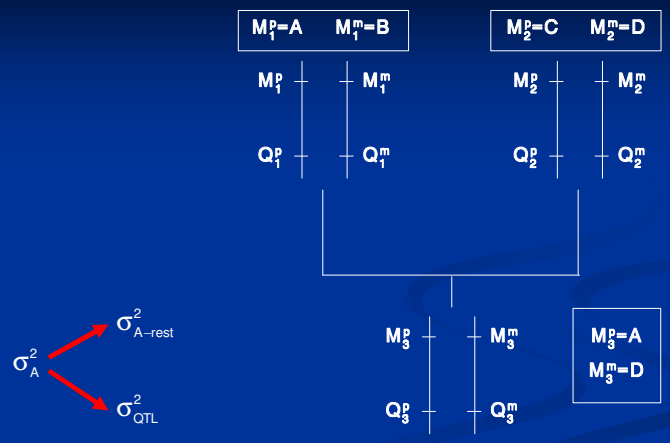
$G_{v|\theta}$ = gametic relationship matrix for the QTL for given θ

$$\alpha_u = \sigma_e^2 / \sigma_u^2 \qquad \alpha_v = \sigma_e^2 / \sigma_v^2$$

σ_e^2 = error variance

σ_u^2 = (residual) additive genetic variance

σ_v^2 = gametic QTL variance



	Q_1^p	Q_1^m	Q_2^p	Q_2^m	Q_3^p	Q_3^m
Q_1^p	1	.	.	.	$(1-\theta)$	.
Q_1^m	.	1	.	.	θ	.
Q_2^p	.	.	1	.	.	θ
Q_2^m	.	.	.	1	.	$(1-\theta)$
Q_3^p	$(1-\theta)$	θ	.	.	1	.
Q_3^m	.	.	θ	$(1-\theta)$	.	1

$$\begin{bmatrix} X'X & X'Z & X'W \\ Z'X & Z'Z + A_u^{-1}\alpha & Z'W \\ W'X & W'Z & W'W + G_{v|\theta}^{-1}\alpha_v \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \\ \hat{v} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \\ W'y \end{bmatrix}$$

- Size of G is twice the number of animals.
- Have to set up the gametic relationship matrix and calculate its inverse

Covariance Matrix of MQTL effect

IBS

WB NL

125/200 125/100

125 allele is IBS

IBD

Gsire Gdam

114/118 127/131

Sire Sire*

114/127 114/127

O O*

114/127 ≡ 114/127

Mutually exclusive

$$Cov(vpo, vpo^*) = Cov(vpo, vpo^* | Qpo \equiv Qpo^*)\, P(Qpo \equiv Qpo^*)$$

$$Cov(vpo, vpo^*) = Var(vpo)\, P(Qpo \equiv Qpo^*)$$

If marker information is available then the r is important

$$P(Qpo \equiv Qpo^*) = P(Qpo \equiv Qps^*)\,(1\text{-}r) + P(Qpo \equiv Qms^*)\,(r)$$

If r = 0.5 then marker info is not available and Qps and Qms have equal probability of being transmitted to O*

Exercise in MA-BLUP

There are 5 animals, all typed.

Id	Sire	Dam	Marker	Pheno
1	0	0	11	1.085
2	0	0	12	2.595
3	1	2	12	2.204
4	0	0	22	2.132
5	3	4	12	0.871

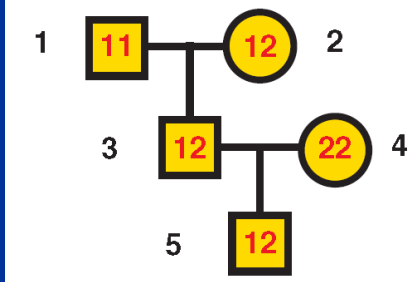
Calculate the IBD probabilities for a QTL located 5 *cM* from the marker for each of the 10 alleles. To ease comparison of our results please label the alleles $1, \ldots, 10$ in the order given in the table.

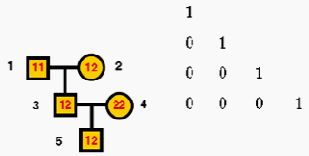
Solve the mixed model equations using the variance components:

Parameter	Symbol	Value
Polygenic variance	$\sigma_g^2 =$	0.4
QTL allele variance	$\sigma_\alpha^2 =$	0.15
Residual variance	$\sigma_\epsilon^2 =$	0.3

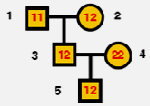
The phenotypes given in the table with data were simulated under model (3) in Fernando & Grossman (1989) with the variance components as shown above.

Id	Sire	Dam	Marker	Pheno
1	0	0	11	1.085
2	0	0	12	2.595
3	1	2	12	2.204
4	0	0	22	2.132
5	3	4	12	0.871

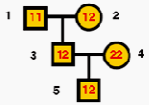




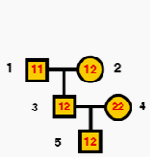
$$\begin{matrix} 1 & & & & \\ 0 & 1 & & & \\ 0 & 0 & 1 & & \\ 0 & 0 & 0 & 1 & \end{matrix}$$



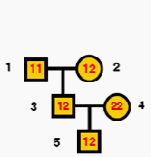
$$\begin{matrix} 1 & & & & \\ 0 & 1 & & & \\ 0 & 0 & 1 & & \\ 0 & 0 & 0 & 1 & \\ \frac{1}{2} & \frac{1}{2} & 0 & 0 & 1 \\ 0 & 0 & \frac{1}{20} & \frac{19}{20} & 0 & 1 \end{matrix}$$



$$\begin{matrix} 1 & & & & & & \\ 0 & 1 & & & & & \\ 0 & 0 & 1 & & & & \\ 0 & 0 & 0 & 1 & & & \\ \frac{1}{2} & \frac{1}{2} & 0 & 0 & 1 & & \\ 0 & 0 & \frac{1}{20} & \frac{19}{20} & 0 & 1 & \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{matrix}$$



$$
\begin{array}{cccccccc}
1 & & & & & & & \\
0 & 1 & & & & & & \\
0 & 0 & 1 & & & & & \\
0 & 0 & 0 & 1 & & & & \\
\frac{1}{2} & \frac{1}{2} & 0 & 0 & 1 & & & \\
0 & 0 & \frac{1}{20} & \frac{19}{20} & 0 & 1 & & \\
0 & 0 & 0 & 0 & 0 & 0 & 1 & \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\
\frac{19}{40} & \frac{19}{40} & \frac{1}{400} & \frac{19}{400} & \frac{19}{20} & \frac{1}{20} & 0 & 0 \quad 1
\end{array}
$$



$$
\begin{array}{cccccccc}
1 & & & & & & & \\
0 & 1 & & & & & & \\
0 & 0 & 1 & & & & & \\
0 & 0 & 0 & 1 & & & & \\
\frac{1}{2} & \frac{1}{2} & 0 & 0 & 1 & & & \\
0 & 0 & \frac{1}{20} & \frac{19}{20} & 0 & 1 & & \\
0 & 0 & 0 & 0 & 0 & 0 & 1 & \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\
\frac{19}{40} & \frac{19}{40} & \frac{1}{400} & \frac{19}{400} & \frac{19}{20} & \frac{1}{20} & 0 & 0 \quad 1 \\
0 & 0 & 0 & 0 & 0 & 0 & \frac{1}{2} & \frac{1}{2} \quad 0 \quad 1
\end{array}
$$

$$\mathbf{Y} = \mathbf{X}\mu + \mathbf{Z}\mathbf{a} + \mathbf{W}\mathbf{q} + \mathbf{e}$$

$$
\begin{pmatrix}
\mathbf{X}'\mathbf{X} & \mathbf{Z}'\mathbf{X} & \mathbf{W}'\mathbf{X} \\
\mathbf{X}'\mathbf{Z} & \mathbf{Z}'\mathbf{Z} + \mathbf{A}^{-1}\alpha_1 & \mathbf{W}'\mathbf{Z} \\
\mathbf{X}'\mathbf{W} & \mathbf{Z}'\mathbf{W} & \mathbf{W}'\mathbf{W} + \mathbf{G}^{-1}\alpha_2
\end{pmatrix}
\begin{pmatrix} \mu \\ \mathbf{a} \\ \mathbf{q} \end{pmatrix}
=
\begin{pmatrix} \mathbf{X}'\mathbf{Y} \\ \mathbf{Z}'\mathbf{Y} \\ \mathbf{W}'\mathbf{Y} \end{pmatrix}
$$

- $\sigma_e^2 = 0.30$
- $\sigma_g^2 = 0.40$
- $\sigma_q^2 = 0.15$
- $\alpha_1 = \frac{\sigma_e^2}{\sigma_g^2}$
- $\alpha_2 = \frac{\sigma_e^2}{\sigma_q^2}$

Predicted Values

ID	$\hat{\mu}$	$\widehat{a_i}$	$\widehat{q_i^1}$	$\widehat{q_i^2}$
1	1.88	-0.27	-0.15	-0.15
2	1.88	0.26	0.09	0.20
3	1.88	0.03	-0.19	0.21
4	1.88	0.01	0.00	0.00
5	1.88	-0.27	-0.19	-0.11

With and Without QTL

ID	y_i	$\widehat{a_i} + \widehat{q_i^1} + \widehat{q_i^2}$	$\widehat{a_i^*}$
1	1.09	-0.57	-0.54
2	2.60	0.55	0.52
3	2.20	0.05	0.05
4	2.13	0.02	0.01
5	0.87	-0.57	-0.53

where $\widehat{a_i^*}$ is predicted using a model without QTL, i.e. $\sigma_g^{2*} = \sigma_g^2 + 2\sigma_q^2$.