

# OHP Picture 1

Recap: covariances between related individuals

□ Reason: MME contain the matrix  $G$   
where  $G = A \cdot \Sigma_u^{-2} = \text{var}(u)$

$\Sigma_u$   
numerator relationship matrix

□ More precisely:  $G^{-1}$  is required for the coefficient matrix of MME

□ Since  $G = A \cdot \Sigma_u^{-2} \Leftrightarrow G^{-1} = A^{-1} \cdot \Sigma_u^{-2}$   
 $\Rightarrow A^{-1}$  required. (In practice  $A^{-1}$  has dimensions  $10^7$  rows  $\times$   $10^7$  columns)

□ Idea: - Construct  $A^{-1}$  without computing  $A$   
- Construction is based on LDL-decomposition of  $A$ , where  $A = L \cdot D \cdot L^T$

where  $L$  is a lower-triangular matrix  
and  $D$  is a diagonal matrix

-  $L$  and  $D$  are "easy" to invert



# OHP Picture 3

Step 2: Full decomposition

□ So far:  $u_i = \frac{1}{2} u_s + \frac{1}{2} u_d + m_i$

□ Continue:  $u_s = \frac{1}{2} u_{ss} + \frac{1}{2} u_{sd} + m_s$

$u_d = \frac{1}{2} u_{sd} + \frac{1}{2} u_{dd} + m_d$

recursively applying simple decomposition through the complete pedigree

□ Example:

$u_1 = m_1$

$u_2 = m_2$

$u_3 = m_3$

$u_4 = \frac{1}{2} u_1 + \frac{1}{2} u_2 + m_4$

$= \frac{1}{2} [m_1] + \frac{1}{2} [m_2] + m_4$

$u_5 = \frac{1}{2} u_3 + \frac{1}{2} u_4 + m_5$

$= \frac{1}{2} m_3 + \frac{1}{2} [m_1 + m_2] + m_5$

$u_6 = \frac{1}{2} u_4 + \frac{1}{2} u_5 + m_6$

$= \frac{1}{2} \left[ \frac{1}{2} m_1 + \frac{1}{2} m_2 + m_4 \right] + \frac{1}{2} \left[ \frac{1}{2} m_3 + \frac{1}{2} m_1 + \frac{1}{2} m_2 + m_5 \right] + m_6$

No changes for animals parents without parents

# OHP Picture 4

$$u_6 = \frac{1}{2} \left[ \frac{1}{2} m_1 + \frac{1}{2} m_2 + m_4 \right] + \frac{1}{2} \left[ \frac{1}{2} m_3 + \frac{1}{2} m_2 + m_5 \right] + m_6$$

$$= \frac{1}{4} m_1 + \frac{1}{4} m_2 + \frac{1}{2} m_4 + \frac{1}{4} m_3 + \frac{1}{4} m_2 + \frac{1}{2} m_5 + m_6$$

$$= \frac{1}{4} m_1 + \frac{1}{2} m_2 + \frac{1}{4} m_3 + \frac{1}{2} m_4 + \frac{1}{2} m_5 + m_6$$

□ Summary:

$$\begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \\ u_6 \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ \frac{1}{2} & \frac{1}{2} & 0 & 1 & 0 & 0 \\ 0 & \frac{1}{2} & \frac{1}{2} & 0 & 1 & 0 \\ \frac{1}{4} & \frac{1}{2} & \frac{1}{4} & \frac{1}{2} & \frac{1}{2} & 1 \end{bmatrix} \cdot \begin{bmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ m_5 \\ m_6 \end{bmatrix}$$

$$u = L \cdot m$$

$\rightarrow 0 \Rightarrow L$  is lower-triangular

# OHP Picture 5

Properties of Matrix L:

$$\begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \\ u_6 \end{bmatrix} = L \begin{bmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ m_5 \\ m_6 \end{bmatrix}$$

Matrix L is shown as:

$$\begin{bmatrix} 1 & & & & & \\ & 1 & & & & \\ & & 1 & & & \\ & 0.5 & 0.5 & & & \\ & & & 1 & & \\ & & & & 1 & \\ & & & & & 1 \end{bmatrix}$$

Red boxes highlight the elements 0.5, 0.5, and 0.25 in the matrix.

$(L)_{61} \Rightarrow$  fraction of  $m_1$  in  $u_6$   
 $m_1$  comes from either father 4 or mother 5

$$u_4 = \frac{1}{2}m_1 + \frac{1}{2}m_2 + m_4$$

$$(L)_{41} = 0.5 = \frac{1}{2} [(L)_{11} + (L)_{21}] \Rightarrow \frac{1}{2} [(L)_{51} + \frac{1}{2}(L)_{41}]$$

fraction of  $m_1$  in  $u_4$  where animals 1 and 2 are parents of animal 4

In general:  $(L)_{ij}$  which is the element in row  $i$  and column  $j$  ( $i > j$  meaning the lower diagonal of L)

$$(L)_{ij} = \frac{1}{2}(L)_{sj} + \frac{1}{2}(L)_{dj}$$

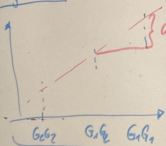
where  $s$  and  $d$  are parents of  $i$

# OHP Picture 6

2 new projects for internships or master thesis

1. Fine mapping quantitative trait loci (QTL) for carcass traits on BTAM in OB classic GWAS: breeding values from bulls & genotypes from bulls  $\rightarrow$  Find association  
*based on offspring*
2. Fine mapping QTL for teat thickness on BTAG Association study with cow phenotypes and genotypes  
in collaboration with Hubert Paauw

Single Locus



Locus G

Locus H

# OHP Picture 8

Matrix  $L$ :

$$u = L \cdot m$$

$$(L)_{ij} = \frac{1}{2}(L)_{sj} + \frac{1}{2}(L)_{tj}$$

Decomposition for  $\text{var}(u)$ :

□ Because  $u = L \cdot m$

$$\begin{aligned}\text{var}(u) &= \text{var}(L \cdot m) \\ &= L \cdot \text{var}(m) \cdot L^T\end{aligned}$$

□ The vector  $m$  contains random mendelian sampling terms ( $m_i$ ) for animal  $i$ :

Full sibs  $i$  and  $j$  with parents  $s$  and  $t$

$$\left. \begin{aligned}u_i &= \frac{1}{2}u_s + \frac{1}{2}u_t + m_i \\ u_j &= \frac{1}{2}u_s + \frac{1}{2}u_t + m_j\end{aligned} \right\} \begin{array}{l} \text{in general } u_i \neq u_j \\ \text{because } i \text{ and } j \\ \text{did not receive the same} \\ \text{sample of random alleles} \\ \text{from parents} \end{array}$$

But  $m_i$  and  $m_j$  are independent  
 $\Rightarrow \text{cov}(m_i, m_j) = 0$

# OHP Picture 9

□  $\text{cov}(m_i, m_j) = 0$  for all  $m_i$  and  $m_j$   
if  $i \neq j$

$$\Rightarrow \text{var}(m) = \begin{bmatrix} \text{var}(m_1) & \text{cov}(m_1, m_2) & \text{cov}(m_1, m_3) \dots \\ \text{cov}(m_2, m_1) & \text{var}(m_2) & \dots \\ \dots & \dots & \dots \end{bmatrix}$$

$= 0$

$\Rightarrow \text{var}(m)$  will be a diagonal matrix

□  $\text{var}(m_1), \text{var}(m_2), \dots, \text{var}(m_i) ?$

□ Using  $u_i = \frac{1}{2}u_s + \frac{1}{2}u_d + m_i$

$$\begin{aligned} \text{var}(u_i) &= \text{var}\left[\frac{1}{2}u_s + \frac{1}{2}u_d + m_i\right] \\ &= \text{var}\left(\frac{1}{2}u_s\right) + \text{var}\left(\frac{1}{2}u_d\right) + \text{var}(m_i) \\ &\quad + 2 \text{cov}\left(\frac{1}{2}u_s, \frac{1}{2}u_d\right) \\ &\quad + 2 \text{cov}\left(\frac{1}{2}u_s, m_i\right) + 2 \text{cov}\left(\frac{1}{2}u_d, m_i\right) \\ &= \frac{1}{4} \text{var}(u_s) + \frac{1}{4} \text{var}(u_d) + \frac{1}{2} \text{cov}(u_s, u_d) + \text{var}(m_i) \end{aligned}$$



# OHP Picture 10

$$\text{var}(u_i) = \frac{1}{4} \text{var}(u_s) + \frac{1}{4} \text{var}(u_d) + \frac{1}{2} \text{cov}(u_s, u_d) + \text{var}(m_i)$$

□ Definition of

$G = A \cdot \bar{v}_u^2$ , we know that

$$\text{var}(u_s) = (1+F_s) \bar{v}_u^2$$

$$\text{var}(u_d) = (1+F_d) \bar{v}_u^2$$

$$\text{cov}(u_s, u_d) = (A)_{sd} \bar{v}_u^2 = 2F_{ik} \bar{v}_u^2$$

where  $F_{ik}$  is the inbreeding coefficient of animal  $k$

□ Solve for  $\text{var}(m_i)$ :

$$\text{var}(m_i) = \text{var}(u_i) - \frac{1}{4} \text{var}(u_s) - \frac{1}{4} \text{var}(u_d) - \frac{1}{2} \text{cov}(u_s, u_d)$$

$$= (1+F_i) \bar{v}_u^2 - \frac{1}{4} (1+F_s) \bar{v}_u^2 - \frac{1}{4} (1+F_d) \bar{v}_u^2 - \frac{1}{2} (2F_{ik} \bar{v}_u^2)$$

$$= \left( \frac{1}{2} - \frac{1}{4} (F_s + F_d) \right) \bar{v}_u^2$$

for known parents  $s$  and  $d$  of animal  $i$

# OHP Picture 11

$$\begin{aligned}\text{var}(u) &= \text{var}(L \cdot m) \\ &= L \cdot \text{var}(m) \cdot L^T\end{aligned}$$

with  $\text{var}(m)$  being a diagonal matrix  $D$  with diagonal elements

$$\sigma_u^2 \cdot (D)_{ii} = \text{var}(m_i) = \begin{cases} \left(\frac{1}{2} - \frac{1}{4}(F_3 + E_1)\right) \sigma_u^2 & (1) \\ \left(\frac{3}{4} - \frac{1}{4}F_3\right) \sigma_u^2 & (2) \\ \sigma_u^2 & (3) \end{cases}$$

where (1) : both parents known  
(2) : only one parent is known  
(3) : no parents known

$$\begin{aligned}\Rightarrow \text{var}(u) &= L \cdot D \sigma_u^2 L^T \quad \text{where } \sigma_u^2 D = \text{var}(m) \\ &= \underbrace{L \cdot D \cdot L^T}_{A} \cdot \sigma_u^2 \\ &= A \cdot \sigma_u^2\end{aligned}$$

# OHP Picture 12

Inverse  $A^{-1}$  of  $A$ :

$$\square A = L \cdot D \cdot L^T$$

$$\Rightarrow A^{-1} = (L^T)^{-1} \cdot \underbrace{D^{-1}}_{\text{Diagonal}} \cdot L^{-1}$$

$\square$  Because  $D$  is diagonal  $\Rightarrow D^{-1}$  is diagonal

with diagonal elements  $(D^{-1})_{ii} = \frac{1}{(D)_{ii}}$

$$D = \begin{bmatrix} \text{var}(m_1) & 0 & \dots & 0 \\ 0 & \text{var}(m_2) & \dots & \dots \\ & & \ddots & \\ & & & \ddots \end{bmatrix}$$

$$D^{-1} = \begin{bmatrix} \frac{1}{\text{var}(m_1)} & 0 & \dots & 0 \\ 0 & \frac{1}{\text{var}(m_2)} & \dots & 0 \\ & & \ddots & \\ & & & \ddots \end{bmatrix}$$

$\square L^{-1}$  ?

# OHP Picture 13

Matrix  $L^{-1}$ :

□ Decompositions:

$$u = P \cdot u + m$$

$$u = L \cdot m$$

} both decompositions  
of the same vector  $u$

$$\Rightarrow u - P \cdot u + m = L \cdot m$$

$$\Rightarrow P \cdot u = L \cdot m - m = (L - I) \cdot m$$

□ Solve both decompositions for  $m$

$$\rightarrow m = u - P \cdot u = (I - P) \cdot u$$

$$m = L^{-1} \cdot u$$

} both equations  
hold for the  
same  $m$

$$\Rightarrow (I - P) \cdot u = L^{-1} \cdot u$$

$$L^{-1} = (I - P)$$

where  $I$  is the identity matrix and  $P$   
is the matrix from the simple decomposition.

# OHP Picture 14

Initialize matrix A in R:

matrix(0, nrow=6, ncol=6)

Function:  $F_i \leftarrow \text{ifelse}(\text{Boolean expression}, \text{"true value"}, \text{false value})$

if Boolean expression is true  
then  $F_i$  will be assigned to  
'true value'  
otherwise  $F_i$  will be assigned  
to the 'false value')