

OHP Picture 1

Recap: Covariances between related individuals

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

\bar{G}
numerator relationship matrix

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

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

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

- Lower D are "easy" to invert

OHP Picture 2

Simple decomposition of U_i of animal i :

$$U_i = \frac{1}{2} U_S + \frac{1}{2} U_d + M_i$$

where U_S : breeding value of parent \Rightarrow } of i
 U_d : " " " " of
 M_i : mendelian sampling term.

$$\begin{aligned} U_1 &= \\ U_2 &= \\ U_3 &= \\ U_4 &= \frac{1}{2} U_1 + \frac{1}{2} U_2 + M_4 \\ U_5 &= \frac{1}{2} U_3 + \frac{1}{2} U_2 + M_5 \\ U_6 &= \frac{1}{2} U_4 + \frac{1}{2} U_5 + [M_6] \end{aligned}$$

$U = P \cdot u + m$

$$\begin{aligned} U_1 &= \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \\ U_2 &= \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \\ U_3 &= \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \\ U_4 &= \begin{bmatrix} \frac{1}{2} & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \\ U_5 &= \begin{bmatrix} 0 & \frac{1}{2} & 0 & 0 & 0 & 0 \end{bmatrix} \\ U_6 &= \begin{bmatrix} 0 & 0 & \frac{1}{2} & \frac{1}{2} & 0 & 0 \end{bmatrix} \end{aligned}$$
$$\begin{bmatrix} U_1 \\ U_2 \\ U_3 \\ U_4 \\ U_5 \\ U_6 \end{bmatrix} + M$$

OHP Picture 3

Step 2: Full decomposition

- So far: $U_1 = \frac{1}{2} U_S + \frac{1}{2} U_D + M_1$
- Continue: $U_S = \frac{1}{2} U_{S1} + \frac{1}{2} U_{S2} + M_S$
 $U_D = \frac{1}{2} U_{D1} + \frac{1}{2} U_{D2} + M_D$

recursively applying simple decomposition through the complete pedigree

- Example:
 - $U_A = M_A$
 - $U_B = M_B$
 - $U_S = M_S$
 - $U_1 = \frac{1}{2} U_A + \frac{1}{2} U_B + M_1$
 - $= \frac{1}{2} [M_A] + \frac{1}{2} [M_B] + M_1$
 - $U_5 = \frac{1}{2} U_S + \frac{1}{2} [U_Z] + M_5$
 $= \frac{1}{2} M_S + \frac{1}{2} M_Z + M_5$
 - $U_6 = \frac{1}{2} U_4 + \frac{1}{2} U_5 + M_6$
 $= \frac{1}{2} \left[\frac{1}{2} M_A + \frac{1}{2} M_B + M_4 \right] +$
 $\quad \frac{1}{2} \left[\frac{1}{2} M_S + \frac{1}{2} M_Z + M_5 \right] + M_6$

No changes for animals parents without parents

OHP Picture 4

$$\begin{aligned} u_6 &= \frac{1}{2} \left[\frac{1}{k} m_1 + \frac{1}{2} m_2 + m_4 \right] \\ &\quad + \frac{1}{2} \left[\frac{1}{2} m_3 + \frac{1}{2} m_2 + m_5 \right] + m_6 \\ &= \frac{1}{4} m_1 + \frac{1}{4} m_2 + \frac{1}{2} m_4 \\ &\quad + \frac{1}{4} m_3 + \frac{1}{4} m_2 + \frac{1}{2} m_5 + m_6 \\ &= \frac{1}{4} m_1 + \frac{1}{2} m_2 + \frac{1}{4} m_3 + \frac{1}{2} m_4 + \frac{1}{2} m_5 + m_6 \end{aligned}$$

→ 0 ⇒ L is lower-triangular

□ Summary:

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

OHP Picture 5

Properties of Matrix L:

$$\begin{bmatrix} u_1 \\ u_2 \\ \vdots \\ u_4 \\ u_5 \\ u_6 \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0.5 & 0.5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0.25 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0.25 \end{bmatrix} \begin{bmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ m_5 \\ m_6 \end{bmatrix}$$

$(L)_{41}$

\uparrow
fraction of m_1 in u_6
 m_1 comes from either father 4 or
mother 5

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

$(L)_{51}$

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

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

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

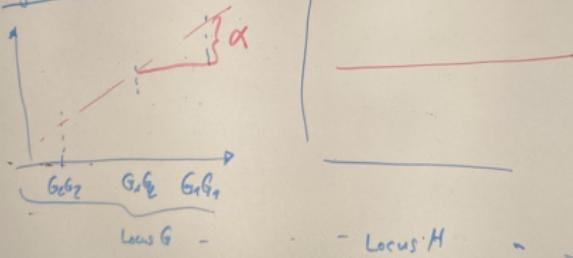
where s and d are
parents of i

OHP Picture 6

2 new projects for internships or master thesis

1. Fine mapping quantitative trait loci (QTL)
for carcass traits on BTAG in OB
Classic GWAS: breeding values from bulls & genotypes from
bulls → Find association
2. Fine mapping QTL for teat thickness on BTAG
Association study with cow phenotypes and genotypes
in collaboration with Hubert Pauchant

Single Locus



OHP Picture 8

Matrix L:

$$u = L \cdot m$$

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

Decomposition for 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 \rightarrow ael o!

$$\left. \begin{aligned} u_i &= \frac{1}{2}u_s + \frac{1}{2}u_d + m_i \\ u_j &= \frac{1}{2}u_s + \frac{1}{2}u_d + m_j \end{aligned} \right\} \text{in general } u_i \neq u_j$$

because i and j did receive the same

sample of random alleles from parents

$m_i \neq m_j$

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 $i \neq j$

$$\Rightarrow \text{var}(m) = \begin{bmatrix} \text{var}(m_1) & \text{cov}(m_1, m_2) & \text{cov}(m_1, m_3) \\ \text{cov}(m_2, m_1) & \text{var}(m_2) & \cdots \\ \vdots & \vdots & \ddots \end{bmatrix}$$
$$= 0$$

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

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

□ Using $u_i = \frac{1}{2}u_{s,i} + \frac{1}{2}u_{d,i} + m_i$

$$\begin{aligned}\text{var}(u_i) &= \text{var}\left[\frac{1}{2}u_{s,i} + \frac{1}{2}u_{d,i} + m_i\right] \\ &= \text{var}\left(\frac{1}{2}u_{s,i}\right) + \text{var}\left(\frac{1}{2}u_{d,i}\right) + \text{var}(m_i) \\ &\quad + 2 \text{cov}\left(\frac{1}{2}u_{s,i}, \frac{1}{2}u_{d,i}\right) \\ &\quad + 2 \text{cov}\left(\frac{1}{2}u_{s,i}, m_i\right) + 2 \text{cov}\left(\frac{1}{2}u_{d,i}, m_i\right) \\ &= \underbrace{\frac{1}{4}\text{var}(u_s) + \frac{1}{4}\text{var}(u_d)}_{=0} + \underbrace{\frac{1}{2}\text{cov}(u_s, u_d)}_{=0} + \text{var}(m_i)\end{aligned}$$

OHP Picture 10

$$\text{var}(u_{ii}) = \frac{1}{4} \text{var}(u_S) + \frac{1}{4} \text{var}(u_D) + \frac{1}{2} \text{cov}(u_S, u_D) + \underline{\text{var}(m_i)}$$

□ Definition of $G = A \cdot \bar{F}_u^2$, we know that

$$\text{var}(u_S) = (1+F_S)\bar{F}_u^2$$

$$\text{var}(u_D) = (1+F_D)\bar{F}_u^2$$

$$\text{cov}(u_D, u_S) = (A)_{SD} \bar{F}_u^2 = 2F_D \bar{F}_u^2$$

where F_k is the inbreeding coefficient
of animal k

□ Solve for $(\text{var}(m_i))$:

$$\text{var}(m_i) = \text{var}(u_{ii}) - \frac{1}{4} \text{var}(u_S) - \frac{1}{4} \text{var}(u_D) - \frac{1}{2} \text{cov}(u_S, u_D)$$

$$= (1+F_i)\bar{F}_u^2 - \frac{1}{4}(1+F_S)\bar{F}_u^2 - \frac{1}{4}(1+F_D)\bar{F}_u^2 - \frac{1}{2}(2F_D \bar{F}_u^2)$$

$$= \underline{\left(\frac{1}{2} - \frac{1}{4}(F_S + F_D) \right) \bar{F}_u^2}$$

for known parents S and D of animal i

OHP Picture 11

$$\text{var}(u) = \text{var}(L \cdot m)$$
$$= L \cdot \text{var}(m) \cdot L^T$$

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

$$\bar{v}_u^2 \cdot (D)_{ii} = \text{var}(m_i) = \begin{cases} \left(\frac{1}{2} - \frac{1}{4}(F_3 + F_4)\right) \bar{v}_u^2 & (1) \\ \left(\frac{3}{4} - \frac{1}{4}F_3\right) \bar{v}_u^2 & (2) \\ \bar{v}_u^2 & (3) \end{cases}$$

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

$$\Rightarrow \text{var}(u) = L \cdot D \bar{v}_u^2 L^T \quad \text{where } \bar{v}_u^2 \cdot D = \text{var}(m)$$
$$= \underbrace{L \cdot D \cdot L^T}_{A} \cdot \bar{v}_u^2$$

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 $(D^{-1})_{ii} = 1/(D)_{ii}$

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

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

$\square L^T ?$

OHP Picture 13

Matrix L^{-1} :

- Decomposition:

$$U = \boxed{P} \cdot U + M \quad \left. \begin{array}{l} \text{both decompositions} \\ \text{of the same vector } U \end{array} \right\}$$
$$U = L \cdot M$$

$$\Rightarrow U - P \cdot U + M = L \cdot M$$

$$\Rightarrow P \cdot U = L \cdot M - M = (L - I)M$$

- Solve both decompositions for M

$$\rightarrow M = U - P \cdot U = (I - P) \cdot U \quad \left. \begin{array}{l} \text{both equations} \\ \text{hold for the} \\ \text{same } M \end{array} \right\}$$
$$M = L^{-1} \cdot U$$

$$\Rightarrow \underbrace{(I - P) \cdot U}_{\substack{\downarrow \\ \downarrow}} = \underbrace{L^{-1} \cdot U}_{\substack{\downarrow \\ \downarrow}}$$

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

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

OHP Picture 14

Initialize matrix A in R:

- $\text{matrix}(\emptyset, \text{nrow}=6, \text{ncol}=6)$

Function: $\text{F}_i = \text{ifelse}$ (

- ↳ "the value"
- ↳ 'Boolean expression'
- ↳ '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')