

Overhead Pictures Lecture 6

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Recap

Recap:

- Two concepts of identity:
 - IBS: identical by state → Alleles identical
 - IBD: identical by descent → Alleles are & copies of the same ancestral allele

For traditional prediction of breeding values only IBD-relations are considered (only with phenotypic observations and pedigree data; without SNP)

Genomic prediction of breeding values, IBS relations are also taken into account.

Data with SNP information on selection candidates

- Quantity to characterize IBD-relations:
 - Coancestry or coefficient of kinship

Definition: Probability of alleles in two individuals being identical by descent.

Example:

Example

Example:

○ = female
□ = male

What is the kinship coefficient between half-sibs?

→ what is the probability of A_1 in half-sib ① is identical by descent with A_1 in half-sib ②

- Probability that half-sib ① inherits A_1 from the father is $1/4$. The same for half-sib ②: $1/4$
- These two events occurring together has probability of $1/4 \cdot 1/4 = 1/16$
- The same applies to the red ancestral allele A_2 . For both offspring to inherit the red A_2 , the probability is $1/16$
- Kinship coefficient: $1/16 + 1/16 = 1/8$

Kinship Coefficient

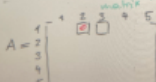
- Kinship coefficient: $\frac{1}{4} + \frac{1}{4} = \frac{1}{2}$
 - Additive genetic relationship which correspond to elements of the numerator relationship matrix F , are two times the kinship coefficient.
- $$(A)_{ij} = 2 \cdot \frac{1}{4} = \frac{1}{2} \text{ if animals } i \text{ and } j \text{ are half-sibs.}$$

Last week:



$$u = \begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \end{bmatrix}$$

$$G = \text{var}(u) = A \cdot \underbrace{\sigma_u^2}_{\substack{\text{numerator} \\ \text{relationship} \\ \text{matrix}}} \rightarrow \text{genetic additive variance}$$



$$(A)_{12} = \frac{\text{cov}(u_1, u_2)}{\sigma_u^2}$$

$$= 0$$

Genetic Relationship

number relationship matrix

$$A = \begin{matrix} & 1 & 2 & 3 & 4 & 5 \\ \begin{matrix} 1 \\ 2 \\ 3 \\ 4 \\ 5 \end{matrix} & & & & & \\ & & \boxed{1} & & & \\ & & & \boxed{1} & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \end{matrix}$$

$$(A)_{42} = \frac{\text{cov}(u_1, u_2)}{\sigma_u^2} = 0$$

$$(A)_{43} = \frac{\text{cov}(u_1, u_3)}{\sigma_u^2} = \frac{\text{cov}(u_1, [\frac{1}{2}u_1 + \frac{1}{2}u_2 + m_3])}{\sigma_u^2}$$

replaced by parents 1 and 2

$$= \frac{\text{cov}(u_1, \frac{1}{2}u_1)}{\sigma_u^2} + \frac{\text{cov}(u_1, \frac{1}{2}u_2)}{\sigma_u^2} + \frac{\text{cov}(u_1, m_3)}{\sigma_u^2}$$

$$= \frac{\frac{1}{2} \text{cov}(u_1, u_1)}{\sigma_u^2} + \frac{\frac{1}{2} \text{cov}(u_1, u_2)}{\sigma_u^2} + 0$$


$$= \frac{1}{2} (A)_{11} + \frac{1}{2} (A)_{12}$$

General Rule

General Rule: for any off diagonal element in A

$$(A)_{ji} = \frac{1}{2} (A)_{js} + \frac{1}{2} (A)_{jd} \quad \text{if animals } s \text{ and } d \text{ are parents of animal } i$$

if j



The diagram shows a square matrix labeled 'A'. A blue diagonal line runs from the top-left to the bottom-right. A green arrow points to this diagonal line with the label 'diagonal (A)_{ii}'. A blue arrow points to a line parallel to the diagonal, slightly to the right, with the label 'off-diagonal (A)_{ji} (i < j)'. The entire matrix diagram is enclosed in a blue oval.

• Diagonal elements $(A)_{ii}$:

$$(A)_{ii} = 1 + F_i$$

where F_i inbreeding coefficient of animal i ; F_i corresponds to $\frac{1}{2}$ times the additive relationship of parents s and d

Example: Pedigree

Example

Example: Pedigree

| Animals | Sire | Dams |
|---------|------|------|
| 1 | NA | NA |
| 2 | NA | NA |
| 3 | 1 | 2 |
| 4 | 1 | NA |
| 5 | 4 | 3 |
| 6 | 5 | 2 |

step 1: Add parents to list of animals
 step 2: Empty matrix A with 6 rows and 6 columns

$A = \begin{matrix} & \begin{matrix} 1 & 2 & 3 & 4 & 5 & 6 \end{matrix} \\ \begin{matrix} 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \end{matrix} & \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix} \end{matrix}$

Example II

Diagonal element:

$$(A)_{11} = 1 + \underline{F_1} = 1 + \frac{1}{2}(A)_{2211} = 1$$

off diagonal:

$$(A)_{12} = \frac{1}{2}(A)_{2111} + \frac{1}{2}(A)_{2112} = 0$$
$$(A)_{13} = \frac{1}{2}(A)_{1212} + \frac{1}{2}(A)_{1213} = \frac{1}{2} \cdot 1 + \frac{1}{2} \cdot 0 = \frac{1}{2}$$
$$(A)_{14} = \frac{1}{2}(A)_{1114} + \frac{1}{2}(A)_{1115} = \frac{1}{2}$$
$$(A)_{15} = \frac{1}{2}(A)_{1414} + \frac{1}{2}(A)_{1415} = \frac{1}{2} \cdot \frac{1}{2} + \frac{1}{2} \cdot \frac{1}{2} = \frac{1}{2}$$
$$(A)_{16} = \frac{1}{2}(A)_{1515} + \frac{1}{2}(A)_{1516} = \frac{1}{2} \cdot \frac{1}{2} + \frac{1}{2} \cdot 0 = \frac{1}{4}$$

Step 3: Because A is symmetric, the first row is copied to the first column

Step 4: Continue with row 2:

Diagonal: $(A)_{22} = 1 + \underline{F_2} = 1 + \frac{1}{2}(A)_{2222} = 1$

Matrix A and BLUP

Remember: Inbreeding Coefficient F_5 of animal 5
From the diagonal element $(A)_{55}$:

Exam $\left\{ \begin{array}{l} F_5 = (A)_{55} - 1 = 0.125 \\ F_5 \neq 1.125 \end{array} \right.$

From BLUP: Mixed Model Equations contain A^{-1}

(Reminder: Inverse A^{-1} is defined such that
 $A \cdot A^{-1} = I$ (identity))

$$\text{MME: } \begin{bmatrix} X^T R^{-1} X & X^T R^{-1} Z \\ Z^T R^{-1} X & I^T R^{-1} Z + G^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X^T R^{-1} y \\ Z^T R^{-1} y \end{bmatrix}$$

$$G = A \cdot \sigma_u^2 \rightarrow G^{-1} = A^{-1} / \sigma_u^2$$

→ MME are based on an animal model which corresponds to a Linear Mixed Effects Model where the breeding values of all animals in the pedigree are modelled as random effects.

First Idea

First idea to compute A^{-1} :

- Compute A
- then invert A to get to A^{-1} (in R: ~~solve~~ solve())
- Small data sets \Rightarrow OK

\Rightarrow Not possible for large data sets

Simple structure of A^{-1} was discovered by Henderson who developed simple rules of computing A^{-1} directly, that means without first computing A .

The rules of computing A^{-1} are based on properties of A and A^{-1} .

- From Linear Algebra it is known that symmetric matrices can be decomposed into a product of three factors:

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

where L is lower triangular matrix \Rightarrow

$$L = \begin{bmatrix} & & \\ & & \\ & & \ominus \end{bmatrix}$$

and D is a diagonal

LDL

and A .

- From Linear Algebra it is known that symmetric matrices can be decomposed into a product of three factors:

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

where L is lower triangular matrix \Rightarrow

$$L = \begin{bmatrix} & & & 0 \\ & & & \\ & & & \\ 0 & & & \end{bmatrix}$$

and D is a diagonal matrix

$$D = \begin{bmatrix} & & & \\ & & & \\ & & & \\ 0 & & & \end{bmatrix}$$

Based on LDL-decomposition of A , we can write

$$A^{-1} = (L^T)^{-1} \cdot D^{-1} \cdot L^{-1}$$

and $(L^T)^{-1}$, D^{-1} and L^{-1} are easy to compute

To get to L and D , we are going to have a look at different decompositions of breeding values:

- breeding value u_i of animal i can be written as

Simple Decomposition

To get to L and D, we are going to have a look at different decompositions of breeding values:

- breeding value U_i of animal i can be written as

$$U_i = \frac{1}{2} U_s + \frac{1}{2} U_d + m_i$$

where U_s is the breeding value of parent's

U_d is the breeding value of parent's

m_i is the Mendelian sampling term of animal i .

→ for example pedigree:

$$\begin{aligned} U_1 &= 0 + 0 + m_1 \\ U_2 &= \frac{1}{2} U_{1A} + \frac{1}{2} U_{1B} + m_2 \\ U_3 &= m_3 \\ U_4 &= \frac{1}{2} U_2 + \frac{1}{2} U_3 + m_4 \\ U_5 &= \frac{1}{2} U_3 + \frac{1}{2} U_4 + m_5 \end{aligned}$$

Set of equations

Write equations in matrix vector notation

$$[U] = [A]^{-1} [m]$$

Simple Decomposition II

$u_5 = \sum u_{45} + \sum u_{35} + m_5$

Write equations in matrix vector notation

vector $u = \begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \end{bmatrix}$ vector $m = \begin{bmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ m_5 \end{bmatrix}$

Define Matrix $P = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{2} & \frac{1}{2} & 0 & 0 \\ 0 & \frac{1}{2} & \frac{1}{2} & 0 & 0 \end{bmatrix}$

$u = P \cdot u + m$; P Links parents to offspring and is a lower triangular matrix

First decomposition of breeding values u .