Overhead Pictures Lecture 6

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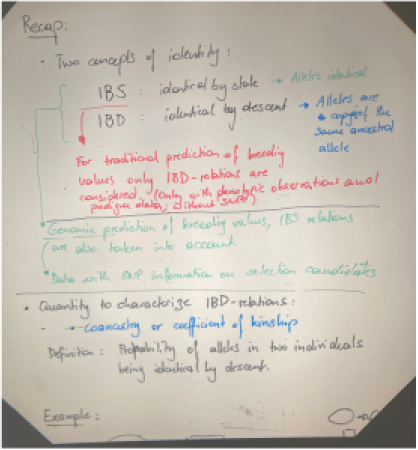
Recap


Recap:

- Two concepts of identity:
  - IBS : identical by state → Alleles identical
  - IBD : identical by descent → Alleles are copy 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)

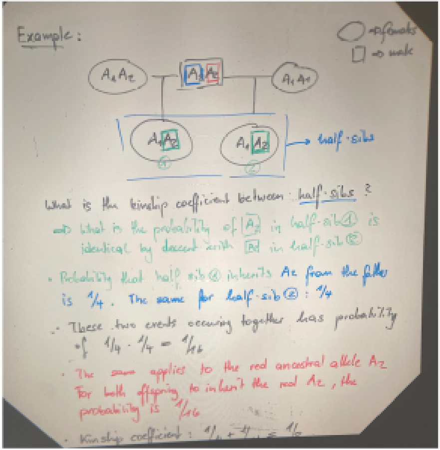
- Genomic prediction of breeding values, IBS relations are also taken into account
- Data with SNP information on selection candidates

- Quantity to characterize IBD-relations:
  - → coancestry or coefficient of kinship

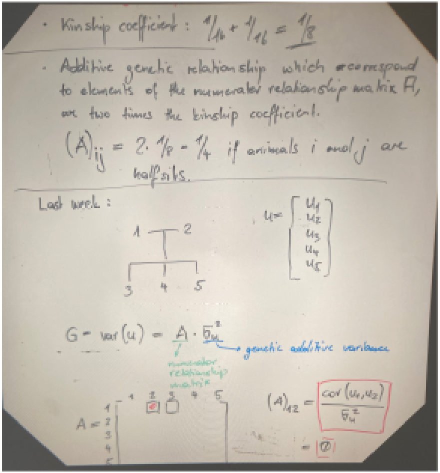
Definition: Probability of alleles in two individuals being identical by descent.

Example:

Example


Example:
→ female
→ male
A1A2
A1A2
A1A1
A1A2
A1A2
→ half-sibs
What is the kinship coefficient between half-sibs?
→ what is the probability of A in half-sib ① is identical by descent with in half-sib ②
Probability that half sib ① inherits A2 from the father is 1/4. The same for half-sib ②: 1/4
∴ These two events occurring together has probability of 1/4 · 1/4 = 1/16
The same applies to the red ancestral allele A2
For both offspring to inherit the red A2, the probability is 1/16
Kinship coefficient:

Kinship Coefficient



Genetic Relationship

numerator relationship matrix

$$A = \begin{array}{c|ccccc} & 1 & 2 & 3 & 4 & 5 \\ \hline 1 & & \boxed{0} & \boxed{} & & \\ 2 & & & & & \\ 3 & & & & & \\ 4 & & & & & \\ 5 & & & & & \end{array}$$

$$(A)_{12} = \boxed{\frac{cov(u_1, u_2)}{\sigma_u^2}} = \boxed{0}$$

$$(A)_{1\boxed{3}} = \frac{cov(u_1, u_3)}{\sigma_u^2} = \frac{cov(u_1, [\frac{1}{2}u_1 + \frac{1}{2}u_2 + m_3])}{\sigma_u^2}$$

replaced by parents 1 and 2

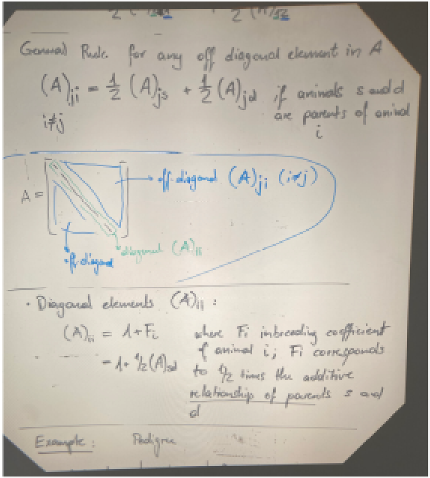
$$u_3 = \frac{1}{2}u_1 + \frac{1}{2}u_2 + m_3$$

$$= \frac{cov(u_1, \frac{1}{2}u_1)}{\sigma_u^2} + \frac{cov(u_1, \frac{1}{2}u_2)}{\sigma_u^2} + \underbrace{\frac{cov(u_1, m_3)}{\sigma_u^2}}_{=0}$$

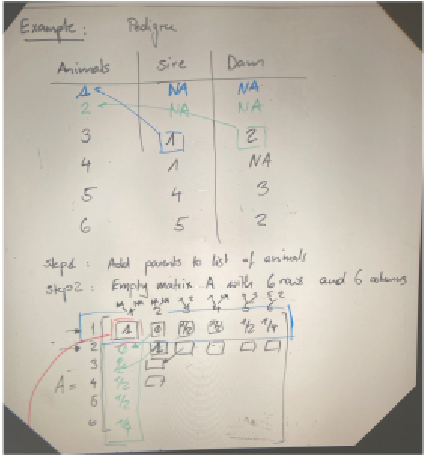
$$= \frac{1}{2}\underbrace{\boxed{\frac{cov(u_1, u_1)}{\sigma_u^2}}}_{(A)_{11}} + \frac{1}{2}\underbrace{\boxed{\frac{cov(u_1, u_2)}{\sigma_u^2}}}_{(A)_{12}}$$

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

General Rule



Example



Example:
Pedigree
Animals
Sire
Dam
1 NA NA
2 NA NA
3 1 2
4 1 NA
5 4 3
6 5 2
step1: Add parents to list of animals
step2: Empty matrix A with 6 rows and 6 columns

Example II

Diagonal element:

$$(A)_{11} = 1 + F_1 = 1 + \frac{1}{2}\underbrace{(A)_{11,11}}_{=0} = 1$$

Off diagonal:

$$(A)_{12} = \frac{1}{2}(A)_{1,11} + \frac{1}{2}(A)_{11,11} = 0$$

$$(A)_{13} = \frac{1}{2}\boxed{(A)_{11}} + \frac{1}{2}(A)_{12} = \frac{1}{2}\cdot 1 + \frac{1}{2}\cdot 0 = \frac{1}{2}$$

$$(A)_{14} = \frac{1}{2}(A)_{11} + \frac{1}{2}(A)_{1,11} = \frac{1}{2}$$

$$(A)_{15} = \frac{1}{2}(A)_{14} + \frac{1}{2}(A)_{13} = \frac{1}{2}\cdot 1/2 + 1/2\cdot 1/2 = 1/2$$

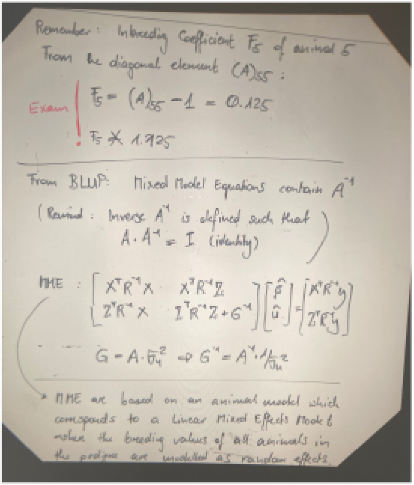
$$(A)_{16} = \frac{1}{2}(A)_{15} + 1/2\,(A)_{12} = 1/2\cdot 1/2 + 1/2\cdot 0 = 1/4$$

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

Step 4: Continue with row 2:

Diagonal: $(A)_{22} = 1 + F_2 = 1 + \frac{1}{2}(A)_{11,11} = 1$

Matrix A and BLUP



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

Exam

$F_5 = (A)_{55} - 1 = 0.125$

$F_5 \neq 1.125$

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

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

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

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

* MME are based on an animal model which corresponds to a Linear Mixed Effects Model when 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 ⇒ Ok

⇒ 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 ⇒

$L = $

and D is a diagonal

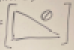
LDL

A.

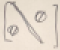
- From Linear Algebra it is known that symmetric matrices can be decomposed into a product of three factors:

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

where L is lower triangular matrix $\Rightarrow$

$L =$ 

and D is a diagonal matrix

$D =$ 

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 d
m_i is the mendelian sampling term of animal i.

→ for example pedigree:

$$\begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \end{bmatrix} \begin{aligned} &= 0 + 0 + m_1 \\ &= \tfrac{1}{2} u_{UA} + \tfrac{1}{2} u_{UA} + m_2 = m_2 \\ &= m_3 \\ &= \tfrac{1}{2} u_1 + \tfrac{1}{2} u_2 + m_4 \\ &= \tfrac{1}{2} u_3 + \tfrac{1}{2} u_2 + m_5 \end{aligned} \quad \Bigg\} \ \boxed{\text{set of equations}}$$

write equations in matrix vector notation

Simple Decomposition II