Isfahan
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Animal Breeding Theory

Introduction

- Genetic models and genetic parameters
  - Basic genetic model – h^2
  - Transmission model
  - Common environmental model – c^2
  - Repeatability model - r
  - Multiple traits – genetic and phenotypic correlations
- Genetic relationships between individuals
  - Additive genetic relationship
  - Inbreeding
  - Tabular method – A-matrix

Introduction

Why do we need genetic models?

Understanding and quantifying resemblance between relatives

Which "part of the resemblance" is due to genetics and what is environmental.

- Estimating breeding values.
- Estimating genetic parameters.

Basic genetic model

- Partitioning of variance
  - P = G + E
  - Var(P) = Var(G+E) = Var(G) + Var(E) + 2 Cov(G,E)
- H^2 = broad sense heritability = proportion of differences that is due to genetics
- Ratio of variances:

$$H^2 = \frac{Var(G)}{Var(P)} = \frac{\sigma_G^2}{\sigma_P^2}$$

  - $H^2 \in [0 \ldots. 1]$

Heritability h^2 (narrow sense)

- Partitioning of variance
  - P = G + E
    = A + D + I + E
  - Var(P) = Var(A) + Var(D) + Var(I) + Var(E)
- h^2 = proportion of differences that is due to differences in breeding values (A):

$$h^2 = \frac{Var(A)}{Var(P)} = \frac{\sigma_A^2}{\sigma_P^2}$$

  - $h^2 \in [0 \ldots. 1]$
  - $h^2 \leq H^2$

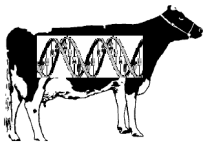
Heritability

Phenotype = Genotype + Environment

High heritability (h^2 =1)

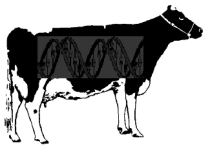
Phenotype = Genetics

"What-you-see-is-what-you-get"



Low heritability (h^2 =0)

Phenotype = Environment



Heritability

Note:

Variances are calculated after the data has been adjusted for systematic environmental effects.

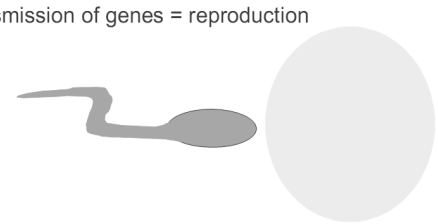
$$\mathbf{y} = \mathbf{X}\,\mathbf{b} + \mathbf{Z}\,\mathbf{u} + \mathbf{e}$$

$\sigma_y^2 \neq \sigma_P^2$

Transmission model

Deals with the transmission of genes from parents to offspring.

Transmission of genes = reproduction



Half of the genes come from the sire, the other half from the dam.

Transmission model

Half of the genes come from the sire, the other half from the dam.

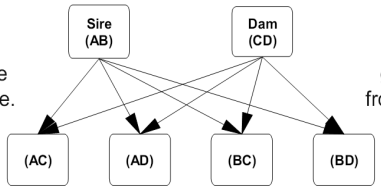
Breeding value offspring: $A_{off} = ½A_{sire} + ½A_{dam}$????

This would imply that full sisters/brothers are identical: they have the same sire and the same dam. Is this the case?

Let's look at the inheritance of a single gene.

Transmission model

Half of the genes come from the sire.



Half of the genes come from the dam.

Which "half" is transmitted by sire or dam is unknown = **Mendelian sampling**

$$A_{Offspring} = \tfrac{1}{2} A_S + \tfrac{1}{2} A_D + MS$$

1/1
1/-1
-1/-1

Simple example:

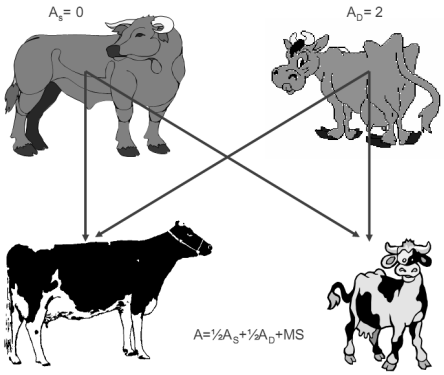
- Three genes
- Additive effect (no dominance)
- Each allele has an effect of 1
- We simply add the effects to obtain the breeding value:
- A_S= 1+1+1-1-1-1 = 0

A_s= 0

A_D= 2

1/1
1/-1
-1/-1

1/-1
1/1
1/-1



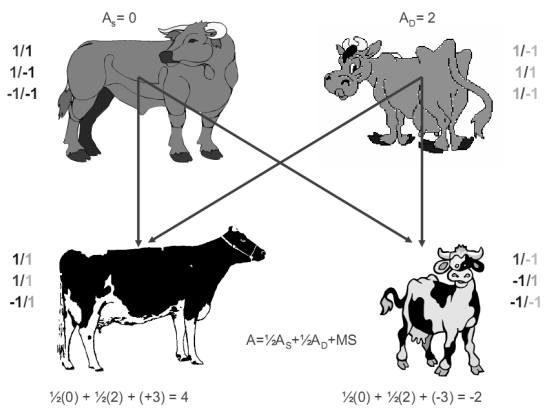
1/1
1/1
-1/1

1/-1
-1/1
-1/-1

A=½A_S+½A_D+MS

½(0) + ½(2) + (+3) = 4

½(0) + ½(2) + (-3) = -2



Transmission model

Variance

$$\mathrm{var}\left(A_{Offspring}\right) = \mathrm{var}\left(\tfrac{1}{2} A_S + \tfrac{1}{2} A_D + MS\right)$$
$$= \mathrm{var}\left(\tfrac{1}{2} A_S\right) + \mathrm{var}\left(\tfrac{1}{2} A_D\right) + \mathrm{var}\left(MS\right)$$
$$\mathrm{var}\left(A_{Offspring}\right) = \tfrac{1}{4}\sigma_A^2 + \tfrac{1}{4}\sigma_A^2 + \mathrm{var}\left(MS\right)$$

➲ Mendelian sampling represents: $\tfrac{1}{2}\sigma_A^2$

$$\mathrm{var}\left(A_{Offspring}\right) = \sigma_A^2 = \tfrac{1}{4}\sigma_A^2 + \tfrac{1}{4}\sigma_A^2 + \tfrac{1}{2}\sigma_A^2$$

- MS = Independent of everything else - uncertainty!!
- Infinitesimal model: Variance of breeding values does not change from one generation to the next

Transmission model

Genetic model (for half sibs):

$$P_{ij} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ji}} + MS_{ij} + E_{ij}$$

P_{ij} = phenotypic observation on offspring j of sire i

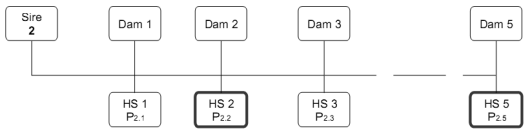
- What is the resemblance between half sibs, i.e. individuals with one parent in common ?

  paternal half sibs and maternal half sibs
- Resemblance for which trait?
- How to quantify resemblance? ➲ covariance

Transmission model

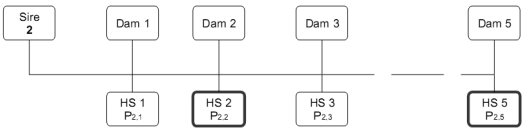
Genetic model (for half sibs):

$$P_{ij} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ji}} + MS_{ij} + E_{ij}$$



What is the resemblance (covariance) in milk production between daughter 2 of sire 2 and daughter 5 of sire 2?

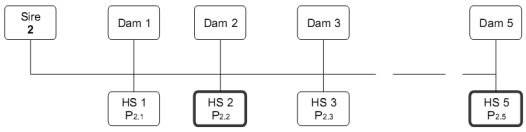
Transmission model



Why would their milk production be similar (show resemblance) ?

They have the same father and therefore they will have partly the same “milk production genes”.

Transmission model



$$P_{2,2} = \mu + \tfrac{1}{2} A_{S_2} + \tfrac{1}{2} A_{D_{2,2}} + MS_{2,2} + E_{2,2}$$

$$P_{2,5} = \mu + \tfrac{1}{2} A_{S_2} + \tfrac{1}{2} A_{D_{2,5}} + MS_{2,5} + E_{2,5}$$

$$Cov(P_{2,2}, P_{2,5}) = ?$$

Transmission model

$$Cov(P_{2,2}, P_{2,5}) =$$
$$Cov(\mu + \tfrac{1}{2} A_{S_2} + \tfrac{1}{2} A_{D_{2,2}} + MS_{2,2} + E_{2,2}\ ,\ \mu + \tfrac{1}{2} A_{S_2} + \tfrac{1}{2} A_{D_{2,5}} + MS_{2,5} + E_{2,5})$$

$$\begin{aligned} Cov(P_{2,2}, P_{2,5}) = \\ & Cov(\tfrac{1}{2} A_{S_2}, \tfrac{1}{2} A_{S_2}) + Cov(\tfrac{1}{2} A_{S_2}, \tfrac{1}{2} A_{D_{2,5}}) + Cov(\tfrac{1}{2} A_{S_2}, MS_{2,5}) + Cov(\tfrac{1}{2} A_{S_2}, E_{2,5}) + \\ & Cov(\tfrac{1}{2} A_{D_{2,2}}, \tfrac{1}{2} A_{S_2}) + Cov(\tfrac{1}{2} A_{D_{2,2}}, \tfrac{1}{2} A_{D_{2,5}}) + Cov(\tfrac{1}{2} A_{D_{2,2}}, MS_{2,5}) + Cov(\tfrac{1}{2} A_{D_{2,2}}, E_{2,5}) + \\ & Cov(MS_{2,2}, \tfrac{1}{2} A_{S_2}) + Cov(MS_{2,2}, \tfrac{1}{2} A_{D_{2,5}}) + Cov(MS_{2,2}, MS_{2,5}) + Cov(MS_{2,2}, E_{2,5}) + \\ & Cov(E_{2,2}, \tfrac{1}{2} A_{S_2}) + Cov(E_{2,2}, \tfrac{1}{2} A_{D_{2,5}}) + Cov(E_{2,2}, MS_{2,5}) + Cov(E_{2,2}, E_{2,5}) \end{aligned}$$

$$Cov(P_{2,2}, P_{2,5}) = Cov(\tfrac{1}{2} A_{S_2}, \tfrac{1}{2} A_{S_2}) = Var(\tfrac{1}{2} A_{S_2}) = \tfrac{1}{4}\sigma_A^2$$

Transmission model

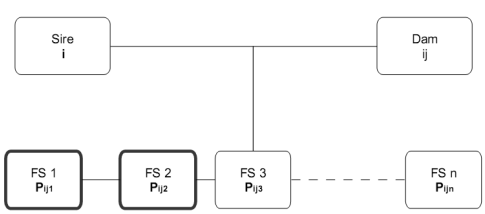
Genetic model (for full sibs):

$$P_{ijk} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ji}} + MS_{ijk} + E_{ijk}$$

P_{ijk} = phenotypic observation on offspring k of sire I and dam ij

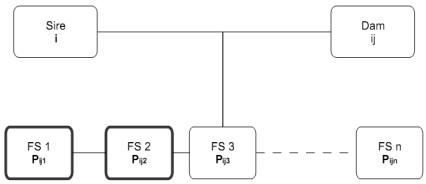
What is the resemblance between full sibs, i.e. individuals with both parents in common ?

Transmission model



What is the resemblance (covariance) in egg production between daughter 1 of sire i and dam ij and daughter 2 of the same sire and dam?

Transmission model



$$P_{ij1} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ji}} + MS_{ij1} + E_{ij1}$$

$$P_{ij2} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ji}} + MS_{ij2} + E_{ij2}$$

$$\begin{aligned}\operatorname{cov}(P_{ij1}, P_{ij2}) = & \quad = \operatorname{cov}\left(\tfrac{1}{2} A_{S_i}, \tfrac{1}{2} A_{S_i}\right) + \operatorname{cov}\left(\tfrac{1}{2} A_{D_{ji}}, \tfrac{1}{2} A_{D_{ji}}\right) \\ & = \tfrac{1}{4}\sigma_A^2 + \tfrac{1}{4}\sigma_A^2\end{aligned}$$

Common environment model

Genetic model for half sibs

$$P_{ij} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ji}} + MS_{ij} + E_{ij}$$

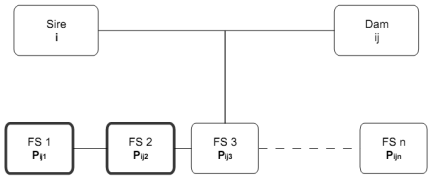
Genetic model for full sibs

$$P_{ijk} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ij}} + MS_{ijk} + E_{ijk}$$

$$P_{ijk} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ij}} + MS_{ijk} + E_{C_{ij}} + E_{ijk}$$

Individuals with the same (father and) mother also share part of their environment

Common environment model



$$P_{ij1} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ji}} + MS_{ij1} + E_{c_{ij}} + E_{ij1}$$

$$P_{ij2} = \mu + \tfrac{1}{2} A_{S_i} + \tfrac{1}{2} A_{D_{ji}} + MS_{ij2} + E_{c_{ij}} + E_{ij2}$$

$$\begin{aligned}\operatorname{cov}(P_{ij1}, P_{ij2}) = & \quad = \operatorname{cov}\left(\tfrac{1}{2} A_{S_i}, \tfrac{1}{2} A_{S_i}\right) + \operatorname{cov}\left(\tfrac{1}{2} A_{D_{ji}}, \tfrac{1}{2} A_{D_{ji}}\right) + \operatorname{cov}\left(E_{c_{ij}}, E_{c_{ij}}\right) \\ & = \tfrac{1}{4}\sigma_A^2 + \tfrac{1}{4}\sigma_A^2 + \sigma_{E_c}^2\end{aligned}$$

Common environment model

lambs in same litter are similar:

- genetics (full sibs)
- mother care
- nutrition
- same pen

Individuals in this case resemble each other not only because the have genes in common but also because the have experienced some of the same environmental effects.

Common environment model

$$c^2 = \frac{\sigma^2_{E_C}}{\sigma^2_P}$$

$c^2_{FS}, c^2_{MZ}, c^2_{DZ}$

The repeatability model

Repeated measures of the <u>same trait on the same individual</u>.

- repeated in time: weight of a fish on 120 days and 130 days.
- measurement of backfat of a lamb at different locations.
- measure the strength of 2 eggs.

The repeatability model

$$P_{ij} = \mu + G_i + E_{p_i} + E_{t_{ij}}$$

P_{ij} = phenotypic observation j on individual i

μ = overall mean

G_i = genetic value of individual 1

E_{p_i} = <u>permanent</u> environmental effect on individual i

$E_{t_{ij}}$ = <u>temporary</u> environmental effect on repeated observation j of individual i

The repeatability model

Backfat measurement lamb 1 location 1 and location 2:

$$P_{1,1} = \mu + G_1 + E_{P_1} + E_{t_{1,1}}$$

$$P_{1,2} = \mu + G_1 + E_{P_1} + E_{t_{1,2}}$$

Covariance between backfat measurement lamb 1 location 1 and location 2:

$$\begin{aligned} Cov(P_{1,1}, P_{1,2}) &= Cov(G_1, G_1) + Cov(E_{P_1}, E_{P_1}) \\ &= Var(G_1) + Var(E_{P_1}) \\ &= \sigma_G^2 + \sigma_{E_P}^2 \end{aligned}$$

The repeatability model

Correlation between repeated observations:

$$\frac{Cov(P_{1,1}, P_{1,2})}{\sqrt{Var(P_{1,1}) * Var(P_{1,2})}} = \frac{\sigma_G^2 + \sigma_{E_P}^2}{\sqrt{\sigma_P^2 * \sigma_P^2}} = \frac{\sigma_G^2 + \sigma_{E_P}^2}{\sigma_P^2} = r$$

i.e. the repeatability.

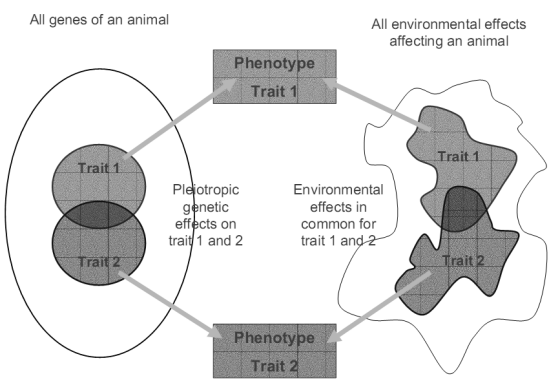
- $r \in [0 \ldots 1]$
- $r \geq h^2$

Repeatability is also being used to asses the quality of a measurement: if we redo a measurement does it give the same result?

Multiple traits

Similarity between traits

- Examples
  - Individuals that eat more also grow faster → positive relationship
  - Cows that produce more milk generally also have poorer fertility → negative relationship
- Causes of similarity between traits
  - Genetics: Traits are affected by the same genes
    genes increasing feed intake also increase growth rate
  - Environment: environmental effects work systematically in the same or opposite direction
    better tasting feed increases both intake and growth rate



Multiple traits

- Measures of similarity: Correlation between traits
- Phenotypic correlation
  - Correlation between phenotypes for both traits
  - Strength of the relationship between the phenotypes for both traits
  - If I know the actual feed intake, how **accurately** do I know the growth rate?

$$r_P = \frac{Cov(P_x, P_y)}{\sqrt{\sigma^2_{P_x} \cdot \sigma^2_{P_y}}}$$

Multiple traits

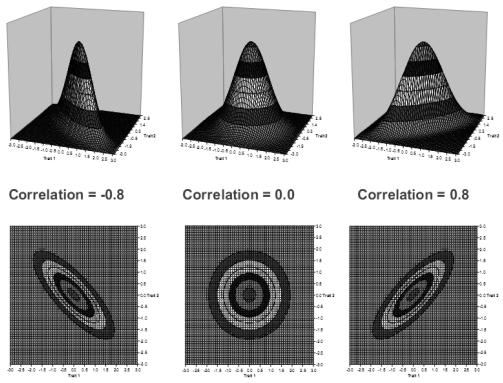
- (Additive) genetic correlation
  - Correlation between the (true) breeding values for both traits.
  - Strength of the relationship between the breeding values for both traits
  - If I know the breeding value for feed intake, how accurately do I know the breeding value for growth rate?

$$r_A = \frac{Cov(A_x, A_y)}{\sqrt{\sigma^2_{A_x} \cdot \sigma^2_{A_y}}}$$

Multiple traits

- Environmental correlation
  - Correlation between the environmental effects on both traits.

$$r_E = \frac{Cov(E_x, E_y)}{\sqrt{\sigma^2_{E_x} \cdot \sigma^2_{E_Y}}}$$



Multiple traits

$$r_P = \frac{Cov(A_x, A_y) + Cov(E_x, E_y)}{\sigma_{P_x}\sigma_{P_y}}$$

$$= \frac{r_A\sigma_{A_x}\sigma_{A_y} + r_E\sigma_{E_x}\sigma_{E_y}}{\sigma_{P_x}\sigma_{P_y}}$$

$$= \frac{r_A\sigma_{A_x}\sigma_{A_y}}{\sigma_{P_x}\sigma_{P_y}} + \frac{r_E\sigma_{E_x}\sigma_{E_y}}{\sigma_{P_x}\sigma_{P_y}}$$

$$r_P = r_A h_x h_y + r_E\sqrt{1-h_x^2}\sqrt{1-h_y^2}$$

Summary

Genetic Models

- Basic genetic model $\boldsymbol{P_i} = \mu + \boldsymbol{G_i} + \boldsymbol{E_i}$
- Transmission model $A_{Offspring} = \frac{1}{2}A_S + \frac{1}{2}A_D + MS$
- Common environmental model $P_{ijk} = \mu + \frac{1}{2}A_{S_i} + \frac{1}{2}A_{D_{ij}} + MS_{ijk} + E_{C_{ij}} + E_{ijk}$
- Repeatability model $\boldsymbol{P_{ij}} = \mu + \boldsymbol{G_i} + \boldsymbol{E_{p_i}} + \boldsymbol{E_{t_{ij}}}$
- Multiple traits

$$P_x = \mu_x + A_x + E_x$$

$$P_y = \mu_y + A_y + E_y$$

Summary

Parameters:

Heritability $\mathbf{h}^2 = \frac{\sigma_A^2}{\sigma_P^2}$

Common environmental effects $\mathbf{c}^2 = \frac{\sigma_{E_C}^2}{\sigma_P^2}$

Repeatability $\mathbf{r} = \frac{\sigma_G^2 + \sigma_{E_P}^2}{\sigma_P^2}$

Phenotypic, genetic and environmental correlations

$$r_P = r_A h_x h_y + r_E\sqrt{1-h_x^2}\sqrt{1-h_y^2}$$

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  - Multiple traits – genetic and phenotypic correlations
- Genetic relationships between individuals
  - Additive genetic relationship
  - Inbreeding
  - Tabular method – A-matrix

Introduction

Introduction

Our interest is in genetics and we want to separate genetic effects from environmental effects.

A tool that we need for that purpose is some way of quantifying resemblance through family ties.

Topics

- The coefficient of kinship
- The additive genetic relationship
- The inbreeding coefficient
- General pedigrees

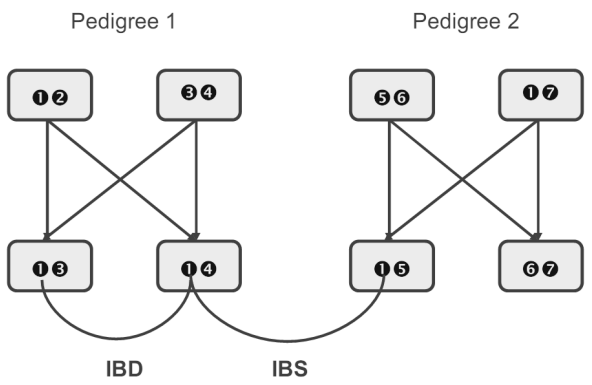
The coefficient of kinship

The coefficient of kinship or

Malecot relationship or

Coefficient of coancestry

the probability that a randomly drawn allele from one individual is identical by descent to a randomly drawn allele from another individual.



The coefficient of kinship

The coefficient of kinship or Malecot relationship or Coefficient of coancestry

the probability that a randomly drawn allele from one individual is identical by descent to a randomly drawn allele from another individual.

The only way in which individuals can have alleles IBD if they have (a) common ancestor(s).

The coefficient of kinship

X (i, j) Y (m, n)

4 possibilities of randomly drawing an allele from X and one from Y:

X	Y	Prob.
i	m	¼
i	n	¼
j	m	¼
j	n	¼

The coefficient of kinship

X (i, j) Y (m, n)

4 possibilities of randomly drawing an allele from X and one from Y:

X	Y	Prob.
i	m	¼
i	n	¼
j	m	¼
j	n	¼

$$f_{X,Y} = \frac{p(i \equiv m) + p(i \equiv n) + p(j \equiv m) + p(j \equiv n)}{4}$$

The additive genetic relationship

$$a_{X,Y} = 2 f_{X,Y}$$

- Kinship: relates to one allele from each individual
- diploid: 2 alleles
- $a_{X,Y}$ = resemblance between breeding values of individual x and y
- depends on the proportion of alleles shared.
- kinship is a probability $\in$ [0 …. 1], additive genetic relationship $\in$ [0 …. 2],

The additive genetic relationship

Formal meaning of $a_{X,Y}$ (when there is no inbreeding):

$a_{X,Y}$ = correlation between breeding values of individual X and individual Y.

resemblance ~ correlation

$$a_{X,Y} = \frac{Cov(A_x, A_Y)}{\sigma_A^2}$$

The additive genetic relationship

Examples:

- $a_{X,X}$: relationship with yourself

$$a_{X,X} = \frac{Cov(A_x, A_X)}{\sigma_A^2} = \frac{\sigma_A^2}{\sigma_A^2} = 1$$

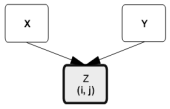
Interpretation: you share 100% of your alleles with yourselves

- $a_{P,O}$: relationship between parent and offspring

$$a_{P,O} = \frac{Cov(A_P, A_O)}{\sigma_A^2} = \frac{Cov(A_P, \tfrac{1}{2} A_P + \tfrac{1}{2} A_{P'} + MS)}{\sigma_A^2} = \frac{\tfrac{1}{2}\sigma_A^2}{\sigma_A^2} = \tfrac{1}{2}$$

Inbreeding coefficient

The inbreeding coefficient (F_i) of an individual is the probability that both alleles at a randomly taken locus are Identical By Descent.

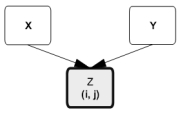


$F_Z = p(i \equiv j)$

i can be regarded as a randomly drawn allele from X and j as a randomly drawn allele from Y.

➲ $F_Z = p(i \equiv j) = f_{X,Y} = \tfrac{1}{2} a_{X,Y}$

Inbreeding coefficient



$F_Z = p(i \equiv j)$

$$f_{Z,Z} = \frac{p(i=i)+p(i=j)+p(j=i)+p(j=j)}{4}$$

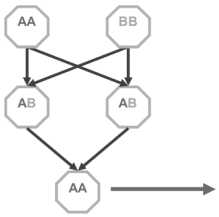
$$= \frac{1+F_Z+F_Z+1}{4} = \tfrac{1}{2}+\tfrac{1}{2}F_Z$$

$a_{Z,Z} = 1+F_Z$

Inbreeding coefficient

$F_{Offspring} = ½a_{S,D}$

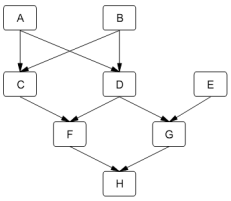
- Offspring is only inbred if the parents are related!!
- Inbreeding = mating of related individuals



Alleles are IBD, F=?

General pedigrees

➲ Additive genetic relationships can be derived based on kinship coefficients.



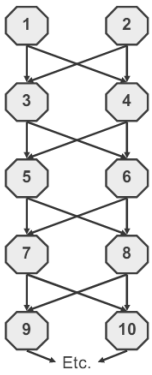
- What is F_H?
- $F_H = ½a_{F,G} = f_{F,G}$
- = probability that randomly drawn allele from F is IBD to randomly drawn allele from G

General pedigrees

Two methods to calculate $a_{X,Y}$ (based on that $f_{X,Y}$ and F_z)

1. Method of tracing paths
   - for small pedigrees $a_{X,Y} = \sum_{i=1}^{n} \left(\frac{1}{2}\right)^{(n_i+p_i)} \left(1+F_{W_i}\right)$
   - use only in simple cases
   - complex pedigree: mistakes are easily made
2. Tabular methods
   - simple to apply to any pedigree
   - a lot of work by hand
   - computer program

Exercise



What is the inbreeding coefficient of individual 7?

Assume that 1 and 2 are not inbred.

$F_{Offspring} = ½ a_{S,D}$

General

Common relationships

relationship	a_{XY}	d_{XY}
mono-zygous twins	1	1
sire-offspring	½	0
dam-offspring	½	0
grandparent - offspring	¼	0
full sibs	½	¼
half sibs	¼	0

Covariances between relatives

Covariances between observations on relatives.

Covariance – quantifies the resemblance

What is the resemblance between the milk production of the mother and the daughter ?

We need a genetic model:

$Cov(X_1,X_2)$

X_1 = milk production daughter = $A_O + E_O$

X_2 = milk production mother = $A_D + E_D$

General

$Cov(X_1,X_2) = Cov(A_O + E_O, A_D + E_D)$

$= Cov(A_O, A_D)$
$+ Cov(A_O, E_D)$
$+ Cov(E_O, A_D)$
$+ Cov(E_O, E_D)$

$= Cov(A_O, A_D)$

General

$Cov(A_O, A_D) = ?$

Transmission model

$A_O = ½A_S + ½A_D + MS$

$A_D = A_D$

Substituting gives:

$Cov(A_O,A_D) =$

$Cov(½A_S, A_D) + Cov(½A_D, A_D) + Cov(MS, A_D)$

General

$Cov(A_1,A_2) =$

$Cov(½A_S, A_D) + Cov(½A_D, A_D) + Cov(MS, A_D)$

$Cov(½A_S, A_D) = 0$

$Cov(MS, A_D) = 0$

$Cov(½A_D, A_D) = \frac{1}{2}\sigma_A^2$

What is the resemblance between the milk production of the mother and the daughter ?

$\frac{1}{2}\sigma_A^2$ ½ is the additive genetic relationship between mother and daughter

General

General:

$$Cov(X_1, X_2) = a_{12}\sigma_A^2$$

More general

$$Cov(X_1, X_2) = a_{12}\sigma_A^2 + d_{12}\sigma_D^2 + c^2\sigma_P^2$$