Variance Components Estimation

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Context

* Breeding organisation wants to include a new trait into an aggregate genotype (breeding goal), alternatively want to start a new breeding goal
* Last week: Model selection
* Assume: Genetic evaluation is done with a mixed linear effect model:

$$y = \boxed{Xb} + \boxed{Zu} + \underline{e}$$

Model selection determines which are relevant fixed effects (b) in our model. The reduction of the number of fixed effects to the relevant set of fixed effects is nessesary to avoid the bias-variance trade-off.

* Variance components estimation, is the topic that tells us how to estimate variance components, and these are included in the variance-covariance matrices of the random effects

var(u) , var(e)

Genetic Variation

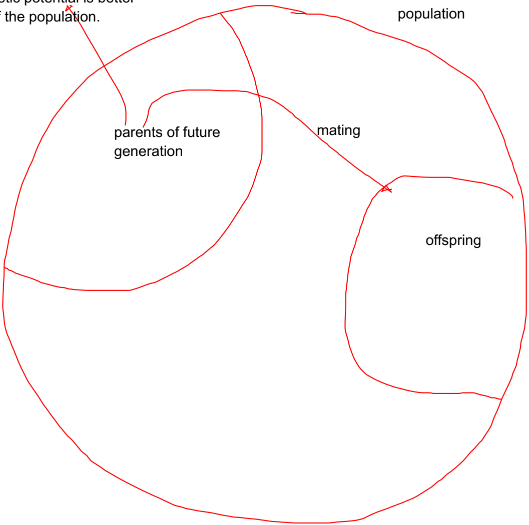
- Requirement for trait to be considered in breeding goal
- Breeding means improvement of next generation via selection and mating
- Only genetic (additive) components are passed to offspring
- Selection should be based on genetic component of trait
- Selection only possible with genetic variation

→ genetic variation indicates how good characteristics are passed from parents to offspring

→ measured by **heritability** $h^2 = \frac{\sigma_a^2}{\sigma_p^2}$

parents are selected from a pool of selection candidates, if their genetic potential is better compared to the rest of the population.

Genetic potential is the value of the random sample of alleles passed from parents to offspring. Value of genetic sample is estimated by the predicted breeding value.



population

parents of future generation

mating

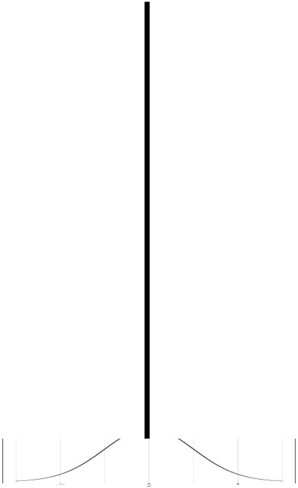
offspring

Selection of parents from a pool of candidates is only possible, if there is variation in the values of the genetic potential. Without any variation, all the values of the genetic potentials would be the same for all animals, and hence no parents could be selected.

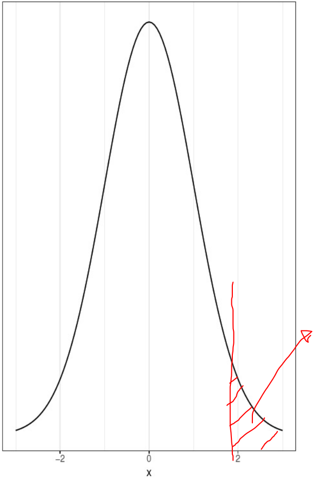
Two Traits

density plots for the genetic potential of two traits

no variation



with variation



parents

Problems

Question: How to quantify the variation of the genetic potential of all animals in the population for our trait of interest?

- Genetic components cannot be observed or measured
- Must be estimated from data
- Data are mostly phenotypic

At the moment: Ignoring the possibility of collecing genomic information for animals in our population

→ topic of variance components estimation

- Model based, that means connection between phenotypic measure and genetic component are based on certain model

Genetic Model:

$$p = g + e$$

quantify the part of the overall variation in the phenotypic observation caused by variation in g

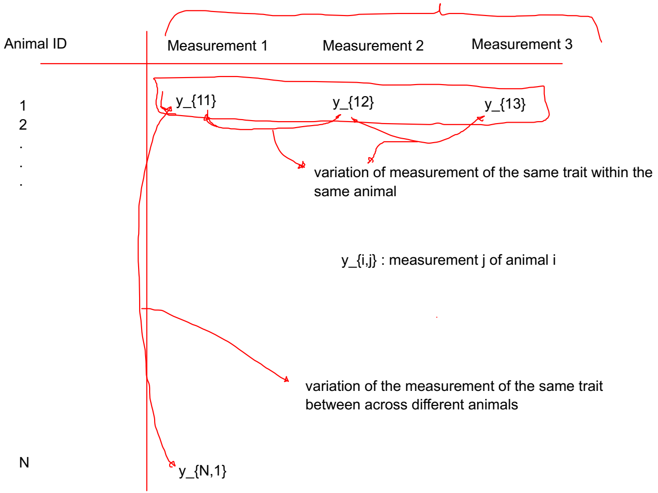
with $cov(g, e) = 0$

- **Goal**: separate variation due to g (σ_a^2) from phenotypic variation

Example of Variance Components Separation

- Estimation of repeatability
- Given repeated measurements of same trait at the same animal
- Repeatability means variation of measurements at the same animal is smaller than variation between measurements at different animals

Repeatability dataset



Example: Weight, height, lactations

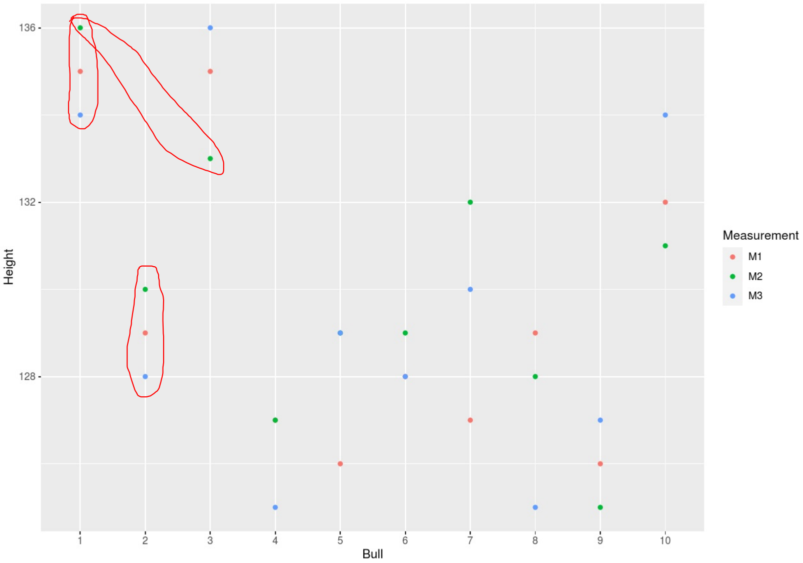
Animal ID	Measurement 1	Measurement 2	Measurement 3
1	y_{11}	y_{12}	y_{13}
2			
.			
.			
.			
N	$y_{N,1}$		

variation of measurement of the same trait within the same animal

$y_{i,j}$: measurement j of animal i

variation of the measurement of the same trait between across different animals

Repeatability Plot



Model

Assume: Measurements are influenced by
animal i and by other factors,
y_{i,j} = animal_i + e_{i,j}
where: animal_i stands for the effect of the
value of y_{ij} caused by animal i

$$y_{ij} = \underbrace{\overset{\text{overall mean, E(y)}}{\boxed{\mu}} + t_i}_{\text{animal\_i}} + \underline{\epsilon_{ij}}$$

where

y_{ij} measurement j of animal i

μ expected value of y

t_i deviation of y_{ij} from μ attributed to animal i

ϵ_{ij} measurement error

Estimation Of Variance Components

Because, effects t_i are defined as deviations

- $E(t_i) = 0$ $\quad \sigma_t^2 = E\left[\left(t - \underbrace{E(t)}_{=0}\right)^2\right] = E(t^2)$
- $\sigma_t^2 = E(t_i^2)$: variance component of total variance (σ_y^2) which can be attributed to the t-effects
- $E(\epsilon_{ij}) = 0$

measurement errors are also deviations

- $\sigma_\epsilon^2 = E(\epsilon_{ij}^2)$: variance component attributed to ϵ-effects
- $\sigma_y^2 = \sigma_t^2 + \sigma_\epsilon^2$ $\Longrightarrow$ $y_{ij} = \mu + t_i + \epsilon_{ij}$

compute the total variance

$$\sigma_y^2 = Var(y_{ij}) = Var(\ldots)$$

- Repeatability w defined as:

$$w = \frac{\sigma_t^2}{\sigma_t^2 + \sigma_\epsilon^2} = \frac{\sigma_t^2}{\sigma_y^2}$$

→ estimate of σ_t^2 needed

Model: $y_{ij} = \underbrace{\mu + t_i + \varepsilon_{ij}}$

Overall variation: $\sigma_y^2 = var(y_{ij}) = var(\mu + t_i + \varepsilon_{ij})$

$$= \overbrace{var(\mu)}^{=0} + var(t_i) + var(\varepsilon_{ij})$$

$$+ 2\underbrace{cov(\mu, t_i) + 2cov(\mu, \varepsilon_{ij}) + 2cov(t_i, \varepsilon_{ij})}_{=0}$$

$$= var(t_i) + var(\varepsilon_{ij})$$

$$= \sigma_t^2 + \sigma_\varepsilon^2$$

Analysis Of Variance (ANOVA)

ANOVA-Table

Sum of Squares

Mean Sum of Squares

Effect	df	Sum Sq	Mean Sq	$E(Mean\ Sq)$
Bull (t)	$r-1$	$SSQ(t)$	$SSQ(t)/(r-1)$	$\sigma_\epsilon^2 + n * \sigma_t^2$
Residual (ϵ)	$N-r$	$SSQ(\epsilon)$	$SSQ(\epsilon)/(N-r)$	σ_ϵ^2

where

Total number of observations

$$SSQ(t) = \left[\frac{1}{n}\sum_{i=1}^{r}\left(\sum_{j=1}^{n} y_{ij}\right)^2\right] - \left(\sum_{i=1}^{r}\sum_{j=1}^{n} y_{ij}\right)^2 / N$$

sum over all squared measurements for animal i

$$SSQ(\epsilon) = \sum_{i=1}^{r}\boxed{\sum_{j=1}^{n}} y_{ij}^2 - \left[\frac{1}{n}\sum_{i=1}^{r}\underbrace{\left(\sum_{j=1}^{n} y_{ij}\right)}_{}^2\right]$$

sum of M

Dataset

Animal	Measurements	Sum of Squares
1	$y_{11}^2 + y_{12}^2 + y_{13}^2 \to$	$\sum_{j=1}^{3} y_{ij}^2$; $i=1$
		+
2	$y_{21}^2 + y_{22}^2 + y_{23}^2 \to$	$\sum_{j=1}^{3} y_{ij}^2$; $i=2$
		+
N		
Total		$\sum_{i=1}^{N} \sum_{j=1}^{3} y_{ij}^2$

Zahlenbeispiel

In R: aov()

```
##              Df Sum Sq Mean Sq F value   Pr(>F)
## Bull          9  286.7   31.85   13.85 8.74e-07 ***
## Residuals    20   46.0    2.30
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Estimate of the residual variance component

Setting expected values of Mean Sq equal to estimates of variance components

$$E(MSQ_t) = \sigma_\varepsilon^2 + n\sigma_t^2 \Rightarrow \hat{\sigma}_t^2 = \frac{MSQ_t - \hat{\sigma}_\varepsilon^2}{n}$$

$$\underbrace{\hat{\sigma}_\epsilon^2 = 2.3}\text{ and }\hat{\sigma}_t^2 = \frac{31.85 - 2.3}{3} = \underset{\sim}{9.85}$$

Estimate of t- variance component

Repeatability

$$\hat{\sigma}_y^2 = \hat{\sigma}_\varepsilon^2 + \hat{\sigma}_t^2$$

$$\hat{w} = \frac{\hat{\sigma}_t^2}{\hat{\sigma}_t^2 + \hat{\sigma}_\epsilon^2} = 0.81$$

Same Strategy for Sire Model

- Sire model is a mixed linear effects model with sire effects s as random components

$$y = Xb + Zs + e$$

- In case where sires are not related, \$var(s) $= I * \sigma_s^2$
- From σ_s^2, we get genetic additive variance as $\sigma_a^2 = 4 * \sigma_s^2$

Dataset for sire model

Animal ID	Sire	Measurement 1	Measurement 2	Measurement 3
10	1	y_{1,10,1}	y_{1,10,2}	
11	1			
12	2			
13	2			
.	2			
.	3			
.	.			
D	5			

ANOVA

Effect	Degrees of Freedom	Sum Sq	Mean Sq	$E(Mean\ Sq)$
Sire $(s \mid b)$	$r - 1$	$SSQ(s \mid b)$	$SSQ(s \mid b)/(r-1)$	$\sigma_e^2 + \underline{k} * \sigma_s^2$
Residual (e)	$N - r$	$SSQ(e)$	$SSQ(e)/(N-r)$	σ_e^2

with

$$k = \frac{1}{r-1}\left[N - \frac{\sum_{i=1}^{r} n_i^2}{N}\right]$$

$$\hat{\sigma}_e^2 = MSQ_e$$

$$\underline{\hat{\sigma}_s^2} = \frac{\boxed{MSQ_s - \hat{\sigma}_e^2}}{k}$$

Estimate of sire variance

In cases where MSQ(e) > MSQ(s), the estimate of the sire variance is negative. Because variance components must be positive, this estimate would be invalid

Maximum Likelihood (ML)

make assumptions about the distribution of the observations. Often, it is assumed that observations follow a normal distribution

- Likelihood

is defined as the conditional density of the obserfations given the parameter

$$L(\theta) = f(y|\theta)$$

- Normal distribution

$$L(\theta) = (2\pi)^{-1/2n}\underline{\sigma}^{-n}|H|^{-1/2} * exp\left\{-\frac{1}{2\underline{\sigma}^2}(y - \underline{Xb})^T H^{-1}(y - Xb)\right\}$$

$$\text{with } var(y) = H * \sigma^2 \text{ and } \underbrace{\theta^T = \begin{bmatrix} b & \sigma^2 \end{bmatrix}}_{\rightarrow \text{ parameters of normal distribution}}$$

Maximization of Likelihood

- Set $\lambda = logL$
- Compute partial derivatives of λ with respect to all unknowns

$$\frac{\partial \lambda}{\partial b}$$

$$\frac{\partial \lambda}{\partial \sigma^2}$$

- Set partial derivatives to 0 and solve for unknowns
- Use solutions as estimates

Restricted Maximum Likelihood (REML)

with REML, we are looking at the likelihood of y corrected for b

first: $y^* = (y - Xb) s^*$

$L^*(\theta^*) = f(y^* | \theta^*)$

fixed effects of the model

- Problem with ML: estimate of σ^2 depends on b → undesirable
- Do transformations Sy and Qy

$y_1^* = Sy$

$y_2^* = Qy$

(i) The matrix S has rank $n - t$ and the matrix Q has rank t

(ii) The result of the two transformations are independent, that means $cov(Sy, Qy) = 0$ which is met when $SHQ^T = 0$

(iii) The matrix S is chosen such that $E(Sy) = 0$ which means $SX = 0$

(iv) The matrix QX is of rank t, so that every linear function of the elements of Qy estimate a linear function of b.

REML II

- From (i) and (ii) it follows that the likelihood L of y is the product of the likelihoods of Sy (L^*) and Qy (L^{**}) that means

$$\lambda = \lambda^* + \lambda^{**}$$

- Variance components are estimated from λ^* which will then be independent of b

Bayesian Estimation

- Proposed already in the 80's
- Full implementation only in 1993
- Requirements:
  - cheap computing and
  - good pseudo-random number generators
- Bayesian estimation is based on conditional posterior distribution of unknowns given the knowns
- Conditional posterior distribution is computed from prior distribution of unknowns times the likelihood

Model

- Univariate Gaussian linear mixed model

$$y = Xb + Zu + e$$

where

y	vector of observations (length n)
b	vector of fixed effects (length p)
u	vector of random breeding values (length q)
e	vector of random residuals (length n)
X	$n \times p$ design matrix linking fixed effects to observations
Z	$n \times q$ design matrix linking breeding values to observations

Likelihood

- Data generating distribution

$$y|b, u, \sigma_e^2 \sim \mathcal{N}(Xb + Zu, I * \sigma_e^2)$$

where I is a $n \times n$ identity matrix and σ_e^2 is the variance of the random residuals.

Priors

- Prior distributions must be specified for all unknowns
- Unknowns in our example are: b, u, σ_e^2 and σ_u^2
- Prior distribution for
  - b is flat, i.e. $p(b) \propto c$
  - u Normal distribution as $u | G, \sigma_u^2 \sim N(0, G * \sigma_u^2)$
  - σ_e^2 scaled inverse χ^2: $p(\sigma_e^2 | \nu_e, s_e^2) \propto (\sigma_e^2)^{-\nu_e/2-1} exp(-\frac{1}{2}\nu_e s_e^2/\sigma_e^2)$
  - σ_u^2 : $p(\sigma_u^2 | \nu_u, s_u^2) \propto (\sigma_u^2)^{-\nu_u/2-1} exp(-\frac{1}{2}\nu_u s_u^2/\sigma_u^2)$
- ν_e, ν_s, s_e^2 and s_u^2 are called hyper-parameters and must be determined

Additional Terms

- Let

$$\theta^T = (b^T, u^T) = (\theta_1, \theta_2, \ldots, \theta_N)$$

$$\theta_{-i} = (\theta_1, \theta_2, \ldots, \theta_{i-1}, \theta_{i+1}, \ldots, \theta_N)$$

- Further, let

$$s^T = (s_u^2, s_e^2)$$

and

$$\nu^T = (\nu_u, \nu_e)$$

Joint Posterior Density

The joint posterior distribution can be written as

$$p(\theta, \sigma_u^2, \sigma_e^2 | y, s, \nu) \propto p(\theta) * p(\sigma_u^2 | \nu_u, s_u^2) * p(\sigma_e^2 | \nu_e, s_e^2) * p(y | \theta, \sigma_e^2)$$

Fully Conditional Posterior Densities of θ

- Density of every single unknown component when setting all other components as known

$$\theta_i | y, \theta_{-i}, \sigma_u^2, \sigma_e^2, s, \nu \sim \mathcal{N}(\tilde{\theta}_i, \tilde{v}_i)$$

where $\tilde{\theta}_i = (r_i - \sum_{j=1,j\neq i}^{N} w_{ij}\theta_j)/w_{ii}$ and $\tilde{v}_i = \sigma_e^2/w_{ii}$.

- vector r is the vector of right-hand side of MME
- matrix W is the coefficient matrix of MME

Fully Conditional Posterior Densities of σ_e^2

- scaled inverted chi-square distribution for σ_e^2

$$\sigma_e^2 | y, \theta, \sigma_u^2, s, \nu \sim \tilde{\nu_e} \tilde{s_e}^2 \chi^{-2}_{\tilde{\nu_e}}$$

- Parameters of the above distribution are defined as

$$\tilde{\nu_e} = n + \nu_e$$

and

$$\tilde{s_e}^2 = \left[(y - Xb - Zu)^T (y - Xb - Zu) + \nu_e s_e^2 \right] / \tilde{\nu_e}$$

Fully Conditional Posterior Densities of σ_u^2

- scaled inverted chi-square distribution for σ_u^2

$$\sigma_u^2|y, \theta, \sigma_e^2, s, \nu \sim \tilde{\nu_u}\tilde{s_u}^2\chi_{\tilde{\nu_u}}^{-2}$$

- Parameters of the above distribution are defined as

$$\tilde{\nu_u} = q + \nu_u$$

and

$$\tilde{s_u}^2 = \left[u^T G^{-1} u + \nu_u s_u^2\right] / \tilde{\nu_u}$$

Implementation

- Step 1: set starting values for θ, σ_e^2 and σ_u^2
- Step 2: draw random number for each component θ_i of θ from fully conditional distribution $\mathcal{N}(\tilde{\theta}_i, \tilde{v}_i)$
- Step 3: draw random number for σ_e^2 from $\tilde{\nu}_e \tilde{s}_e{}^2 \chi^{-2}_{\tilde{\nu}_e}$
- Step 4: draw random number for σ_u^2 from $\tilde{\nu}_u \tilde{s}_u{}^2 \chi^{-2}_{\tilde{\nu}_u}$
- Repeat steps 2-4 many times and store random numbers
- Step 5: compute means of random numbers to get Bayesian estimates of unknowns θ, σ_e^2 and σ_u^2