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Modelos Matemáticos e Aplicações

Módulo 2: Modelos lineares mistos

Linear Mixed Models

Some particular cases and respective application

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Exercise 1

A field trial was installed in Vila Nova de Fozcoa, with a random sample of genotypes (196 genotypes) of the variety, to evaluate the genetic variability of the yield of the Touriga Nacional variety. In the field, each genotype was randomly assigned in 5 plots (trial with 5 replicates). The yield (kg/plant) data obtained in 1994 is available in *data.frame* touriga.

a) Describe the adequate model to study the yield genetic variability of the variety.

Random model (one factor of random effects), balanced, with G and R diagonal matrices

$$Y_{ij} = \mu + u_i + e_{ij}$$

for $i = 1, \dots, a, j = 1, \dots, b\ , n = ab.$

Y_{ij} is the jth observation in the ith level of factor A;

μ is a general mean (population);

u_i is the effect of the level i of the factor A (random effects);

e_{ij} is the random error associated to the observation Y_{ij}.

- $u_i, i.i.d., \mathcal{N}\left(0, {\sigma^2}_u\right), \forall i$
- $e_{ij}, i.i.d., \mathcal{N}\left(0, {\sigma^2}_e\right), \forall ij$
- $\mathrm{cov}(u_i, e_{i'j'}) = 0, \forall i, i' \mathrm{e\ j'}$

Exercise 1 (cont.)

b) Fit the model previously described, with the restricted maximum likelihood (REML) method.

(i) Use *lme* of the package“nlme”, and *lmer* of the package “lme4”; Apply the command *summary* to the two objects created above and identify the REML estimates for the variance components.

(ii) Knowing that $\bar{Y}.. = 1.196$ kg/plant and $\bar{Y}_{c0101.} = 1.6044$ kg/plant, what is the empirical best linear unbiased predictor of the yield genotypic effect of the genotype c0101?

(iii) What is the yield fitted value for clone c0101 in repetition 2?

(iv) Explore commands *ranef* and *fitted* of packages “nmle” and “lme4”.

Example: for a random model with one factor of random effects, balanced (factor with a levels, b observations per level), the empirical best linear unbiased predictor of u_i (for the level i) is:

$$EBLUP(u_i) = \frac{b\hat{\sigma}^2{}_u}{b\hat{\sigma}^2{}_u + \hat{\sigma}^2{}_e}(\bar{Y}_{i.} - \bar{Y}_{..})$$

c) The ANOVA TABLE for a random model with one factor of random effects (Factor A), balanced, with ***G*** and ***R*** diagonal matrices, is described as follows:

	G.L.	S.Q.	QM	E[QM]
Factor A	$a-1$	$SQA=\sum_{i=1}^{a} b\,(\bar{y}_{i.}-\bar{y}_{..})^2$	$QMA=\frac{SQA}{a-1}$	$b\sigma_u{}^2\ +\sigma_e{}^2$
Resíduals	$a(b-1)$	$SQRE=\sum_{i=1}^{a}\sum_{j=1}^{b}\left(y_{ij}-\bar{y}_{i.}\right)^2$	$QMRE=\frac{SQRE}{a(b-1)}$	$\sigma_e{}^2$
TOTAL	$ab-1$	$SQT=\sum_{i=1}^{a}\sum_{j=1}^{b}\left(y_{ij}-\bar{y}_{..}\right)^2$		

i) What are the estimators for the variance components (procedure based on expected mean squares from the analysis of variance)?

Exercise 1 (cont.)

d) In fact, the Touriga Nacional field trial described above was planted according to a randomized complete block design (5 blocks).

(i) Fit a new model considering the block effect (assuming a random effects factor). Use package *lme4*.

(ii) Carry out hypotesis tests for the variance components of the model.

(iii) Compute AIC and BIC for both fitted models and select the best one according to the criteria.

Likelihood ratio tests for variance component ${\sigma_u}^2$

- Hypotheses: $H_0: {\sigma_u}^2 = 0 \quad vs \quad H_1: {\sigma_u}^2 > 0$
- The REML likelihood ratio statistic :

$$\Lambda = 2\left(l_{R_1} - l_{R_0}\right) \sim \chi^2_\nu$$

being l_{R_1} the REML log-likelihood of the more general model (full model) and l_{R_0} the REML log-likelihood of the reduced model (that is, the REML log-likelihood under the null hypothesis). Under regularity conditions and under the null hypothesis, the likelihood ratio statistic, has an approximate χ^2_ν distribution with the degrees of freedom (ν) equal to the difference in the number of parameters between the two models. However, when we test a variance component, under the null hypothesis the parameter falls on the boundary of the parameter space. Theoretically it can be shown that for a single variance component, the asymptotic distribution of the REMLRT is a mixture of χ^2 variates , where the mixing probabilities are 0.5, one with 0 degrees of freedom and the other with one degree of freedom. As a consequence we can perform the likelihood ratio test as if the standard conditions apply, and divide the resulting p-value by two.

- The REML likelihood ratio test is only valid if the fixed effects are the same for both model.
- Significance level: α
- Rejection region: upper (right-hand) tail

Reject H_0 if $\Lambda_{calc} > {\chi^2}_{\alpha(\nu)}$

Case 2

Linear mixed model: one factor of fixed effects, one factor of random effects, balanced, without interaction and with interaction, with $\boldsymbol{G}$ and $\boldsymbol{R}$ diagonal matrices (*G*=$\sigma_u{}^2\ \boldsymbol{I}_q$, *R*=$\sigma_e{}^2\ \boldsymbol{I}_n$)

Exercise 3

Consider the *data.frame* terrenos. The objective of the study is to compare the yield between four wheat varieties. In addition, 13 sites with different soil conditions were identified. Consider that those soils constitute a random sample of the soils where the four varieties of wheat will be grown. The four varieties were assigned randomly within sites, each variety once per site.

a) Fit the adequate model for this study (for example, using *package nlme*, function *lme*).

Linear mixed model: one factor of fixed effects (factor A), one factor of random effects (factor B), balanced, without interaction

$$Y_{ijk} = \mu_1 + \beta_i + u_j + e_{ijk}$$

for $i = 1, \dots, a, j = 1, \dots, b, k = 1, \dots, c, n = abc$, with $\beta_1 = 0.$

Y_{ijk} is the observation in the ith level of factor A and jth level of factor B;
μ_1 is a general mean (population) in the level 1 of factor A;
β_i is the effect of the level i of the factor A (the increased concerning to μ_1), fixed;
u_j is the effect of the level j of the factor B, random;
e_{ijk} is the random error associated to the observation Y_{ijk} .

- $u_j, i.i.d., \mathcal{N}\left(0, \sigma^2{}_u\right), \forall j$
- $e_{ijk}, i.i.d., \mathcal{N}\left(0, \sigma^2{}_e\right), \forall ijk$

The sums of squares are defined as :

$$SQT = \sum_{i=1}^{a}\sum_{j=\mathbf{1}}^{b}\sum_{k=1}^{c}\left(Y_{ijk} - \bar{Y}_{...}\right)^2$$

$$SQA = \sum_{i=1}^{a} bc\left(\bar{Y}_{i..} - \bar{Y}_{..,}\right)^2$$

$$SQB = \sum_{j=1}^{b} ac\left(\bar{Y}_{.j.} - \bar{Y}_{...,}\right)^2$$

$$SQRE = \sum_{i=1}^{a}\sum_{j=1}^{b}\sum_{k=1}^{c}\left(Y_{ijk} - \bar{Y}_{i..} - \bar{Y}_{.j.} + \bar{Y}_{...,}\right)^2$$

$$SQT = SQA + SQB + SQRE$$

- **Estimators for variance components:** procedure based on expected mean squares from the analysis of variance (ANOVA)

$$\boxed{\begin{aligned} &\mathrm{E}[SQB] = (b-1)\left(ac{\sigma_u}^2 \ + {\sigma_e}^2\ \right) \\ &\mathrm{E}[QMB] = \frac{E[SQB]}{(b-1)} = ac{\sigma_u}^2 \ + {\sigma_e}^2 \end{aligned}}$$

$$\boxed{\begin{aligned} &E[SQRE] = n-(a+b-1){\sigma_e}^2 \\ &E[QMRE] = \frac{E[SQRE]}{n-(a+b-1)} = {\sigma_e}^2 \end{aligned}}$$

The estimators are:

$$\hat{\sigma}_e{}^2 \ = \frac{SQRE}{n-(a+b-1)} = QMRE \qquad \hat{\sigma}_u{}^2 \ = \frac{QMB-QMRE}{ac}$$

- **The maximum likelihood estimators for variance components are($\hat{\sigma}_u{}^2 \geq 0$)**

$$\hat{\sigma}_e{}^2 = \left[1 - \frac{a-1}{b(ac-1)}\right] QMRE,$$

$$\hat{\sigma}_u{}^2 = \frac{SQB/b - \hat{\sigma}_e{}^2}{ac}$$

- **The restricted maximum likelihood estimators for variance components are ($\hat{\sigma}_u{}^2 \geq 0$):**

$$\hat{\sigma}_e{}^2 = \frac{SQRE}{n-(a+b-1)} = QMRE \qquad \hat{\sigma}_u{}^2 = \frac{QMB - QMRE}{ac}$$

Asymptotic variance matrix for REML estimators

$$\boxed{\operatorname{var}\begin{bmatrix}\hat{\sigma}_e{}^2\\ \hat{\sigma}_u{}^2\end{bmatrix}\approx\frac{2\sigma_e{}^4}{b(ac-1)}\begin{bmatrix}1 & \dfrac{-1}{ac}\\ \dfrac{-1}{ac} & \left[\dfrac{1+(ac-1)(1+ac\sigma_u{}^2/\sigma_e{}^2)^2}{a^2c^2}\right]\end{bmatrix}}$$

Exercise 3 (cont.)

b)

i) Carry out the hypothesis test for fixed effects of the model. For the calculation of the test statistic recall the hypothesis tests for linear combinations of fixed effects of the linear mixed model given in the theoretical classes. Consider the estimated covariance matrix of the fixed effects estimators (vcov (terrenolme1)), define the matrix L, create the vector with the fixed effects estimates and, with the help of R, compute the test statistic. For your conclusions, use the significance level of 0.05. At the end, run anova (terrenolme1).

Tests of hypotheses for linear combinations of the fixed effects of the mixed model ($\boldsymbol{L}^{\boldsymbol{T}}[\boldsymbol{\beta}]$), when $\boldsymbol{L}$ is a matrix (rank of $\boldsymbol{L}$ greater than 1)

- Hypotheses: $H_o: \boldsymbol{L}^{\boldsymbol{T}}[\boldsymbol{\beta}] = \boldsymbol{0}$ vs. $H_1: not\ all\ \boldsymbol{L}^{\boldsymbol{T}}[\boldsymbol{\beta}] = \boldsymbol{0}$
- Test statistic : $\mathrm{F} = \dfrac{[\widehat{\boldsymbol{\beta}}]^{\boldsymbol{T}} \boldsymbol{L}\left(\boldsymbol{L}^{\boldsymbol{T}} \widehat{\boldsymbol{C}_{\mathbf{11}}} \boldsymbol{L}\right)^{-\mathbf{1}} \boldsymbol{L}^{\boldsymbol{T}}[\widehat{\boldsymbol{\beta}}]}{\boldsymbol{rank}(\boldsymbol{L})} \sim \boldsymbol{\mathcal{F}}_{v_1,v_2}$, sob H_0

F in general has an approximate F-distribution, with $v_1 = rank(\boldsymbol{L})$ and v_2 must be estimated (for example, using *Satterthwaite approximation).* This not happen only for particular cases for data exhibiting certain types of balance and for some special unbalanced cases with the elements of the vectors $\boldsymbol{u}$ e $\boldsymbol{e}$ being *i.i.d*. random variables. In these cases, $v_2 = n - r(\boldsymbol{W})$, where $r(\boldsymbol{W})$ is the rank of the matrix **W** which contains the columns of matrices $\boldsymbol{X}$ and $\boldsymbol{Z}$. $\widehat{\boldsymbol{C}}_{\mathbf{11}} = \left(\boldsymbol{X}^{\boldsymbol{T}} \widehat{\boldsymbol{V}}^{-\mathbf{1}} \boldsymbol{X}\right)^{-\mathbf{1}}$ was defined in theoretical part **(**slides 61 and 62).

- Significance level : α
- Rejection region: upper (right-hand) tail; Reject H_0 if $F_{calc} > f_{\alpha(v_1,v_2\ )}$

Some considerations

- For random or complex mixed models there are no exact statistical tests for certain model effects (the numerator and denominator of the F statistics are linear combinations of mean squares). In these cases, approximate F tests are performed. One of the classic methods most used for this approach is the method of Satterthwaite (1941). However, other methods are implemented in more complex mixed models frequently reported in the literature and commonly used in several packages, for example, the methods of Giesbrecht and Burns (1985) and Kenward and Roger (1997). (next slide, additional information)

❑ Example: Satterthwaite Degrees of freedom Approximation

Satterthwaite showed that given the ratio

$$\frac{X^2_{num}/_{\nu_1}}{X^*_2/_{\upsilon^*_2}}$$

where $X^2_{num} \cap \chi^2_{\nu_1}$ and X^*_2 is a linear combination of chi-square random variable all independent of X^2_{num}, the $X^*_2 \cap \chi^2_{\upsilon^*_2}$, where

$$\upsilon^*_2 \cong \frac{\left(\sum_m l_m X^2_m\right)^2}{\sum_m \left(l_m X^2_m\right)^2 / df_m},$$

X^2_m denotes the $\chi^2_{df_m}$ random variables, l_m denote the constants in the linear combination, df_m the degrees of freedom for the respective X^2_m.

Hypothesis test for fixed effects

- Hypotheses $H_0\colon \beta_i = 0,\ \ \forall_{i=2,\ldots a}\ \ vs\ \ H_1\colon \exists_{i=2,\ldots,a} : \beta_i \neq 0$

- Test statistic : $F = \frac{QMA}{QMRE} \cap F_{(a-1,n-(a+b-1)\ )}$, sob H_0

- Significance level : α

- Rejection region : upper (right-hand) tail

Rejeitar H_0 se $F_{calc} > f_{\alpha(a-1,n-(a+b-1)))}$

Note: the test for fixed effects is similar to what was described in the context of fixed effects ANOVA

Exercise 3 (cont.)

ii) Is the mean yield of variety B equal to the mean yield of variety A (for $\alpha = 0.05$)?

Tests of hypotheses for linear combinations of the fixed effects of the mixed model ($\boldsymbol{L}^T[\boldsymbol{\beta}]$), being $\boldsymbol{L}$ a non random vector

- Hypotheses : $H_o: \boldsymbol{L}^T[\boldsymbol{\beta}] = \mathbf{0}$ vs $H_1: \boldsymbol{L}^T[\boldsymbol{\beta}] \neq \mathbf{0}$

- Test statistic: $T = \dfrac{\boldsymbol{L}^T[\hat{\boldsymbol{\beta}}]}{\sqrt{(\boldsymbol{L}^T\hat{\boldsymbol{C}}_{11}\boldsymbol{L})}} \sim t_{\upsilon_2}$, under H_0

Under the assumed normality of $\boldsymbol{u}$ and $\boldsymbol{e}$, T has an exact t-distribution only for data exhibiting certain types of balance and for some special unbalanced cases. In general, it is only approximately t-distributed, and its degrees of freedom must be estimated (for example, using *Satterthwaite approximation).* This not happen only for particular cases for data exhibiting certain types of balance and for some special unbalanced cases with the elements of the vectors $\boldsymbol{u}$ e $\boldsymbol{e}$ being *i.i.d*. random variables. In these cases, $\upsilon_2 = n - r(\boldsymbol{W})$, where $r(\boldsymbol{W})$ is the rank of the matrix **W** which contains the columns of matrices $\boldsymbol{X}$ and $\boldsymbol{Z}$.

$\sqrt{(\boldsymbol{L}^T\hat{\boldsymbol{C}}_{11}\boldsymbol{L})}$ is a scalar, is the standard error of the estimator of the parameter being tested, matrix $\hat{\boldsymbol{C}}_{11} = (\boldsymbol{X}^T\hat{\boldsymbol{V}}^{-1}\boldsymbol{X})^{-1}$ was defined in theoretical part (slides 61 and 62).

- Significance level: α

- Rejection region: two-tailed; Reject H_0 if $|T_{calc}| > t_{\alpha/_2\,(\upsilon_2\,)}$

Exercise 4

The data set *Machines* (Pinheiro e Bates, 2000) is available in both *libraries nlme* and *lme4* of R. The objective of the experiment is to compare three brands of machines used in an industrial process. Six workers were chosen randomly among the employees of a factory to operate each machine three times. The response variable is an overall productivity score taking into account the number and quality of components produced.

a) Describe the appropriate model for this study. Fit the model using R, with function *lmer* of package *lme4*. Use the commands plot.design (Machines) and interaction.plot (Machine,Worker,score) and comment.

b) What are the restrict maximum likelihood estimates for the variance components of the model?

c) Would the values of the variance components estimates obtained by the maximum likelihood method be higher or lower than the estimates given in the previous item ?

Linear mixed model: one factor of fixed effects (factor A), one factor with random effects (factor B), balanced, with interaction

$$Y_{ijk} = \mu_1 + \beta_i + u_j + (\beta u)_{ij} + e_{ijk}$$

for $i = 1, \dots, a, j = 1, \dots, b, k = 1, \dots, c, n = abc,$ with $\beta_1 = 0$.

Y_{ijk} is the kth observation in the ith level of factor A and jth level of factor B;

μ_1 is a general mean (population) in the level 1 of factor A;

β_i is the effect of the level i of the factor A (the increased concerning to μ_1), fixed;

u_j is the effect of the level j of the factor B, random;

$(\beta u)_{ij}$ is the interaction effect of the ith level of factor A with the jth level of factor B, random;

e_{ijk} is the random error associated to the observation Y_{ijk}.

- $u_j, i.i.d., \mathcal{N}\left(0, \sigma^2{}_u\right), \forall j$
- $(\beta u)_{ij}, i.i.d., \mathcal{N}\left(0, \sigma^2{}_{\beta u}\right), \forall ij$
- $e_{ijk}, i.i.d., \mathcal{N}\left(0, \sigma^2{}_e\right), \forall ijk$

The sums of squares are defined as :

$$SQT = \sum_{i=1}^{a}\sum_{j=\mathbf{1}}^{b}\sum_{k=1}^{c}\left(Y_{ijk} - \bar{Y}_{...}\right)^2$$

$$SQA = \sum_{i=1}^{a} bc\,(\bar{Y}_{i..} - \bar{Y}_{...})^2$$

$$SQB = \sum_{j=1}^{b} ac\left(\bar{Y}_{.j.} - \bar{Y}_{...}\right)^2$$

$$SQAB = \sum_{i=1}^{a}\sum_{j=1}^{b} c\left(Y_{ij.} - \bar{Y}_{i..} - \bar{Y}_{.j.} + \bar{Y}_{...}\right)^2$$

$$SQRE = \sum_{i=1}^{a}\sum_{j=1}^{b}\sum_{k=1}^{c}\left(Y_{ijk} - \bar{Y}_{ij.}\right)^2$$

$$SQT = SQA + SQB + SQAB + SQRE$$

- **Estimators for variance components:** procedure based on expected mean squares from the analysis of variance (ANOVA)

$$\mathrm{E}[SQB] = (b-1)\left(ac{\sigma_u}^2 + c{\sigma_{\beta u}}^2 + {\sigma_e}^2\right)$$

$$\mathrm{E}[QMB] = \frac{E[SQB]}{(b-1)} = ac{\sigma_u}^2 + c{\sigma_{\beta u}}^2 + {\sigma_e}^2$$

$$\mathrm{E}[SQAB] = (a-1)(b-1)\left(c{\sigma_{\beta u}}^2 + {\sigma_e}^2\right)$$

$$\mathrm{E}[QMAB] = \frac{E[SQAB]}{(a-1)(b-1)} = c{\sigma_{\beta u}}^2 + {\sigma_e}^2$$

$$E[SQRE] = ab(c-1){\sigma_e}^2$$

$$E[QMRE] = \frac{E[SQRE]}{ab(c-1)} = {\sigma_e}^2$$

These yield the estimators

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

$$\hat{\sigma}_{\beta u}{}^2 = \frac{QMAB - QMRE}{c}$$

$$\hat{\sigma}_u{}^2 = \frac{QMB - QMAB}{ac}$$

- **The maximum likelihood estimators for variance components are** $(\hat{\boldsymbol{\sigma}}_{\boldsymbol{u}}{}^{2} \geq \mathbf{0}, \hat{\boldsymbol{\sigma}}_{\boldsymbol{\beta u}}{}^{2} \geq \mathbf{0})$

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

$$\hat{\sigma}_u{}^2 = \frac{(1-\frac{1}{b})(QMB-QMAB)}{ac}$$

$$\hat{\sigma}_{\beta u}{}^2 = \frac{(1-\frac{1}{b})QMAB - QMRE}{c}$$

- **The restricted maximum likelihood estimators for variance components are** $(\hat{\boldsymbol{\sigma}}_{\boldsymbol{u}}{}^{2} \geq \mathbf{0}, \hat{\boldsymbol{\sigma}}_{\boldsymbol{\beta u}}{}^{2} \geq \mathbf{0})$

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

$$\hat{\sigma}_{\beta u}{}^2 = \frac{QMAB - QMRE}{c}$$

$$\hat{\sigma}_u{}^2 = \frac{QMB - QMAB}{ac}$$

Asymptotic variance matrix for REML estimators

$$\operatorname{var}\begin{bmatrix}\hat{\sigma}_e{}^2\\ \hat{\sigma}_u{}^2\\ \hat{\sigma}_{\beta u}{}^2\end{bmatrix} \approx \frac{2}{b}\begin{bmatrix}\dfrac{\sigma_e{}^4}{a(c-1)} & 0 & \dfrac{-\sigma_e{}^4}{ac(c-1)}\\ & \dfrac{\dfrac{(\sigma_e{}^2+c\sigma_{\beta u}{}^2)^2}{a-1}+(\sigma_e{}^2+c\sigma_{\beta u}{}^2+ac\sigma_u{}^2)^2}{a^2c^2} & \dfrac{-(\sigma_e{}^2+c\sigma_{\beta u}{}^2)^2}{ac^2(a-1)}\\ & & \dfrac{1}{c^2}\left[\dfrac{(\sigma_e{}^2+c\sigma_\beta{}^2)^2}{a-1}+\dfrac{\sigma_e{}^4}{a(c-1)}\right]\end{bmatrix}$$

ANOVA TABLE: linear mixed model, one factor of fixed effects (factor A) and one factor of random effects (factor B), balanced, with interaction

$$Y_{ijk} = \mu_1 + \beta_i + u_j + (\beta u)_{ij} + e_{ijk}$$

for $i = 1, \dots, a, j = 1, \dots, b, k = 1, \dots, c, n = abc$, with $\beta_1 = 0$.

- $u_j, i.i.d., \mathcal{N}\left(0, {\sigma^2}_u\right), \forall j; (\beta u)_{ij}, i.i.d., \mathcal{N}\left(0, {\sigma^2}_{\beta u}\right), \forall ij; e_{ijk}, i.i.d., \mathcal{N}\left(0, {\sigma^2}_e\right), \forall ijk$

	G.L.	S.Q.	QM	E[QM]	F*
Factor A	$a-1$	SQA	QMA	$\frac{bc}{a-1}\sum_{i=1}^{a}(\beta_i - \bar{\beta}_.)^2 + {\sigma_e}^2 + c{\sigma_{\beta u}}^2$	$\frac{QMA}{QMAB}$
Factor B	$b-1$	SQB	QMB	${\sigma_e}^2 + c{\sigma_{\beta u}}^2 + ca{\sigma_u}^2$	$\frac{QMB}{QMAB}$
Interaction	$(a-1)(b-1)$	$SQAB$	$QMAB$	${\sigma_e}^2 + c{\sigma_{\beta u}}^2$	$\frac{QMAB}{QMRE}$
Resíduals	$ab(c-1)$	$SQRE$	$QMRE$	${\sigma_e}^2$	
TOTAL	$n-1$	SQT			

*** The appropriate F-statistic is a quotient of QM that is chosen such that the expected value of the numerator and the expected value of the denominator differ only in the fixed effects (or variance component) of the factor being tested.**

Tests of hypotheses , fixed effects of factor A

- Hypotheses: $H_0: \beta_i = 0, \ \forall_{i=2,\ldots a} \ \ vs \ \ H_1: \exists_{i=2,\ldots,a}$ tal que $\beta_i \neq 0$
- Test statistic: $F = \frac{QMA}{QMAB} \cap F_{(a-1,(a-1)(b-1))}$, sob H_0
- Significance level: α
- Rejection region: upper (right-hand) tail: unilateral direita

Rejeitar H_0 se $F_{calc} > f_{\alpha(a-1,(a-1)(b-1))}$

Exercise 4 (cont.)

d) Carry out the hypothesis test for worker×machine interaction. Use a significance level of 0.01.

e) Carry out the hypothesis test for the variability associated to worker. Use a significance level of 0.01.

f) Carry out an appropriate hypothesis test to assess if there are any major effects associated with machine brands. Use a significance level of 0.01.

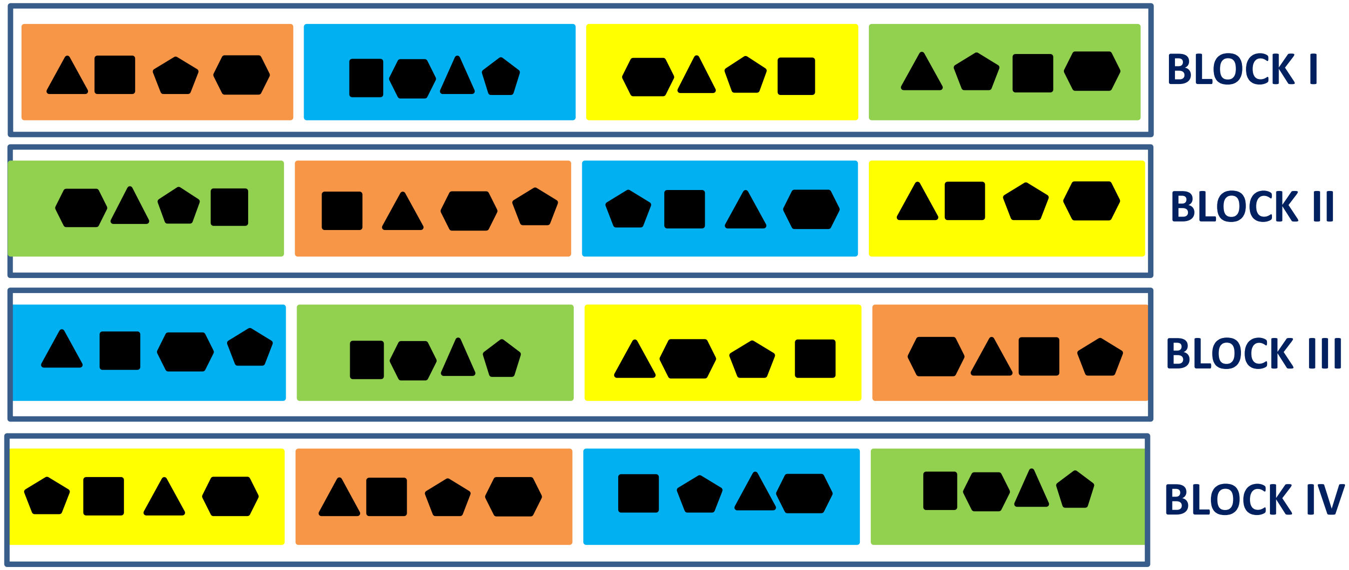
Case 3

Linear mixed models for analysis of split plot experiments

The split-plot design on a RCB

- Main treatments (levels of factor A) are assigned at random within blocks, each treatment once per block; they are divided further into additional independent units (subplots) to which another set of treatments (levels of factor B) are randomly assigned.
- The number of blocks is the number of replications.
- Any main treatment can be adjacent to any other treatment, but not to the same treatment within the block.

Example:
Different colors represent different main treatments (levels of factor A) ; each row represents a block. There are 4 blocks (I-IV) each of 4 main treatments (colors) divided into 4 additional independent units (subplots) to which another set of treatments (levels of factor B, symbols) are randomly assigned.



Considering two factors with fixed effects (factors A and B) and random blocks. The model can be described as:

$$Y_{ijk} = \mu_{11} + \alpha_i + u_j + (\alpha u)_{ij} + \beta_k + (\alpha\beta)_{ik} + (\beta u)_{kj} + e_{ijk}$$

with $i = 1, \dots, a, j = 1, \dots, b, k = 1, \dots, c, n = abc,$
and $\alpha_1 = 0$, $\beta_1 = 0$, $(\alpha\beta)_{1k} = 0, \forall_k,$ $(\alpha\beta)_{i1} = 0, \forall_i.$
Where:

Y_{ijk}, is the observation from i^th level of factor *A* (*whole-plot i*), block *j*, and *k*^th level of factor *B* (*sub-plot* or *split-plot k*);

μ_{11}, is the general mean (population) in the level 1 of factor *A* with level 1 of factor *B*;

α_i, is the effect of the level *i* of the factor *A* (increase), assigned to whole-plot (fixed);

u_j, is the effect of block *j* (random);

$(\alpha u)_{ij}$, is the interaction effect of the i^th level of factor *A* with block *j*, named as *whole-plot error* (random);

β_k, is the effect of the level *k* of the factor *B* (increase), assigned to *sub-plot* (fixed);
$(\alpha\beta)_{ik}$, is the interaction effect of the ith level of factor *A* with the kth level of factor *B* (increase) (fixed);
$(\beta u)_{kj}$, is the interaction effect of the k^th level of factor *B* with block *j* (random);
e_{ijk}, is the random error associated to the observation Y_{ijk}.

In the common approach, the effect $(\beta u)_{jk}$ is set to zero (thus, $(\beta u)_{jk}$ is incorporated in e_{ijk}). The random error includes $(\beta u)_{jk}$ and $(\alpha\beta u)_{ijk}$, and is called as *within plot error*.

Therefore, the common assumptions are:

$u_j, i.i.d., \ \mathcal{N}\left(0, \sigma^2{}_u \ \right), \forall j; \ (\alpha u)_{ij}, i.i.d., \mathcal{N}\left(0, \sigma^2{}_{\alpha u} \ \right), \forall ij;$
$e_{ijk}, i.i.d., \mathcal{N}\left(0, \sigma^2{}_e \ \right), \forall ijk; \ Cov\left(u_j, (\alpha u)_{ij}\right) = 0; \ Cov\left(u_j, e_{ijk}\right) = 0;$
$Cov\left((\alpha u)_{ij}, e_{ijk}\right) = 0.$

ANOVA TABLE, considering a balance design, Considering two factors with fixed effects (factors A and B) and random blocks, :

	G.L.	S.Q.	QM	E[QM]	F*
Factor A	$a-1$	SQA	QMA	$\mathrm{c}\sigma_{\alpha u}{}^{2} + \sigma_e{}^{2} + bc\frac{\sum_{i=1}^{a}(\alpha_i - \bar{\alpha}_{.})^2}{a-1}$	$\frac{QMA}{\text{QMWError}}$
Block	$b-1$	SQBL	QMBL	$ac\sigma_u{}^{2}\ \mathrm{c}\sigma_{\alpha u}{}^{2} + \sigma_e{}^{2}$	
Interaction FactorA×Block (*Whole-plot error*)	$(a-1)(b-1)$	SQWError	QMWError	$\mathrm{c}\sigma_{\alpha u}{}^{2} + \sigma_e{}^{2}$	
Factor B	$c-1$	SQB	QMB	$\sigma_e{}^{2} + ab\frac{\sum_{k=1}^{c}\left(\beta_k - \bar{\beta}_{.}\right)^2}{c-1}$	$\frac{QMB}{QMRE}$
Interaction FactorA×FactorB	$(a-1)(c-1)$	$SQAB$	$QMAB$	$\sigma_e{}^{2} + b\frac{\sum_{i=1}^{a}\sum_{k=1}^{c}\left(\alpha\beta_{ik} - \overline{\alpha\beta}_{..}\right)^2}{(a-1)(c-1)}$	$\frac{QMAB}{QMRE}$
Residuals (*Within plot error*)	$a(b-1)(c-1)$	$SQRE$	$QMRE$	$\sigma_e{}^{2}$	

*** The appropriate F-statistic is a quotient of QM that is chosen such that the expected value of the numerator and the expected value of the denominator differ only in the fixed effects (or variance component) of the factor being tested.**

Exercise 6

In *package* “*nlme*” of R, there is a data set named “*Alfalfa*”.

```
> head(Alfalfa)
Grouped Data: Yield ~ Date | Block/Variety
  Variety Date Block Yield
1   Ladak None     1  2.17
2   Ladak   S1     1  1.58
3   Ladak  S20     1  2.29
4   Ladak   O7     1  2.23
5   Ladak None     2  1.88
6   Ladak   S1     2  1.26
      …
```

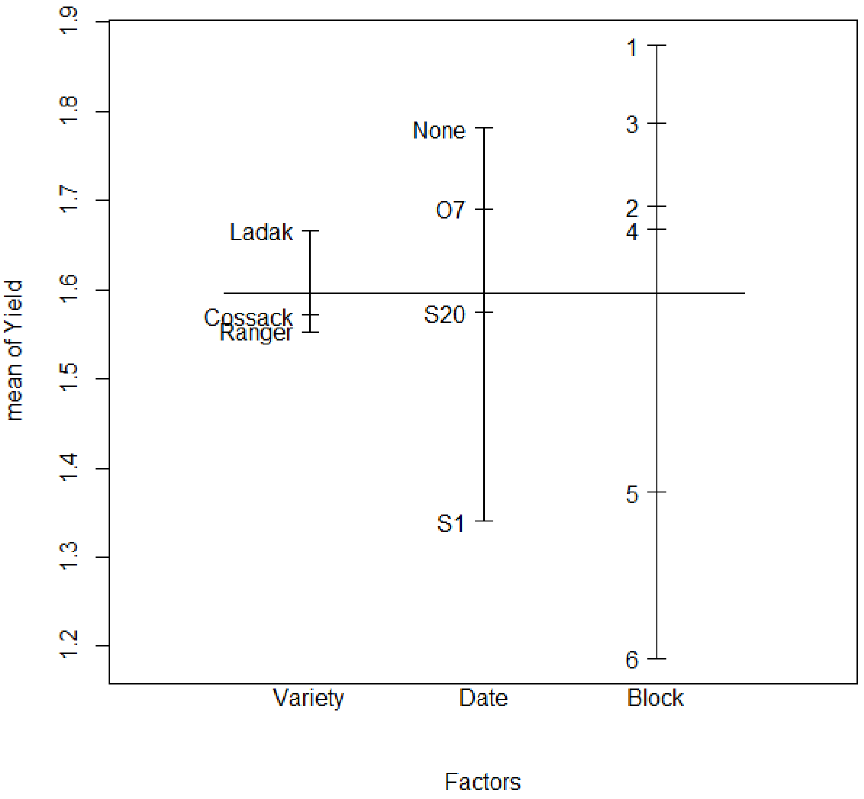
Exercise 6

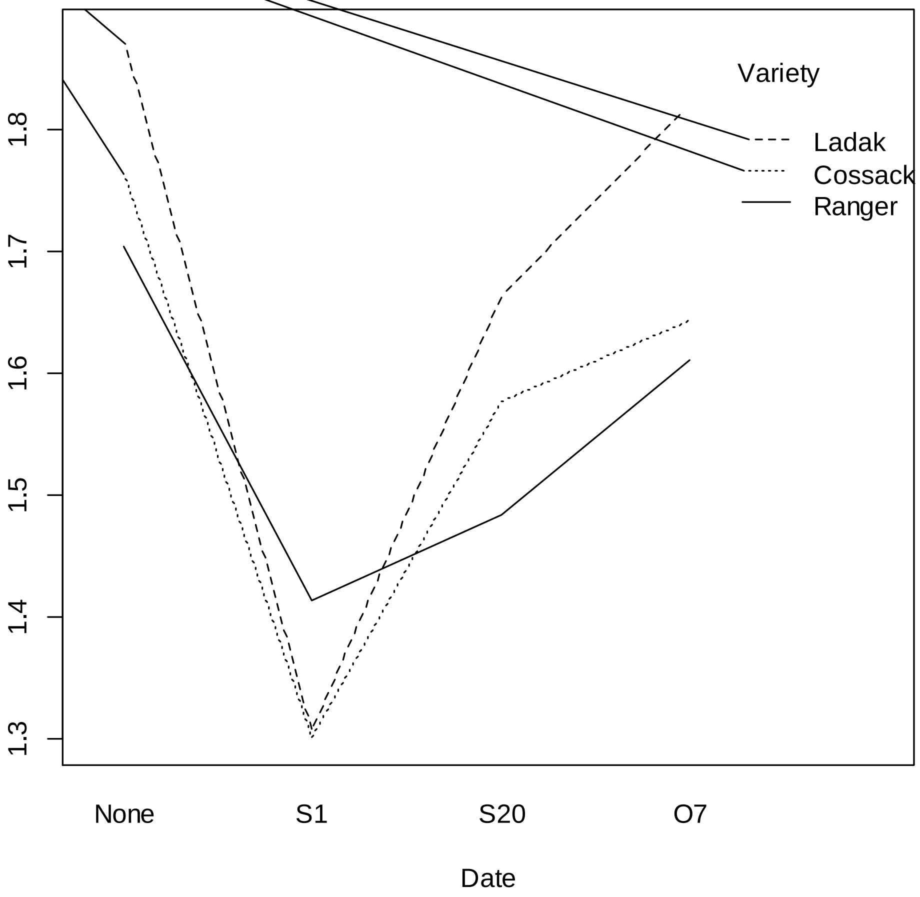
This data is described in Snedecor & Cochran (1980) as an example of a *split-plot design* (Pinheiro and Bates, 2000). The objective is to study if the yield (T/acre) of alfalfa (*Medicago sativa*) is afected by variety and date of third cutting. Therefore, there are two factors: variety of alfalfa, with 3 levels (*Cossac*, *Ladak* e *Ranger*) and date of third cutting, with 4 levels (*none*–sem corte, *S1*– Sep1; *S20* – Sep20; and *O7* – Oct7). The treatment structure used in the experiment was a 3×4 full factorial. The experimental units were arranged into 6 blocks, each block was divided into 3 plots (*whole plots: the largest experimental units)*, where the varieties of alfalfa were randomly assigned; and each whole plot was divided into four subplots (split plots), where the dates of third cutting were randomly assigned.

a) Describe the appropriate model for this study.

Exercise 6 (cont.)

b) Plot the data using *plot.design (Alfalfa)* and *interaction.plot (Date, Variety, Yield)*. Comment.





Exercise 6 (cont.)

c) Fit the model described in item a) in R using *lmer* of package "*lme4*".

d) Carry out the hypothesis tests that answer the objectives of the study.

e) Compare the previous results with those obtained with command "*aov(Yield~Date*Variety+Error(Block*Variety), data=Alfalfa)*".

Some considerations

(1) Factors A and B with random effects;

(2) Factor A with fixed effects and factor B with random effects.

(1) **ANOVA table:** factors A and B with random effects, balanced:

	G.L.	QM	E[QM]	F*
Factor A	$a-1$	QMA	$bc\sigma_{\alpha}{}^{2} + \mathrm{c}\sigma_{\alpha u}{}^{2} + b\sigma_{\alpha\beta}{}^{2} + \sigma_{e}{}^{2}$	$\frac{QMA+QMRE}{\mathrm{QMWError}+QMAB}$ **
Block	$b-1$	$QMBL$	$ac\sigma_{u}{}^{2}\ \mathrm{c}\sigma_{\alpha u}{}^{2} + \sigma_{e}{}^{2}$	
Interaction FactorA×Block (Whole-plot error)	$(a-1)(b-1)$	$QMWError$	$\mathrm{c}\sigma_{\alpha u}{}^{2} + \sigma_{e}{}^{2}$	
Factor B	$c-1$	QMB	$ab\sigma_{\beta}{}^{2} + b\sigma_{\alpha\beta}{}^{2} + \sigma_{e}{}^{2}$	$\frac{QMB}{QMAB}$
Interaction FactorA×FactorB	$(a-1)(c-1)$	$QMAB$	$b\sigma_{\alpha\beta}{}^{2} + \sigma_{e}{}^{2}$	$\frac{QMAB}{QMRE}$
Residuals	$a(b-1)(c-1)$	$QMRE$	$\sigma_{e}{}^{2}$	

*A estatística F apropriada é um quociente de QM que é escolhido de tal forma que o valor esperado do numerador e o valor esperado do denominador diferem apenas na componente de variância a ser testada (ou efeitos fixos do factor a ser testado).

**Approximate degrees of freedom. For example, *Satterthwaite* method:

$$\nu_1 = \frac{(QMA+QMRE)^2}{\frac{(QMA)^2}{a-1}+\frac{(QMRE)^2}{a(b-1)(c-1)}},\ \nu_2 = \frac{(\mathrm{QMWError}+QMAB)^2}{\frac{(\mathrm{QMWError})^2}{(a-1)(b-1)}+\frac{(QMAB)^2}{(a-1)(c-1)}}$$

(2) ANOVA table: factor A with fixed effects and factor B with random effects**,** balanced:

	G.L.	QM	E[QM]	F*
Factor A	$a-1$	QMA	$c\sigma_{\alpha u}{}^2 + b\dfrac{a}{a-1}\sigma_{\alpha\beta}{}^2 + \sigma_e{}^2 + bc\dfrac{\sum_{i=1}^{a}(\alpha_i-\bar{\alpha}_{.})^2}{a-1}$	$\dfrac{QMA+QMRE}{\mathrm{QMWError}+QMAB}$**
Block	$b-1$	QMBL	$ac\sigma_u{}^2\ c\sigma_{\alpha u}{}^2 + \sigma_e{}^2$	
Interaction FactorA×Block (Whole-plot error)	$(a-1)(b-1)$	QMWError	$c\sigma_{\alpha u}{}^2 + \sigma_e{}^2$	
Factor B	$c-1$	QMB	$ab\sigma_\beta{}^2 + \sigma_e{}^2$	$\dfrac{QMB}{QMRE}$
Interaction FactorA×FactorB	$(a-1)(c-1)$	$QMAB$	$b\dfrac{a}{a-1}\sigma_{\alpha\beta}{}^2 + \sigma_e{}^2$	$\dfrac{QMAB}{QMRE}$
Residuals	$a(b-1)(c-1)$	$QMRE$	$\sigma_e{}^2$	

*A estatística F apropriada é um quociente de QM que é escolhido de tal forma que o valor esperado do numerador e o valor esperado do denominador diferem apenas na componente de variância a ser testada (ou efeitos fixos do factor a ser testado).

**Approximate degrees of freedom. For example, *Satterthwaite* method:

$$\nu_1 = \frac{(QMA+QMRE)^2}{\frac{(QMA)^2}{a-1}+\frac{(QMRE)^2}{a(b-1)(c-1)}},\ \nu_2 = \frac{(\mathrm{QMWError}+QMAB)^2}{\frac{(\mathrm{QMWError})^2}{(a-1)(b-1)}+\frac{(QMAB)^2}{(a-1)(c-1)}}$$

Case 4

The following is an example of the application of linear mixed models with categorical and numerical predictor variables (covariance analysis) and in which the observations are made in the same individual over time*

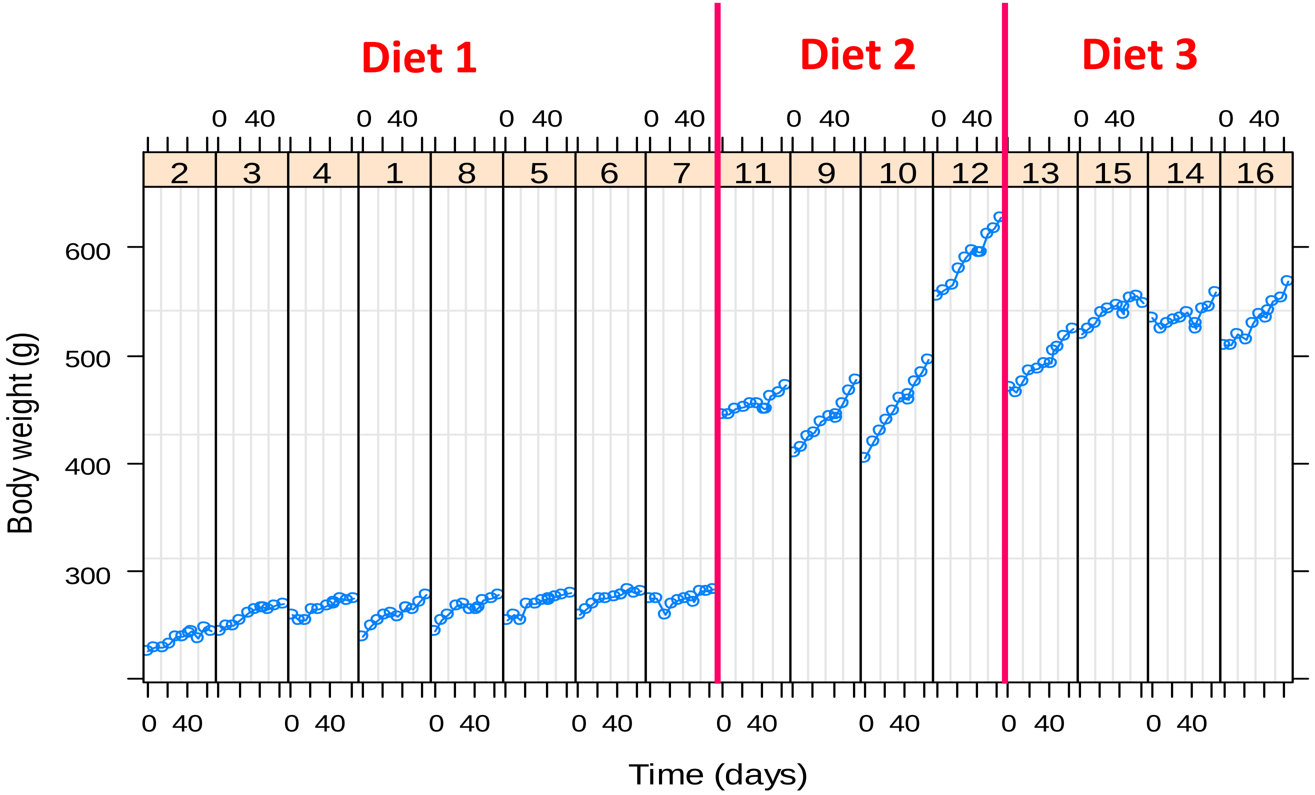
* The correlation matrices used for this type of analysis are used in time series and spatial statistics. For its understanding would be necessary theoretical bases on time series and spatial statistics, which is not part of this UC. Therefore, we will only exemplify its application, so that it is recorded that these instruments are currently widely used in mixed models context.

Exercise 8

Data set *BodyWeight* (Pinheiro e Bates, 2000) is available in R, and is related to the body weights of rats measured over 64 days. The body weights of the rats (in grams) are measured on day 1 and every seven days thereafter until day 24, with an extra measurement on day 44. There are 3 groups of rats, each on a different diet.

```
> head(BodyWeight)
Grouped Data: weight ~ Time | Rat
  weight Time Rat Diet
1    240    1   1    1
2    250    8   1    1
3    255   15   1    1
4    260   22   1    1
```

a) Plot the data using *plot(BodyWeight)* and comment.



- differences among the three diet groups can be observed;
- there is evidence of a rat in diet group 2 with an unusually high initial body weight;
- the body weights appear to grow linearly with time, possibly with different intercepts and slopes for each diet.

b) In R use *lme* of package “*nlme4*” to fit the appropriate model for this study (consider intercept and slope random effects to account for rat-to-rat variation). Use the commands *summary*, *anova*, *ranef* and *fitted*. Explain how each fitted value is obtained.

c) The observations are made in the same individual over time. In this context, the dependence among the within-group errors can be modelled. The observations are not equally spaced in time, as an extra observation is taken at 44 days. In this case, we can use a spatial correlation structure for random errors. Several correlation structures are available in package *nlme*, for example, corEXp, corGaus, corSpher. Use the commands:

```
bodyw2.lme<-update(bodyw1.lme, corr=corExp(form=~Time))
bodyw3.lme<-update(bodyw1.lme, corr=corGaus(form=~Time))
bodyw4.lme<-update(bodyw1.lme, corr=corSpher(form=~Time)).
```

According to AIC and BIC criteria, what is the best correlation structure?

d) Is the model selected in item c) significantly better than the model fitted in item b?

e) Does the model selected in d) differ significantly from the model fitted in b)?