ORIGIN := 0

**Randomized Block Designs with Replicates** 

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Randomized Block Designs with Replicates extends the use of one or more random factors (Blocks or Subjects) and fixed factors (Treatments) to the question of interactions within different levels of Blocks and Treatments. This example, from Ch. 1 of Pinheiro & Bates (PB) 2004, *Mixed-Effects models in S and S-PLUS*, was worked in the traditional way in *Biostatistics* Worksheet 301 following the chart in Zar 2010, *Biostatistical Analysis 5th edition*, Table 12.3 p. 262. Using the newer methods described by PB involving maximum likelihood & REML iterative estimates, similar but not exactly the same results are calculated below. The new method are much more useful since they allow unbalanced data and permit more sophisticated modeling including, as shown below, different interpretations of interaction between fixed and random effects. PB use this example along with several others to display a wide range of problems covered by linear mixed modeling using their {nlme} package in R. Their discussion, somewhat hard to follow at first, is nevertheless highly recommended.

## **Example:**

Machines Data from PB Section 1.3 p. 21.

#LMM 021 BLOCK DESIGN ANOVA WITH REPLICATES         library(nlme)       # {nlme} for lme()         library(help=nlme) # prototype for finding package index         #PINHEIRO & BATES MIXED-EFFECTS MODELS         #READING DATA IN STANDARD FORMAT         setwd("c:/BATData")         M=read.table("Machines.txt")         M\$fWorker=factor(M\$Worker)         M         groupedData plot:         #PLOTTING GROUPED DATA OBJECT:         MG=         plot(MG)							
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		1		I		I	
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	5		000			600	0 0
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factor(Worker)	, ,				0	0	0 0 00
	3				Ŭ Ŵ	Ŭ	0 0 00
	2		0	00	000 000		
	1		0	00	00	0 00	>
		45	50	55	60	65	70
				sc	core		

> [	٨G				
Gro	ouped Da	ata: sco	re ~ Ma	achine	factor(Worker)
	Worker	Machine	score	fWorker	factor(Worker)
1	1	A	52.0	1	1
2	1	A	52.8	1	1
3	1	A	53.1	1	1
4	2	A	51.8	2	2
5	2	A	52.8	2	2
6	2	A	53.1	2	2
7	3	A	60.0	3	3
8	3	A	60.2	3	3
9	3	A	58.4	3	3
10	4	A	51.1	4	4
11	4	A	52.3	4	4
12	4	A	50.3	4	4
13	5	A	50.9	5	5
14	5	A	51.8	5	5
15	5	A	51.4	5	5
16	6	A	46.4	6	6
17	6	A	44.8	6	6
18	6	A	49.2	6	6
19	1	В	62.1	1	1
20	1	В	62.6	1	1
21	1	В	64.0	1	1
22	2	В	59.7	2	2
23	2	В	60.0	2	2
24	2	В	59.0	2	2
25 26	3 3	B	68.6 65.8	3 3	3 3
20	3	B	69.7	3	3
28	4	B	63.2	4	4
29	4	B	62.8	4	4
30	4	B	62.2	4	4
31	5	В	64.8	5	5
32	5	В	65.0	5	5
33	5	В	65.4	5	5
34	6	B	43.7	6	6
35	6	В	44.2	6	6
36	6	В	43.0	6	6
37	1	С	67.5	1	1
38	1	С	67.2	1	1
39	1	С	66.9	1	1
40	2	С	61.5	2	2
41	2	С	61.7	2	2
42	2	С	62.3	2	2
43	3	С	70.8	3	3
44	3	С	70.6	3	3
45	3	С	71.0	3	3
46	4	С	64.1	4	4
47	4	С	66.2	4	4
48	4	С	64.0	4	4
49	5	С	72.1	5	5
50	5	С	72.0	5	5
51	5	С	71.1	5	5
52	6	С	62.0	6	6
53	6	C	61.4	6	6
54	6	С	60.5	6	6

# Linear Fixed Model ANOVA:

#FIXED FACTOR MODEL INCLUDING INTERACTION LM1=Im (score~Machine\*fWorker, data=M) summary(LM1) anova(LM1) #FIXED FACTOR MODEL NO INTERACTION LM2=Im (score~Machine+fWorker, data=M) #LINEAR MODEL WITH "treatments" CONTRASTS summary(LM2) anova(LM2) #COMPARISON OF FIXED FACTOR MODELS: anova(LM2,LM1)

#### > anova(LM1)

Analysis of Variance Table

Machine/Worker interactions are statistically significant here. >

Note: although results of the F-test for Interaction can be read directly, F-ratios for Treatment and Block effects following Zar's table require hand calculation as shown in *Biostatistics* Worksheet 301, but not repeated here.

Response: score Df Sum Sq Mean Sq F value Pr(>F) 2 1755.26 877.63 949.17 < 2.2e-16 \*\*\* Machine fWorker 5 1241.89 248.38 268.63 < 2.2e-16 \*\*\* 42.65 46.13 < 2.2e-16 \*\*\* Machine: fWorker 10 426.53 Residuals 36 33.29 0.92 \_\_\_ Signif. codes: 0 `\*\*\*' 0.001 `\*\*' 0.01 `\*' 0.05 `.' 0.1 `' 1 > anova(LM2) Analysis of Variance Table Response: score Df Sum Sq Mean Sq F value Pr(>F) Machine 2 1755.26 877.63 87.798 < 2.2e-16 \*\*\* fWorker 5 1241.89 248.38 24.848 4.867e-12 \*\*\* Residuals 46 459.82 10.00 \_\_\_ Signif. codes: 0 `\*\*\*' 0.001 `\*\*' 0.01 `\*' 0.05 `.' 0.1 `' 1 > anova(LM2,LM1) Analysis of Variance Table Model 1: score ~ Machine + fWorker Model 2: score ~ Machine \* fWorker Res.Df RSS Df Sum of Sq F Pr(>F) 1 46 459.82 36 33.29 10 426.53 46.13 < 2.2e-16 \*\*\* 2 \_\_\_ Signif. codes: 0 `\*\*\*' 0.001 `\*\*' 0.01 `\*' 0.05 `.' 0.1 `' 1

#### **Linear Mixed Model Without Interaction:**

$\mathbf{V} = \mathbf{R} + \mathbf{h} + \mathbf{c}$	where: $Y_{ij}$ is the response variable "score", $\beta_j$ = fixed cell
$\mathbf{Y}_{ijk} = \boldsymbol{\beta}_j + \mathbf{b}_i + \boldsymbol{\varepsilon}_{ijk}$	means for different levels j of Treatment "Machine", b <sub>i</sub> =
$b_i \sim N(0,\sigma_b^2), \epsilon_{iik} \sim N(0,\sigma^2)$	random offset from overall mean attributable to each
$b_i \sim 1(0,0_b)$ , $c_{ijk} \sim 1(0,0)$	Block "Worker", $\varepsilon_{iik}$ = error, with i as index of Blocks, j
	is index of Treatment levels, and k the index of replicates.

 $y_i = X_i\beta + Z_ib_i + \varepsilon_i$  < Matrix formulation in terms of each Block, with  $X_i$  being the matrix of fixed contrasts,  $\varepsilon_{ii} \sim N(0,\sigma^2 I)$  Z<sub>i</sub> the matrix of random contrasts, and I the Identity matrix.

Y~X + (1 | B) < formula representation with Y the response variable, X the Treatment, and B the block.</pre>

## Linear Mixed Model Without Interaction using lme() in R:

```
#MIXED LINEAR MODEL:
LMe1=lme(score~Machine,random=~1|fWorker,data=M)
summary(LMe1)
anova(LMe1)
anova(LMe1,type="marginal")
intervals(LMe1) #95% CONFIDENCE INTERVALS OF PARAMETERS
                                       > summary(LMe1)
                                       Linear mixed-effects model fit by REML
                                        Data: M
                                             AIC BIC logLik
                                         296.8782 306.5373 -143.4391
                                       Random effects:
                                        Formula: ~1 | fWorker
                                         (Intercept) Residual
                                       StdDev: 5.146552 3.161647
                                       Fixed effects: score ~ Machine
                                              Value Std.Error DF t-value p-value
                                       (Intercept) 52.35556 2.229312 46 23.48507 0
                                       MachineB 7.96667 1.053883 46 7.55935
                                                                                   0
                                       MachineC 13.91667 1.053883 46 13.20514
                                                                                   0
                                        Correlation:
```

### Linear Mixed Model With Interaction as a Nested Design:

	where: $Y_{ij}$ is the response variable "score", $\beta_j$ = fixed cell
$\mathbf{V} = \mathbf{\beta} + \mathbf{b} + \mathbf{b} + \mathbf{s}$	means for different levels j of Treatment "Machine", b <sub>i</sub> =
$\mathbf{Y}_{ijk} = \boldsymbol{\beta}_j + \mathbf{b}_i + \mathbf{b}_{ij} + \boldsymbol{\epsilon}_{ijk}$	random offset from overall mean attributable to each Block
$\mathbf{b}_{i} \sim N(0,\sigma_{1}^{2}), \mathbf{b}_{ii} \sim N(0,\sigma_{2}^{2}), \mathbf{\varepsilon}_{iik} \sim N(0,\sigma^{2})$	"Worker", b <sub>ii</sub> = effect of Machine within (i.e., related to)
$b_i = 1(0,0_1), b_{ij} = 1(0,0_2), c_{ijk} = 1(0,0)$	Worker, $\varepsilon_{iik}$ = error, with i as index of Blocks, j is index of
	Treatment levels, and k the index of replicates within Blocks.
$\mathbf{v} = \mathbf{V}\mathbf{\beta} + 7\mathbf{b} + 7\mathbf{b} + \mathbf{s}$	

(Intr) MachnB

Number of Observations: 54

Number of Groups: 6

Standardized Within-Group Residuals:

Min O1 Med O3

-2.7248806 -0.5232891 0.1327564 0.6513056 1.7559058

MachineB -0.236 MachineC -0.236 0.500

$\mathbf{y}_{i} = \mathbf{A}_{i}\mathbf{p} + \mathbf{Z}_{i}\mathbf{v}_{i} + \mathbf{Z}_{ij}\mathbf{v}_{ij} + \mathbf{\varepsilon}_{i}$	< Matrix formulation in terms of each Block i, with X <sub>i</sub> being the matrix of fixed
$\epsilon_{ii} \sim N(0, \sigma^2 I)$	contrasts, $Z_i \& Z_{ij}$ the matrices of random contrasts, and I the Identity matrix.

Y ~ X + (1|B/X) < formula representation with Y the response variable, X the Treatment, B/X the block B with interaction effect of X within B.

score ~ Machine + (1 | fWorker/Machine)

## Linear Mixed Model With Interaction as a Nested Design using lme() in R:

#NESTED DESIGN MIXED MODEL: LMe2=Ime(score~Machine,random=~1|fWorker/Machine,data=M) summary(LMe2) anova(LMe2) anova(LMe2,type="marginal") intervals(LMe2) Max

> summary(LMe2) Linear mixed-effects model fit by REML Data: M AIC BIC logLik 227.6876 239.2785 -107.8438 Random effects: Formula: ~1 | fWorker (Intercept) StdDev: 4.78105 Formula: ~1 | Machine %in% fWorker (Intercept) Residual StdDev: 3.729532 0.9615771 Fixed effects: score ~ Machine Value Std.Error DF t-value p-value (Intercept) 52.35556 2.485828 36 21.061613 0.0000 MachineB 7.96667 2.176972 10 3.659518 0.0044 MachineC 13.91667 2.176972 10 6.392672 0.0001 Correlation: (Intr) MachnB MachineB -0.438 MachineC -0.438 0.500 Standardized Within-Group Residuals: Min Q1 Med Q3 Max -2.26958675 -0.54846580 -0.01070594 0.43936568 2.54005792 Number of Observations: 54 Number of Groups: fWorker Machine %in% fWorker 6 18

# **Linear Mixed Model With General Interaction:**

$Y_{ijk} = \beta_j + b_i + \varepsilon_{ijk}$ $b_i \sim N(0, \Psi), \ \varepsilon_{ij} \sim N(0, \sigma^2 I)$	where: $Y_{ij}$ is the response variable "score", $\beta_j$ = fixed cell means for different levels j of Treatment "Machine", $b_i$ = random offset from overall mean attributable to each Block/Treatment interaction, $\varepsilon_{ijk}$ = error, with i as index of Blocks, j is index of Treatment levels, and k the index of replicates within Blocks.
$\mathbf{y}_{i} = \mathbf{X}_{i}\boldsymbol{\beta} + \mathbf{Z}_{i}\mathbf{b}_{i} + \boldsymbol{\epsilon}_{i}$	< Matrix formulation in terms of each Block i, with $X_i$ being the fixed contrasts, $Z_i$ the matrix of random cell mean contrasts, $\Psi$ the matrix of all variance/covariances between $b_i$ , and I the Identity matrix.
$\mathbf{Y} \sim \mathbf{X} + (\mathbf{X} \mid \mathbf{B})$ < formu	la representation with Y the response variable, X the Treatment, the block B

but also with random effect of X (analyzed with cell-mean constrasts for convenience).

score ~ Machine + (Machine | fWorker)

#### Linear Mixed Model With General Interaction using lme() in R:

#MIXED MODEL RANDOM VARIANCE MATRIX ANY POSITIVE-DEFINITE: LMe3=lme(score~Machine,random=~Machine|fWorker,data=M) summary(LMe3) anova(LMe3) anova(LMe3,type="marginal") intervals(LMe3)

#### Randomized Block ANOVA with Replicates

#### > summary(LMe3)

Linear mixed-effects model fit by REML Data: M BIC logLik AIC 228.3112 247.6295 -104.1556 Random effects: Formula: ~Machine - 1 | fWorker Structure: General positive-definite, Log-Cholesky parametrization StdDev Corr MachineA 4.0792807 MachnA MachnB MachineB 8.6252908 0.803 MachineC 4.3894795 0.623 0.771 Residual 0.9615766 Fixed effects: score ~ Machine Value Std.Error DF t-value p-value (Intercept) 52.35556 1.680711 46 31.150834 0.0000 MachineB 7.96667 2.420851 46 3.290854 0.0019 MachineC 13.91667 1.540100 46 9.036211 0.0000 Correlation: (Intr) MachnB MachineB 0.463 MachineC -0.374 0.301 Standardized Within-Group Residuals: Min Q1 Med Q3 Max -2.39354008 -0.51377575 0.02690829 0.47245472 2.53338699 Number of Observations: 54 Number of Groups: 6 > anova(LMe1) numDF denDF F-value p-value (Intercept) 1 46 773.5703 <.0001 Machine 2 46 87.7982 <.0001 > anova(LMe2) numDF denDF F-value p-value (Intercept) 1 36 773.5709 <.0001 2 10 20.5762 3e-04 Machine > anova(LMe3) numDF denDF F-value p-value (Intercept) 1 46 2351.8063 <.0001 Machine 2 46 41.0038 <.0001 > anova(LMe1,LMe2) Model df AIC BIC logLik Test L.Ratio p-value LMe1 1 5 296.8782 306.5373 -143.4391 LMe2 2 6 227.6876 239.2785 -107.8438 1 vs 2 71.19063 <.0001 > anova(LMe1,LMe3) Model df AIC BIC logLik Test L.Ratio p-value 1 5 296.8782 306.5373 -143.4391 T.Me1 2 10 228.3112 247.6295 -104.1556 1 vs 2 78.56698 <.0001 LMe3 > anova(LMe2,LMe3) Test L.Ratio p-value Model df AIC BIC logLik LMe2 1 6 227.6876 239.2785 -107.8438 LMe3 2 10 228.3112 247.6295 -104.1556 1 vs 2 7.37635 0.1173

^ Preference is seen for models LMe2 or LMe3 with interactions over LMe1 without interactions. Difference between Nested model of interactions LMe2 and General Model LMe3 is not significant, so model LMe2 with fewer estimated parameters (see df) and lower AIC is preferred.

#COMPARISON OF MODELS: anova(LMe1,LMe2) anova(LMe1,LMe3) anova(LMe2,LMe3)