$$
\begin{array}{lll}
\text { ORIGIN }:=0 & \text { Randomized Block Designs with Replicates } & \text { prepared by } \\
\text { Wm Stein }
\end{array}
$$

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. $P B$ 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 Ime() library(help=nlme) \# prototype for finding package index

```
#PINHEIRO & BATES MIXED-EFFECTS MODELS
#READING DATA IN STANDARD FO RMAT
setwd("c:/BATData")
M=read.table("Machines.txt")
M$fWorker=factor(M$Worker)
M
```


## groupedData plot:

\#PLOTTING GROUPED DATA OBJECT:
MG=groupedData(score~Machine|factor(Worker),data=M)
MG
plot(MG)

> MG
Grouped Data: score ~ Machine | factor(Worker) Worker Machine score fWorker factor(Worker)


## 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)
```


## 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.

```
> anova(LM1)
Analysis of Variance Table
Response: score
    Df Sum Sq Mean Sq F value Pr(>F)
Machine 2 1755.26 877.63 949.17< 2.2e-16 ***
fWorker 5 1241.89 248.38 268.63< 2.2e-16 ***
Machine:fWorker 10 426.53 42.65 46.13 < 2.2e-16 ***
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
2 36 33.29 10 426.53 46.13 < 2.2e-16 ***
Signif. codes: 0 `***' 0.001 `**' 0.01 '*' 0.05 '.' 0.1 ', 1
```


## Linear Mixed Model Without Interaction:

$\mathbf{Y}_{\mathrm{ijk}}=\beta_{\mathrm{j}}+\mathbf{b}_{\mathrm{i}}+\varepsilon_{\mathrm{ijk}}$
$\mathbf{b}_{\mathbf{i}} \sim \mathbf{N}\left(\mathbf{0}, \sigma_{\mathrm{b}}{ }^{2}\right), \varepsilon_{\mathrm{ijk}} \sim \mathbf{N}\left(\mathbf{0}, \sigma^{2}\right)$
$\mathbf{y}_{\mathbf{i}}=\mathbf{X}_{\mathbf{i}} \beta+\mathbf{Z}_{\mathbf{i}} \mathbf{b}_{\mathbf{i}}+\varepsilon_{\mathbf{i}}<$ Matrix formulation in terms of each Block, with $\mathbf{X}_{\mathbf{i}}$ being the matrix of fixed contrasts, $\varepsilon_{\mathrm{ij}} \sim \mathbf{N}\left(0, \sigma^{2} \mathrm{I}\right) \quad \mathrm{Z}_{\mathrm{i}}$ the matrix of random contrasts, and I the Identity matrix.
$\mathbf{Y} \sim \mathbf{X}+(1 \mid B) \quad$ formula representation with $Y$ the response variable, $X$ the Treatment, and $B$ the block.
score $\sim$ Machine + (1 | fWorker)
where: $\mathbf{Y}_{\mathrm{ij}}$ is the response variable "score", $\beta_{\mathrm{j}}=$ fixed cell means for different levels $j$ of Treatment "Machine", $b_{i}=$ random offset from overall mean attributable to each Block "Worker", $\varepsilon_{\mathrm{ijk}}=$ error, with i as index of Blocks, j is index of Treatment levels, and $k$ the index of replicates.

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

```
#MIXED LINEAR MODEL:
LMe1=Ime(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
$296.8782306 .5373-143.4391$
Random effects:
Formula: ~1 | fWorker
(Intercept) Residual
StdDev: 5.1465523 .161647
Fixed effects: score ~ Machine
Value Std.Error DF t-value p-value
(Intercept) 52.355562 .2293124623 .48507 0
$\begin{array}{llllll}\text { MachineB } & 7.96667 & 1.053883 & 46 & 7.55935 & 0\end{array}$
$\begin{array}{llllll}\text { MachineC } \quad 13.91667 & 1.053883 & 46 & 13.20514 & 0\end{array}$
Correlation:
(Intr) MachnB
MachineB -0.236
MachineC -0.236 0.500
Standardized Within-Group Residuals:

| Min | Q1 | Med | Q3 | Max |
| ---: | ---: | ---: | ---: | ---: |
| -2.7248806 | -0.5232891 | 0.1327564 | 0.6513056 | 1.7559058 |

Number of Observations: 54
Number of Groups: 6

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

$\mathbf{Y}_{\mathrm{ijk}}=\beta_{\mathrm{j}}+\mathbf{b}_{\mathbf{i}}+\mathbf{b}_{\mathrm{ij}}+\varepsilon_{\mathrm{ijk}}$
$b_{i} \sim N\left(0, \sigma_{1}{ }^{2}\right), b_{i j} \sim N\left(0, \sigma_{2}{ }^{2}\right), \varepsilon_{i \mathrm{ijk}} \sim N\left(0, \sigma^{2}\right)$
where: $Y_{i j}$ is the response variable "score", $\beta_{j}=$ fixed cell means for different levels $\mathbf{j}$ of Treatment "Machine", $\mathbf{b}_{\mathbf{i}}=$ random offset from overall mean attributable to each Block "Worker", $b_{i j}=$ effect of Machine within (i.e., related to) Worker, $\varepsilon_{i j k}=$ error, with $i$ as index of Blocks, $j$ is index of Treatment levels, and $k$ the index of replicates within Blocks.
$\mathbf{y}_{\mathbf{i}}=\mathbf{X}_{\mathrm{i}} \boldsymbol{\beta}+\mathbf{Z}_{\mathrm{i}} \mathbf{b}_{\mathbf{i}}+\mathbf{Z}_{\mathrm{ij}} \mathbf{b}_{\mathbf{i j}}+\varepsilon_{\mathbf{i}}$ $\varepsilon_{i j} \sim \mathbf{N}\left(\mathbf{0}, \sigma^{2} \mathbf{I}\right)$
$Y \sim X+(1 \mid B / X) \quad<$ formula representation with $Y$ the response variable, $X$ the Treatment, $B / X$ the block $B$ with interaction effect of $X$ within $B$.
score $\sim$ Machine + (1 | fWorker/Machine)

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

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

```
> 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 
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:
\begin{tabular}{rrrrr} 
Min & Q1 & Med & Q3 & Max \\
-2.26958675 & -0.54846580 & -0.01070594 & 0.43936568 & 2.54005792
\end{tabular}
Number of Observations: 54
Number of Groups:
    fWorker Machine %in% fWorker
```


## Linear Mixed Model With General Interaction:

$\mathbf{Y}_{\mathrm{ijk}}=\beta_{\mathrm{j}}+\mathbf{b}_{\mathbf{i}}+\varepsilon_{\mathrm{ijk}}$
$b_{i} \sim N(0, \Psi), \varepsilon_{i j} \sim N\left(0, \sigma^{2} I\right)$
$\mathbf{y}_{\mathbf{i}}=\mathbf{X}_{\mathbf{i}} \boldsymbol{\beta}+\mathbf{Z}_{\mathbf{i}} \mathbf{b}_{\mathbf{i}}+\varepsilon_{\mathbf{i}}$
where: $\mathbf{Y}_{\mathrm{ij}}$ is the response variable "score", $\beta_{\mathrm{j}}=$ fixed cell means for different levels $j$ of Treatment "Machine", $b_{i}=$ random offset from overall mean attributable to each Block/Treatment interaction, $\varepsilon_{i j \mathrm{jk}}=$ error, with i as index of Blocks, $j$ is index of Treatment levels, and $k$ the index of replicates within Blocks.
< Matrix formulation in terms of each Block $\mathbf{i}$, with $\mathbf{X}_{\mathbf{i}}$ 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.
$Y \sim X+(X \mid B) \quad<$ formula 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 $\sim$ Machine + (Machine | fWorker)

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

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

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

```
    > summary(LMe3)
    Linear mixed-effects model fit by REML
        Data: M
            AIC BIC logLik
    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: 
Number of Observations: 54
Number of Groups: 6
> anova(LMe1)
numDF denDF F-value p-value
(Intercept) 1 46773.5703<.0001
Machine 2 46 87.7982 <.0001
> anova(LMe2)
\begin{tabular}{lrrrr} 
& numDF & denDF & F-value & p-value \\
(Intercept) & 1 & 36 & 773.5709 & \(<.0001\) \\
Machine & 2 & 10 & 20.5762 & \(3 e-04\)
\end{tabular}
> 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)
```


${ }^{\wedge}$ 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.

