

Pharmaceutical Example: Nested Design (Sites as Fixed)

We return to Example 17.11 from Ott and Longnecker. This is a two-stage nested design with batch nested within site (and tablet nested with batch). For this analysis, we are treating site as fixed.

Notes:

1. In this case we cannot use the A/B notation because we want to treat sites as fixed, but batches as random.
2. When there is nesting, I prefer to work with unique names to prevent confusion/mistakes! See previous example for details.
3. Use of EMSanova is primarily for illustration. Not required for routine analysis.

```
library(lme4)
library(lmerTest)
library(pbkrtest)
library(emmeans)
library(EMSaov)
Tablet <- read.csv("C:/hess/STAT512/RNotes/Random1/R1_Pharm_Nested.csv", header=TRUE)
str(Tablet)
```

```
## 'data.frame': 30 obs. of 3 variables:
## $ site : int 1 1 1 1 1 1 1 1 1 1 ...
## $ batch : int 1 1 1 1 1 2 2 2 2 2 ...
## $ content: num 5.03 5.1 5.25 4.98 5.05 4.64 4.73 4.82 4.95 5.06 ...
```

#Important: Need to define site and batch as factors!!!!

```
Tablet$site <- as.factor(Tablet$site)
Tablet$batch <- as.factor(Tablet$batch)
Modell1 <- lmer( content ~ site + (1|site:batch), data = Tablet)
summary(Modell1)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: content ~ site + (1 | site:batch)
## Data: Tablet
##
## REML criterion at convergence: -29.8
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -1.9919 -0.4455 -0.1840  0.4677  2.3623
##
## Random effects:
## Groups      Name                Variance Std.Dev.
## site:batch (Intercept) 0.02028  0.1424
## Residual                0.01209  0.1100
## Number of obs: 30, groups: site:batch, 6
##
## Fixed effects:
##              Estimate Std. Error    df t value Pr(>|t|)
## (Intercept)  5.01867    0.08699 4.00000  57.694  5.4e-07 ***
## site2        0.04933    0.12302 4.00000   0.401    0.709
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##      (Intr)
## site2 -0.707
```

```
anova(Model1, ddf="Kenward-Roger")
```

```
## Type III Analysis of Variance Table with Kenward-Roger's method
##      Sum Sq   Mean Sq NumDF DenDF F value Pr(>F)
## site 0.0019445 0.0019445     1     4  0.1608 0.7089
```

```
emmeans(Model1, pairwise ~ site)
```

```
## $emmeans
##   site emmean    SE df lower.CL upper.CL
## 1      5.02 0.087  4      4.78      5.26
## 2      5.07 0.087  4      4.83      5.31
##
## Degrees-of-freedom method: kenward-roger
## Confidence level used: 0.95
##
## $contrasts
##   contrast estimate    SE df t.ratio p.value
## 1 - 2      -0.0493 0.123  4  -0.401  0.7089
```

```
EMS <- EMSanova(content ~ site + batch, data = Tablet,
                 type = c("F", "R"),
                 nested = c(NA, "site"))
```

```
EMS
```

```
##           Df          SS          MS Fvalue Pvalue Sig
## site         1 0.01825333 0.01825333 0.1608 0.7089
## batch(site)  4 0.45401333 0.11350333 9.3869 1e-04 ***
## Residuals    24 0.29020000 0.01209167
##
##           EMS
## site      Error+5batch(site)+15site
## batch(site) Error+5batch(site)
## Residuals      Error
```