Statistics 514: Design of Experiments

Topic 10

Topic Overview

This topic will cover

- Mixed Effects Designs
- Nested Factors
- Split-plot Designs
- Computing Standard Errors
- Repeated Measures Analysis

Factorial Experiments with Random Effects

- Much of the previous discussion has focused on fixed effects
  - Always use MSE in denominator of F-test
  - Use MSE in linear combinations and CI's
- Not always true when random factors present
  - May use interaction MS or combination of MS's
- Will now use EMS as guide for tests
- Two models: Random model, Mixed model

Two-Factor Random Model

$$y_{i,j,k} = \mu + \tau_i + \beta_j + (\tau\beta)_{i,j} + \epsilon_{i,j,k} \begin{cases} i = 1, 2, \ldots, a \\ j = 1, 2, \ldots, b \\ k = 1, 2, \ldots, n \end{cases}$$

$$\tau_i \sim N(0, \sigma^2_\tau) \quad \beta_j \sim N(0, \sigma^2_\beta) \quad (\tau\beta)_{i,j} \sim N(0, \sigma^2_{\tau\beta})$$

- $\text{Var}(y_{i,j,k}) = \sigma^2 + \sigma^2_\tau + \sigma^2_\beta + \sigma^2_{\tau\beta}$
- Expected MS's similar to one-factor random model
  - $\text{E}(\text{MS}_E) = \sigma^2$

- $E(MS_A) = \sigma^2 + bn\sigma_\tau^2 + n\sigma_{\tau\beta}^2$
- $E(MS_B) = \sigma^2 + an\sigma_\beta^2 + n\sigma_{\tau\beta}^2$
- $E(MS_{AB}) = \sigma^2 + n\sigma_{\tau\beta}^2$

- EMS determine which MS to use in denominator
  - $H_0 : \sigma_\tau^2 = 0 \rightarrow MS_A/MS_{AB}$
  - $H_0 : \sigma_\beta^2 = 0 \rightarrow MS_B/MS_{AB}$
  - $H_0 : \sigma_{\tau\beta}^2 = 0 \rightarrow MS_{AB}/MS_E$
- No hierarchical testing. Look at all tests.

Estimating Variance Components

- Using ANOVA method
  - $\hat{\sigma}^2 = MS_E$
  - $\hat{\sigma}_\tau^2 = (MS_A - MS_{AB})/bn$
  - $\hat{\sigma}_\beta^2 = (MS_B - MS_{AB})/an$
  - $\hat{\sigma}_{\tau\beta}^2 = (MS_{AB} - MS_E)/n$
- Sometimes results in negative estimates
- `proc varcomp` and `proc mixed` compute estimates
- Can use different estimation procedures
  - ANOVA method – `Method = type1`
  - RMLE method – `Method = reml`(default)
- `proc mixed`
  - Variance component estimates
  - Hypothesis tests and confidence intervals

```
             Gauge Capability Example in Text 13-2

options nocenter ps=60 ls=80;

data randr;
 input part operator resp @@;
 cards;
1 1 21 1 1 20 1 2 20 1 2 20 1 3 19 1 3 21
2 1 24 2 1 23 2 2 24 2 2 24 2 3 23 2 3 24
3 1 20 3 1 21 3 2 19 3 2 21 3 3 20 3 3 22
```

```
4 1 27 4 1 27 4 2 28 4 2 26 4 3 27 4 3 28
5 1 19 5 1 18 5 2 19 5 2 18 5 3 18 5 3 21
6 1 23 6 1 21 6 2 24 6 2 21 6 3 23 6 3 22
7 1 22 7 1 21 7 2 22 7 2 24 7 3 22 7 3 20
8 1 19 8 1 17 8 2 18 8 2 20 8 3 19 8 3 18
9 1 24 9 1 23 9 2 25 9 2 23 9 3 24 9 3 24
10 1 25 10 1 23 10 2 26 10 2 25 10 3 24 10 3 25
11 1 21 11 1 20 11 2 20 11 2 20 11 3 21 11 3 20
12 1 18 12 1 19 12 2 17 12 2 19 12 3 18 12 3 19
13 1 23 13 1 25 13 2 25 13 2 25 13 3 25 13 3 25
14 1 24 14 1 24 14 2 23 14 2 25 14 3 24 14 3 25
15 1 29 15 1 30 15 2 30 15 2 28 15 3 31 15 3 30
16 1 26 16 1 26 16 2 25 16 2 26 16 3 25 16 3 27
17 1 20 17 1 20 17 2 19 17 2 20 17 3 20 17 3 20
18 1 19 18 1 21 18 2 19 18 2 19 18 3 21 18 3 23
19 1 25 19 1 26 19 2 25 19 2 24 19 3 25 19 3 25
20 1 19 20 1 19 20 2 18 20 2 17 20 3 19 20 3 17
;

proc glm;
 class operator part;
 model resp=operator|part;
 random operator part operator*part / test;
 test H=operator E=operator*part;
 test H=part E=operator*part;

proc mixed cl=wald maxiter=20 covtest method=type1;
 class operator part;
 model resp = ;
 random operator part operator*part;

proc mixed cl maxiter=20 covtest;
 class operator part;
 model resp = ;
 random operator part operator*part;
run;
```

Dependent Variable: resp

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	59	1215.091667	20.594774	20.77	<.0001
Error	60	59.500000	0.991667		
Corrected Total	119	1274.591667			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
operator	2	2.616667	1.308333	1.32	0.2750
part	19	1185.425000	62.390789	62.92	<.0001
operator*part	38	27.050000	0.711842	0.72	0.8614

Source	Type III Expected Mean Square
operator	Var(Error) + 2 Var(operator*part) + 40 Var(operator)
part	Var(Error) + 2 Var(operator*part) + 6 Var(part)
operator*part	Var(Error) + 2 Var(operator*part)

Tests of Hypotheses Using the Type III MS for operator*part as an Error Term

Source	DF	Type III SS	Mean Square	F Value	Pr > F
operator	2	2.616667	1.308333	1.84	0.1730
part	19	1185.425000	62.390789	87.65	<.0001

Tests of Hypotheses for Random Model Analysis of Variance

Dependent Variable: resp

Source	DF	Type III SS	Mean Square	F Value	Pr > F
operator	2	2.616667	1.308333	1.84	0.1730
part	19	1185.425000	62.390789	87.65	<.0001
Error	38	27.050000	0.711842		

Error: MS(operator*part)

Source	DF	Type III SS	Mean Square	F Value	Pr > F
operator*part	38	27.050000	0.711842	0.72	0.8614
Error: MS(Error)	60	59.500000	0.991667		

Type 1 Analysis of Variance

Source	DF	Sum of Squares	Mean Square
operator	2	2.616667	1.308333
part	19	1185.425000	62.390789
operator*part	38	27.050000	0.711842
Residual	60	59.500000	0.991667

Type 1 Analysis of Variance

Source	Expected Mean Square	Error Term	Error DF
operator	Var(Residual) + 2 Var(operator*part) + 40 Var(operator)	MS(operator*part)	38
part	Var(Residual) + 2 Var(operator*part) + 6 Var(part)	MS(operator*part)	38
operator*part	Var(Residual) + 2 Var(operator*part)	MS(Residual)	60
Residual	Var(Residual)	.	.

Covariance Parameter Estimates

Cov Parm	Estimate	Standard Error	Z Value	Pr Z	Alpha	Lower	Upper
operator	0.01491	0.03296	0.45	0.6510	0.05	-0.04969	0.07952
part	10.2798	3.3738	3.05	0.0023	0.05	3.6673	16.8924
operator*part	-0.1399	0.1219	-1.15	0.2511	0.05	-0.3789	0.09903
Residual	0.9917	0.1811	5.48	<.0001	0.05	0.7143	1.4698

The Mixed Procedure

```
                     Iteration History
Iteration    Evaluations    -2 Res Log Like       Criterion
        0              1       624.67452320
        1              3       409.39453674      0.00003340
        2              1       409.39128078      0.00000004
        3              1       409.39127700      0.00000000
                   Convergence criteria met.

                           Covariance Parameter Estimates
                          Standard       Z
Cov Parm         Estimate     Error   Value       Pr Z   Alpha      Lower      Upper
operator          0.01063   0.03286    0.32     0.3732    0.05   0.001103   3.737E12
part              10.2513    3.3738    3.04     0.0012    0.05     5.8888    22.1549
operator*part           0         .       .          .       .          .          .
Residual           0.8832    0.1262    7.00     <.0001    0.05     0.6800     1.1938
```

Confidence Intervals for Variance Components

- Can use asymptotic variance estimates to form CI
- Known as Wald's approximate CI
- `mixed`: option `cl = wald` or `method = type1`

  Use standard normal → 95% CI uses 1.96
  $\hat{\sigma}^2_\beta \pm 1.96(0.0330) = (-0.05, 0.08)$
  $\hat{\sigma}^2_\tau \pm 1.96(3.3738) = (3.67, 16.89)$

- In general `proc mixed` uses Satterthwaite CI

  Default method – REML
  Versions < 6.12 computed Wald CI
  Current uses Satterthwaite's Approximation
  Will discuss this CI construction later

Rules for Expected Mean Squares (13-5)

- In models so far, EMS fairly straightforward
- Could show EMS using brute force expectation method
- For mixed models, good to have formal procedure
- Montgomery describes procedure for **restricted** model

1. Write the error term in the model as $\epsilon_{(i,j,..)m}$, where m represents the replication subscript.
2. Write each variable term in the model as a row heading in a two-way table

3. Write the subscripts in the model as column headings. Over each subscript, write "F" if factor fixed and "R" if random. Over this, write down the levels of each subscript.
4. For each row, copy the number of observations under each subscript, providing the subscript does not appear in the row variable term.
5. For any bracketed subscripts in the model, place a 1 under those subscripts that are inside the brackets.
6. Fill in remaining cells with a 0 (if subscript represents a fixed factor) or a 1 (if random factor).
7. To find the remaining mean square of any term (row), cover the entries in the columns that contain non-bracketed subscript letters in this term in the model. For the rows with at least the same subscripts, multiply the remaining numbers to get coefficient for corresponding terms in the model.

2-Factor Fixed Model

$$y_{i,j,k} = \mu + \tau_i + \beta_j + (\tau\beta)_{i,j} + \epsilon_{i,j,k}$$

	F	F	R	
	a	b	n	Expected
Factor	i	j	k	Mean Square
τ_i	0	b	n	$\sigma^2 + \frac{bn\sum\tau_i^2}{a-1}$
β_j	a	0	n	$\sigma^2 + \frac{an\sum\beta_j^2}{b-1}$
$(\tau\beta)_{i,j}$	0	0	n	$\sigma^2 + \frac{n\sum\sum(\tau\beta)_{i,j}^2}{(a-1)(b-1)}$
$\epsilon_{(i,j),k}$	1	1	1	σ^2

2-Factor Random Model

$$y_{i,j,k} = \mu + \tau_i + \beta_j + (\tau\beta)_{i,j} + \epsilon_{i,j,k}$$

	R	R	R	
	a	b	n	Expected
Factor	i	j	k	Mean Square
τ_i	1	b	n	$\sigma^2 + n\sigma_{\tau\beta}^2 + bn\sigma_\tau^2$
β_j	a	1	n	$\sigma^2 + n\sigma_{\tau\beta}^2 + an\sigma_\beta^2$
$(\tau\beta)_{i,j}$	1	1	n	$\sigma^2 + n\sigma_{\tau\beta}^2$
$\epsilon_{(i,j),k}$	1	1	1	σ^2

2-Factor Mixed Model (A Fixed)

$$y_{i,j,k} = \mu + \tau_i + \beta_j + (\tau\beta)_{i,j} + \epsilon_{i,j,k}$$

	F	R	R	
	a	b	n	Expected
Factor	i	j	k	Mean Square
τ_i	0	b	n	$\sigma^2 + n\sigma^2_{\tau\beta} + \frac{bn\sum\tau_i^2}{a-1}$
β_j	a	1	n	$\sigma^2 + an\sigma^2_{\beta}$
$(\tau\beta)_{i,j}$	0	1	n	$\sigma^2 + n\sigma^2_{\tau\beta}$
$\epsilon_{(i,j),k}$	1	1	1	σ^2

3-Factor Mixed Model (*A* Fixed)

$$y_{i,j,k} = \mu + \tau_i + \beta_j + \delta_k + (\tau\beta)_{i,j} + (\tau\delta)_{i,k} + (\beta\delta)_{j,k} + \epsilon_{i,j,k,\ell}$$

	F	R	R	R	
	a	b	c	n	
Factor	i	j	k	ℓ	Expected Mean Squares
τ_i	0	b	c	n	$\sigma^2 + cn\sigma^2_{\tau\beta} + bn\sigma^2_{\tau\gamma} + n\sigma^2_{\tau\beta\gamma} + \frac{bcn\sum\tau_i^2}{a-1}$
β_j	a	1	c	n	$\sigma^2 + an\sigma^2_{\beta\gamma} + acn\sigma^2_{\beta}$
γ_k	a	b	1	n	$\sigma^2 + an\sigma^2_{\beta\gamma} + abn\sigma^2_{\gamma}$
$(\tau\beta)_{i,j}$	0	1	c	n	$\sigma^2 + n\sigma^2_{\tau\beta\gamma} + cn\sigma^2_{\tau\beta}$
$(\tau\gamma)_{i,k}$	0	b	1	n	$\sigma^2 + n\sigma^2_{\tau\beta\gamma} + bn\sigma^2_{\tau\gamma}$
$(\beta\gamma)_{j,k}$	a	1	1	n	$\sigma^2 + an\sigma^2_{\beta\gamma}$
$(\tau\beta\gamma)_{i,j,k}$	0	1	1	n	$\sigma^2 + n\sigma^2_{\tau\beta\gamma}$
$\epsilon_{i,j,k,\ell}$	1	1	1	1	σ^2

Construction of Hasse Diagram

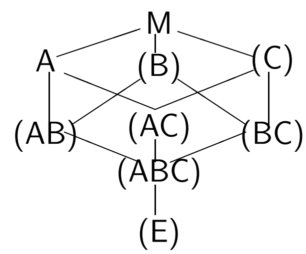
- Described in Oehlert.
- Used for both *restricted* and *unrestricted* models
- Provide graphical view of design
- Shows nested/crossed and random/fixed structure
- Every term in model is a node
- Terms/nodes placed in layered structure

  Term U is above term V if all terms in U are in V.

- Join nodes based on nested/cross structure
- Brackets placed around random terms

3-Factor Mixed Model

- Denominator for U is leading eligible random term(s)
- Leading: Closest connected random term below U
- Eligible:
  - Unrestricted: Any random term possible
  - Restricted: Any without fixed factor not in U



Restricted Model:
A: Leading random terms are AB and AC $\rightarrow$ approximate test
B: Leading random term is BC because AB has fixed factor A
BC: Leading term is E because ABC has fixed factor A

Unrestricted Model:
A: Leading random terms are AB and AC $\rightarrow$ approximate test
B: Leading random terms is AB and BC $\rightarrow$ approximate
BC: Leading term is ABC

Two-Factor Mixed Effects Model

- Same model but different parameter restrictions
- Assume A fixed and B random

1	$\sum \tau_i = 0$ and $\beta \sim N(0, \sigma^2_\beta)$	usual assumptions
2	$(\tau\beta)_{i,j} \sim N(0, (a-1)\sigma^2_{\tau\beta}/a)$	$(a-1)/a$ simplifies EMS
3	$\sum_j (\tau\beta)_{i,j} = 0$ for β level j	added restriction

- Due to added restriction
  - Not all $(\tau\beta)_{i,j}$ independent, $\text{Cov}((\tau\beta)_{i,j}, (\tau\beta)_{i',j}) = -\frac{1}{a}\sigma^2_{\tau\beta}$
- Known as **restricted** mixed effects model
- This model coincides with EMS algorithm
  - $\text{E}(MS_E) = \sigma^2$

- $\mathrm{E}(MS_A) = \sigma^2 + bn\sum\tau_i^2/(a-1) + n\sigma^2_{\tau\beta}$
- $\mathrm{E}(MS_B) = \sigma^2 + an\sigma^2_\beta$
- $\mathrm{E}(MS_{AB}) = \sigma^2 + n\sigma^2_{\tau\beta}$

NOTE: If $X_i \sim N(0,\sigma^2)$ then $\begin{cases} X_i - \bar{X} \sim N(0, \frac{n-1}{n}\sigma^2) \\ \mathrm{Cov}(X_i - \bar{X}, X_j - \bar{X}) = -\frac{1}{n}\sigma^2 \end{cases}$

Hypothesis Tests and Diagnostics

- Hypothesis Tests

$$\begin{aligned} \mathrm{H}_0 &: \tau_1 = \tau_2 = \ldots = 0 \to MS_A/MS_{AB} \\ \mathrm{H}_0 &: \sigma^2_\beta = 0 \to MS_B/MS_E \\ \mathrm{H}_0 &: \sigma^2_{\tau\beta} = 0 \to MS_{AB}/MS_E \end{aligned}$$

- Variance Estimates (Using ANOVA method)

$$\begin{aligned} \hat{\sigma}^2 &= MS_E \\ \hat{\sigma}^2_\beta &= (MS_B - MS_E)/an \\ \hat{\sigma}^2_{\tau\beta} &= (MS_{AB} - MS_E)/n \end{aligned}$$

Diagnostics

- Histogram or QQplot

  Normality or Unusual Observation

- Residual Plots

  Constant variance or Unusual Observations

Multiple Comparisons

$$y_{i,j,k} = \mu + \tau_i + \beta_j + (\tau\beta)_{i,j} + \epsilon_{i,j,k}$$

$$\begin{aligned} \bar{y}_{i..} &= \mu + \tau_i + \bar{\beta}_. + (\bar{\tau\beta})_{i.} + \bar{\epsilon}_{i..} \\ \mathrm{Var}(\bar{y}_{i..}) &= \sigma^2_\beta/b + (a-1)\sigma^2_{\tau\beta}/ab + \sigma^2/bn \\ \bar{y}_{i..} - \bar{y}_{i'..} &= \tau_i - \tau_{i'} + (\bar{\tau\beta})_{i.} - (\bar{\tau\beta})_{i'.} + \bar{\epsilon}_{i..} - \bar{\epsilon}_{i'..} \\ \mathrm{Var}(\bar{y}_{i..} - \bar{y}_{i'..}) &= 2\sigma^2_{\tau\beta}/b + 2\sigma^2/bn \\ &= 2(n\sigma^2_{\tau\beta} + \sigma^2)/bn \end{aligned}$$

- Need to plug in variance estimates to compute $\mathrm{Var}(\bar{y}_{i..})$
- What are the DF?
- For pairwise comparisons, use estimate $2MS_{AB}/bn$
- Use df_{AB} for t-statistic

Sample Size Calculations

Use Charts V and VI

Random Effects Model

Factor	λ	df_{num}	df_{den}
A	$\sqrt{1+\frac{bn\sigma_\tau^2}{\sigma^2+n\sigma_{\tau\beta}^2}}$	$a-1$	$(a-1)(b-1)$
B	$\sqrt{1+\frac{an\sigma_\beta^2}{\sigma^2+n\sigma_{n\tau\beta}^2}}$	$b-1$	$(a-1)(b-1)$
AB	$\sqrt{1+\frac{n\sigma_{\tau\beta}^2}{\sigma^2}}$	$(a-1)(b-1)$	$ab(n-1)$

Mixed Effects Model

Factor	λ or Φ	df_{num}	df_{den}
A	$\sqrt{\frac{bn\sum\tau_i^2}{a(\sigma^2+n\sigma_{\tau\beta}^2)}}$	$a-1$	$(a-1)(b-1)$
B	$\sqrt{1+\frac{an\sigma_\beta^2}{\sigma^2}}$	$b-1$	$ab(n-1)$
AB	$\sqrt{1+\frac{n\sigma_{\tau\beta}^2}{\sigma^2}}$	$(a-1)(b-1)$	$bn(n-1)$

```
          /* Gauge Capability Example in Text 12-3 */

options nocenter ps=40 ls=75;

data randr;
 input part operator resp @@;
 cards;
1 1 21 1 1 20 1 2 20 1 2 20 1 3 19 1 3 21
2 1 24 2 1 23 2 2 24 2 2 24 2 3 23 2 3 24
3 1 20 3 1 21 3 2 19 3 2 21 3 3 20 3 3 22
4 1 27 4 1 27 4 2 28 4 2 26 4 3 27 4 3 28
5 1 19 5 1 18 5 2 19 5 2 18 5 3 18 5 3 21
6 1 23 6 1 21 6 2 24 6 2 21 6 3 23 6 3 22
7 1 22 7 1 21 7 2 22 7 2 24 7 3 22 7 3 20
8 1 19 8 1 17 8 2 18 8 2 20 8 3 19 8 3 18
9 1 24 9 1 23 9 2 25 9 2 23 9 3 24 9 3 24
10 1 25 10 1 23 10 2 26 10 2 25 10 3 24 10 3 25
11 1 21 11 1 20 11 2 20 11 2 20 11 3 21 11 3 20
12 1 18 12 1 19 12 2 17 12 2 19 12 3 18 12 3 19
13 1 23 13 1 25 13 2 25 13 2 25 13 3 25 13 3 25
14 1 24 14 1 24 14 2 23 14 2 25 14 3 24 14 3 25
15 1 29 15 1 30 15 2 30 15 2 28 15 3 31 15 3 30
16 1 26 16 1 26 16 2 25 16 2 26 16 3 25 16 3 27
17 1 20 17 1 20 17 2 19 17 2 20 17 3 20 17 3 20
18 1 19 18 1 21 18 2 19 18 2 19 18 3 21 18 3 23
19 1 25 19 1 26 19 2 25 19 2 24 19 3 25 19 3 25
20 1 19 20 1 19 20 2 18 20 2 17 20 3 19 20 3 17;
```

```
proc glm;
 class operator part;
 model resp=operator|part;
 random part operator*part / test;
 means operator / tukey lines E=operator*part;
 lsmeans operator / adjust=tukey E=operator*part tdiff stderr;

proc mixed alpha=.05 cl covtest;
 class operator part;
 model resp=operator / ddfm=kr;
 random part operator*part;
 lsmeans operator / alpha=.05 cl diff adjust=tukey;
run;
quit;
```

```
Dependent Variable: resp
                                    Sum of
Source                      DF     Squares   Mean Square  F Value  Pr > F
Model                       59  1215.091667    20.594774    20.77  <.0001
Error                       60    59.500000     0.991667
Corrected Total            119  1274.591667

Source                      DF  Type III SS  Mean Square  F Value  Pr > F
operator                     2     2.616667     1.308333     1.32  0.2750
part                        19  1185.425000    62.390789    62.92  <.0001
operator*part               38    27.050000     0.711842     0.72  0.8614

Source                   Type III Expected Mean Square
operator                 Var(Error) + 2 Var(operator*part) + Q(operator)
part                     Var(Error) + 2 Var(operator*part) + 6 Var(part)
operator*part            Var(Error) + 2 Var(operator*part)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: resp
Source                      DF  Type III SS  Mean Square  F Value  Pr > F
operator                     2     2.616667     1.308333     1.84  0.1730
part                        19  1185.425000    62.390789    87.65  <.0001
Error                       38    27.050000     0.711842
Error: MS(operator*part)

Source                      DF  Type III SS  Mean Square  F Value  Pr > F
operator*part               38    27.050000     0.711842     0.72  0.8614
Error: MS(Error)            60    59.500000     0.991667

Alpha                                     0.05
Error Degrees of Freedom                    38
Error Mean Square                     0.711842
Critical Value of Studentized Range  3.44902
Minimum Significant Difference          0.4601

Means with the same letter are not significantly different.
```

```
          Mean      N    operator

A       22.6000     40    3
A
A       22.3000     40    1
A
A       22.2750     40    2
```

Standard Errors and Probabilities Calculated Using the Type III MS for operator*part as an Error Term

operator	resp LSMEAN	Standard Error	Pr > |t|	LSMEAN Number
1	22.3000000	0.1334018	<.0001	1
2	22.2750000	0.1334018	<.0001	2
3	22.6000000	0.1334018	<.0001	3

Least Squares Means for Effect operator
t for H0: LSMean(i)=LSMean(j) / Pr > |t|
Dependent Variable: resp

i/j	1	2	3
1		0.132514	-1.59017
		0.9904	0.2622
2	-0.13251		-1.72269
	0.9904		0.2100
3	1.590173	1.722688	
	0.2622	0.2100	

The Mixed Procedure

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	622.27805725	
1	2	409.45998838	0.00002843
2	1	409.45716449	0.00000003
3	1	409.45716136	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Estimate	Standard Error	Z Value	Pr Z	Alpha	Lower
part	10.2513	3.3738	3.04	0.0012	0.05	5.8888
operator*part	0	.	.	.	.	.
Residual	0.8832	0.1262	7.00	<.0001	0.05	0.6800

Covariance Parameter Estimates

Cov Parm	Upper
part	22.1549
operator*part	.

```
Residual          1.1938

           Fit Statistics
-2 Res Log Likelihood           409.5
AIC (smaller is better)         413.5

    Type 3 Tests of Fixed Effects

              Num     Den
Effect         DF      DF    F Value    Pr > F
operator        2      98       1.48    0.2324  *** KR adjustment
```

Restricted model

$$
\begin{aligned}
\mathrm{Var}(\bar{y}_{1..}) &= (\sigma^2 + n\sigma^2_{\tau\beta} + n\sigma^2_{\beta})/bn = (0.8832 + 2(10.2513))/40 \\
\mathrm{Var}(\bar{y}_{1..} - \bar{y}_{2..}) &= 2(\sigma^2 + n\sigma^2_{\tau\beta})/bn = 0.8832/20
\end{aligned}
$$

```
                          Least Squares Means
                              Standard
Effect    operator  Estimate     Error    DF  t Value  Pr > |t|   Alpha
operator  1          22.3000    0.7312  20.1    30.50    <.0001    0.05
operator  2          22.2750    0.7312  20.1    30.46    <.0001    0.05
operator  3          22.6000    0.7312  20.1    30.91    <.0001    0.05

          Least Squares Means
Effect    operator     Lower      Upper
operator  1          20.7752    23.8248
operator  2          20.7502    23.7998
operator  3          21.0752    24.1248

                    Differences of Least Squares Means

                                         Standard
Effect    operator  _operator  Estimate     Error    DF  t Value  Pr > |t|
operator  1         2           0.02500    0.2101    98     0.12    0.9055
operator  1         3           -0.3000    0.2101    98    -1.43    0.1566
operator  2         3           -0.3250    0.2101    98    -1.55    0.1252

              Differences of Least Squares Means
Effect    operator  _operator  Adjustment        Adj P     Alpha
operator  1         2          Tukey-Kramer     0.9922      0.05
operator  1         3          Tukey-Kramer     0.3308      0.05
operator  2         3          Tukey-Kramer     0.2739      0.05

                   Differences of Least Squares Means
                                                      Adj        Adj
Effect    operator  _operator     Lower      Upper      Lower      Upper
operator  1         2           -0.3920     0.4420    -0.4751     0.5251
operator  1         3           -0.7170     0.1170    -0.8001     0.2001
operator  2         3           -0.7420    0.09201    -0.8251     0.1751
```

Other Mixed Models

- SAS uses different mixed model in analysis
- Reduce parameter restrictions

  $\sum \tau_i = 0$ and $\beta \sim N(0, \sigma_\beta^2)$
  $(\tau\beta)_{i,j} \sim N(0, \sigma_{\tau\beta}^2)$

- Known as *unrestricted* mixed model
- For two-factor model

$$
\begin{aligned}
\mathrm{E}(MS_E) &= \sigma^2 \\
\mathrm{E}(MS_A) &= \sigma^2 + bn \sum \tau_i^2/(a-1) + n\sigma_{\tau\beta}^2 \\
\mathrm{E}(MS_B) &= \sigma^2 + an\sigma_\beta^2 + n\sigma_{\tau\beta}^2 \\
\mathrm{E}(MS_{AB}) &= \sigma^2 + n\sigma_{\tau\beta}^2
\end{aligned}
$$

- `random` statement is SAS also gives these results
- Differences
  - Test $\mathrm{H}_0 : \sigma_\beta^2 = 0$ using MS_{AB} in denominator
  - Often more conservative test, $\hat{\sigma}_\beta^2 = (MS_B - MS_{AB})/an$

To decide which is appropriate, suppose you ran experiment again and sampled (by chance) the same random effects levels. Should this mean you also have the same set of interaction effects?

Yes: Restricted No: Unrestricted

General Mixed Effects Model

- In terms of linear model

$$Y = X\beta + Z\delta + \epsilon$$

  β is a vector fixed-effect parameters
  δ is a vector of random-effect parameters
  ϵ is the error vector

- δ and ϵ assumed uncorrelated
  - means 0
  - covariance matrices G and R (allows correlation)
- $\mathrm{Cov}(Y) = ZGZ' + R$

- If $R = \sigma^2 I$ and $Z = 0$, back to standard linear model
- SAS `proc mixed` allows one to specify G and R
- G through `random`; R through `repeated`
- Unrestricted linear mixed model is default

Example

A corporation wants to compare two different sunscreens for protecting the skin of adults age 20-25 from burning/tanning. A random sample of 10 subjects ages 20-25 were chosen for the study. With each person, four squares on the back were marked, and each sunscreen was randomly applied to two of the squares. The color of skin was noted prior to treatment and then after a two hour period of sun bathing. The difference was recorded. A large positive difference means less protection.

- What are the factors in the model?
- Which are random and which are fixed?

Results

	Sunscreen			
Subject	1		2	
1	8.2	7.6	6.1	6.8
2	3.6	3.5	4.3	4.7
3	10.7	10.3	9.6	9.2
4	3.9	4.4	2.3	2.5
5	12.9	12.1	12.4	12.8
6	5.5	5.9	4.8	4.0
7	9.1	9.7	8.3	8.6
8	13.7	13.2	12.9	13.6
9	8.1	8.7	8.0	7.5
10	2.5	2.8	2.1	2.5

Which appears to be better?

```
options nocenter ls=75 ps=60;

data new;
infile "h:\System\Desktop\sunscreen.dat";
input subject lotion resp;

proc mixed covtest cl maxiter=20;
 class subject lotion;
 model resp=lotion /ddfm=kr;
 random subject subject*lotion;
 lsmeans lotion / diff cl;
```

```
run;
quit;

                    Covariance Parameter Estimates
                           Standard       Z
Cov Parm         Estimate     Error   Value      Pr Z   Alpha     Lower
subject           14.2086    6.7767    2.10    0.0180    0.05    6.6748
subject*lotion     0.2660    0.1579    1.68    0.0460    0.05    0.1084
Residual           0.1320   0.04174    3.16    0.0008    0.05   0.07726

    Type 3 Tests of Fixed Effects
              Num     Den
Effect         DF      DF    F Value    Pr > F
lotion          1       9       6.76    0.0287

1.  Significant source of variation due to combination
      - one lotion may not be best for all subjects
2.  Significant subject-to-subject variability
3.  Lotion 2 ''on average'' offers more protection
4.  Is difference practically significant?

                         Least Squares Means
                             Standard
Effect   lotion   Estimate      Error     DF   t Value   Pr > |t|    Alpha
lotion   1          7.8200     1.2058   9.21      6.49     0.0001     0.05
lotion   2          7.1500     1.2058   9.21      5.93     0.0002     0.05

         Least Squares Means
Effect   lotion      Lower       Upper
lotion   1          5.1015     10.5385
lotion   2          4.4315      9.8685

                    Differences of Least Squares Means
                                        Standard
Effect   lotion   _lotion   Estimate       Error     DF   t Value   Pr > |t|
lotion   1        2           0.6700      0.2577      9      2.60     0.0287
```

For restricted model –
$\mathrm{Var}(\bar{y}_{i..}) = (\sigma^2 + (a-1)n\sigma^2_{\tau\beta}/a + n\sigma^2_{\beta})/bn = (0.1320 + 0.2660 + 2(14.2086))/20 = 1.44$, which is slightly larger than the unrestricted model.

Approximate F-tests and Confidence Intervals

- For some models, no exact F-test exists
- Recall 3-Factor Mixed Model (A - fixed)
- No exact test for A based on EMS

Assume $a = 3$, $b = 2$, $c = 3$, $n = 2$ and following MS were obtained

Source	DF	MS	EMS	F	p
A	2	0.7866	$\phi_A + 6\sigma^2_{AB} + 4\sigma^2_{AC} + 2\sigma^2_{ABC} + \sigma^2$	?	?
B	1	0.0010	$18\sigma^2_B + 6\sigma^2_{BC} + \sigma^2$	0.33	0.622
AB	2	0.0056	$6\sigma^2_{AB} + 2\sigma^2_{ABC} + \sigma^2$	2.24	0.222
C	2	0.0560	$12\sigma^2_C + 6\sigma^2_{BC} + \sigma^2$	18.87	0.051
AC	4	0.0107	$4\sigma^2_{AC} + 2\sigma^2_{ABC} + \sigma^2$	4.28	0.094
BC	2	0.0030	$6\sigma^2_{BC} + \sigma^2$	10.00	0.001
ABC	4	0.0025	$2\sigma^2_{ABC} + \sigma^2$	8.33	0.001
Error	18	0.0003	σ^2		

Could assume some variances negligible: not recommended without "conclusive" evidence

Examples

- If assume σ^2_{ABC} and σ^2_{AB} equals 0

Source	DF	MS	EMS	F	p
A	2	0.7866	$\phi_A + 2\sigma^2_{ABC} + \sigma^2$	314.64	0.001
B	1	0.0010	$18\sigma^2_B + 6\sigma^2_{BC} + \sigma^2$	0.33	0.622
C	2	0.0560	$12\sigma^2_C + 6\sigma^2_{BC} + \sigma^2$	18.87	0.051
BC	2	0.0030	$6\sigma^2_{BC} + \sigma^2$	1.2	0.319
ABC	4	0.0025	$2\sigma^2_{ABC} + \sigma^2$	1.0	0.427
Error	24	0.0025	σ^2		

Could test interactions and then possibly remove

- Based on first table.

  AC and AB found insignificant.
  Test A over $ABC \rightarrow F = 314.64$ and $p < 0.001$.

- Both Type I and Type II errors possible
- What level to test insignificance?

Pooling Mean Squares with Error

- Variation of previous approach
- Works well when df for error is small (< 6)
- Often test significance at $\alpha = 0.25$
- May pool together something that is different from zero
- Use high α to protect against that

Pooling Procedure

1. Test highest order interaction vs error
2. If ABC found insignificant, pool together mean squares

$$MS'_E = \frac{SS_E + SS_{ABC}}{df_E + df_{ABC}}$$

3. Continue by testing AB, AC, BC over new error and pool accordingly
4. In SAS, pooling accomplished by simply dropped term from model

- Procedure primarily used for error, not interactions
- If higher order interaction found significant – stop
- Pooling procedure of no benefit in example

Satterthwaite's Approximate F-test

Use linear combination of mean squares

- To test certain factor, choose numerator and denominator such that the difference in MS is a multiple of the effect of interest
- Ratio approximately F where

$$\begin{aligned} F_{p,q} &= \frac{MS_r \pm \ldots \pm MS_s}{MS_u \pm \ldots \pm MS_v} \\ p &= \frac{(MS_r \pm \ldots \pm MS_s)^2}{MS_r^2/f_r + \ldots + MS_s^2/f_s} \\ q &= \frac{(MS_u \pm \ldots \pm MS_v)^2}{MS_u^2/f_u + \ldots + MS_v^2/f_v} \end{aligned}$$

- f_i is the degrees of freedom associated with MS_i
- No MS in both num and denom (indep)
- Caution when subtraction is used

Example

For the 3 factor model,

$$\frac{MS_A}{MS_{AB} + MS_{AC} - MS_{ABC}} = \frac{0.7866}{0.0107 + 0.0056 - 0.0025} = 57.0$$

$$p = 2 \quad q = \frac{0.0138^2}{0.0107^2/4 + 0.0056^2/2 + 0.0025^2/4} = 4.15$$

- Interpolation needed

$$\Pr(F_{2,4} > 57) = 0.0011 \quad \Pr(F_{2,5} > 57) = 0.0004$$

$$p = 0.85(0.0011) + 0.15(0.0004) = 0.001$$

- SAS can be used to compute p-values and quantile values for F and χ^2 values with non-integer degrees of freedom.

  p-values: `probf(x, df1, df2)` and `probchi(x, df)`
  Quantiles: `finv(p, df1, df2)` and `cinv(p, df)`

```
data pvalue;
  p = 1-probf(57, 2.0, 4.15);
  f = finv(0.95, 2.0, 4.15);
  c1 = cinv(0.025, 18.57);
  c2 = cinv(0.975, 18.57);

proc print p f c1 c2;
```

```
Obs            p        f          c1         c2
 1     .000959732    6.71564    8.61485    32.2833
```

Example

For the 3 factor model (avoiding subtraction),

$$\frac{MS_A + MS_{ABC}}{MS_{AB} + MS_{AC}} = \frac{0.7866 + 0.0025}{0.0107 + 0.0056} = 48.41$$

$$p = \frac{0.7891^2}{0.7866^2/2 + 0.0025^2/4} = 2.01 \quad q = \frac{0.0163^2}{0.0107^2/4 + 0.0056^2/2} = 6.00$$

This is again found significant.

Confidence Intervals

- Use Satterthwaite's pseudo F-tests to create CI
- Recall $df_E MSE/\sigma^2 \sim \chi^2$

$$\frac{df_E MSE}{\chi^2_{\alpha/2, df_E}} \leq \sigma^2 \leq \frac{df_E MSE}{\chi^2_{1-\alpha/2, df_E}}$$

- Use pseudo F-tests, $\hat{\sigma}^2 = MS' - MS''$
- Both MS are independent and have similar χ^2 distribution
- Assume linear combination of χ^2 is χ^2 with df

$$\frac{(MS_r + \ldots + MS_s - MS_u - \ldots - MS_v)^2}{MS_r^2/f_r + \ldots + MS_s^2/f_s + MS_u^2/f_u + \ldots + MS_v^2/f_v}$$

- Use same CI formula as above

Random Effects Example 13-2

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	59	1215.091667	20.594774	20.77	<.0001
Error	60	59.500000	0.991667		
Corrected Total	119	1274.591667			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
operator	2	2.616667	1.308333	1.32	0.2750
part	19	1185.425000	62.390789	62.92	<.0001
operator*part	38	27.050000	0.711842	0.72	0.8614

$$df = \frac{(62.39 - 0.71)^2}{62.39^2/19 + 0.71^2/38} = 18.57$$

CI: $(18.57(10.28)/32.28, 18.57(10.28)/8.61) = (5.91, 22.17)$
$\hat{\sigma}^2_\beta = (1.31 - 0.71)/40 = 0.015$

$$df = \frac{(1.31 - 0.71)^2}{1.31^2/2 + 0.71^2/38} = 0.413$$

CI: $(0.413(0.015)/3.079, 0.413(0.015)/2.29 \times 10^{-8}) = (0.002, 270781)$

Example of Restricted vs Unrestricted Models

There are various ways to compact a gold filling to make it harder. Fillings need to be hard in order to wear well. There are three standard ways to do this:

1. *Condensing:* The dentist uses a special hand tool (a condenser to pack the gold into the cavity).

2. *Hand-malleting:* The dentist holds the condenser in place, and an assistant taps it with a small hammer.

3. *Mechanical malleting:* Like Method 2, except the hammer is built into the condenser, and tapping is done by machine.

Five dentists are chosen from the UCLA School of Dentistry, and the factors are crossed: each dentist uses each of the three methods to pack gold into a small cavity drilled into a block of ivory. Hardness was measured by pushing a pyramid-shaped diamond into the filling and recording the size of the indentation. Each method is used twice, and order is assumed not to be a factor.

Method is **fixed**, while dentist is **random**.

Restricted and Unrestricted Models for Mixed Effects

		Restricted	**Unrestricted**
Model	For each dentist, the interaction terms are ...	random, but restricted to add to zero across Methods negatively correlated	random and unrestricted uncorrelated
EMS's and denominators	EMS(Dentist) =	Dentists + Error	Dentists + Inter + Error
	Denominator MS for testing Dentist effects is	Error	Interaction
Interpretation	F-ratio for Dentists tests the null hypothesis that	"true" Dentist averages are equal	for each Dentist, the observed response values are uncorrelated

Properties of Restricted and Unrestricted Models

Restricted: Negatively correlated interaction terms
Unrestricted: Random terms are independent

Restricted: "If Dentists effects are zero, Dentists averages must be equal (as in fixed effects model)."
Unrestricted: "Dentist effects are zero" mean within factor correlation is 0.

Remember: SAS uses unrestricted model

"Limited Resources" Interpretation of Restricted Model

- Covariance between observations in restricted models could be negatively correlated
- If responses are linked to a resource of limited supply, then a negative correlation is to be expected

Examples

Enzyme concentration on two sites: brain and heart
Plants competing for nutrients

Pooling

- Lots of ways to choose best models (e.g., AIC, BIC, C_p)
- Usually check all possible models for "best fit".

  Not always interested if effects are "true" (or practical)
  Lots of refitting (which takes up computation) involved

- Not always clear what to do with interaction in mixed model
  - Often only consider models with higher order interaction if lower order interactions containing terms is included

  - Sometimes narrow constraint to interaction with fixed terms in lower orders
  - Book gives prescription for pooling interaction effects ($df < 6, p > 0.25$) in lower orders.

    Basically, shouldn't pool if it makes test "less sensitive".

One way around mixed model issues is to assume every factor is fixed.

- Random effects are not discussed at all in Wu and Hamada.
- Allows everything to be cast as linear regression.
- Reason: Maximum Likelihood with fixed effects $\equiv$ Least Squares estimates.
- However, for mixed effects models, Least Squares estimates are Method of Moments estimates.

Likelihood

Let $x_1, \ldots, x_n$ be n observations with distribution $f(x_i, \theta_i)$

Likelihood Function:

$$L(\theta) = f(x_1; \theta_1) \cdots f(x_n; \theta_n)$$

Maximum Likelihood Estimator (MLE)

$$\hat{\theta}_{MLE} = \arg\max_{\theta} L(\theta)$$

Can be a computationally intensive maximization.

Example: Fixed Effects Model (1 factor)

$$L(\mu_1, \ldots, \mu_a, \sigma^2) = [(2\pi)^N \sigma^2]^{-1/2} \exp(-\frac{\sigma^2}{2}(y - \mu)'(y - \mu))$$

where

$$\mu = (\mu_1, \ldots, \mu_1, \ldots, \mu_a, \ldots, \mu_a)'$$

Since maximizing L is equivalent to minimizing $(y - \mu)'(y - \mu)$, $ML \equiv LS$.

Second Example: Random Effects Model ($a = b = n = 2$)

$$y_{i,j,k} = \mu + \tau_i + \beta_j + (\tau\beta)_{i,j} + \epsilon_{i,j,k}$$

$$\text{Cov}(y_{i,j,k}, y_{i',j',k'}) = \sigma^2 I(i = i', j = j', k = k') + \sigma^2_\tau I(i = i') + \sigma^2_\beta I(j = j') + \sigma^2_{\tau\beta} I(i = i', j = j')$$

Observations $y_{1,1}, \ldots, y_{2,2}$ come from normal distribution with 8×8 covariance matrix Σ (page 517)

$$L(\mu, \sigma^2_\tau, \sigma^2_\beta, \sigma^2_{\tau\beta}, \sigma^2) = [(2\pi)^N |\Sigma|]^{-N/2} \exp[-\frac{1}{2}(y - \mu\mathbf{j}_n)'\Sigma^{-1}(y - \mu\mathbf{j}_n)],$$

where $\mathbf{j}$ is $N \times 1$ vector of 1's.

Restricted Maximum Likelihood: maximize L under the constraints $\sigma^2 \geq 0$, $\sigma^2_\tau \geq 0$, $\sigma^2_\beta \geq 0$, $\sigma^2_{\tau\beta} \geq 0$. (Montgomery's definition)

Mixed Model: Similar but slightly more complicated
Standard Errors: Use asymptotic estimates

Nested Factors: Definitions

- Factors A and B are considered *crossed* if

  Every level of B occurs with every level of A
  A factorial model involves crossed factors

	Factor A			
Factor B	1	2	3	4
1	xx	xx	xx	xx
2	xx	xx	xx	xx
3	xx	xx	xx	xx

A	1			2			3			4		
B	1	2	3	1	2	3	1	2	3	1	2	3
$Resp_1$	x	x	x	x	x	x	x	x	x	x	x	x
$Resp_2$	x	x	x	x	x	x	x	x	x	x	x	x

- Factors A and B considered *nested* if

  Levels of B occur with only one level of A
  Recall replicated Latin square designs
  One can arbitrarily number levels of B

A	1			2			3			4		
B	1	2	3	4	5	6	7	8	9	10	11	12
$Resp_1$	x	x	x	x	x	x	x	x	x	x	x	x
$Resp_2$	x	x	x	x	x	x	x	x	x	x	x	x

Replication as a Nested Factor

- Consider CRD $y_{i,j} = \mu + \tau_i + \epsilon_{i,j}$
- Can write design where $a = 3$ and $n = 4$ as

Treatment	1				2				3			
Replicate	1	2	3	4	5	6	7	8	9	10	11	12
Response	x	x	x	x	x	x	x	x	x	x	x	x

- Thus, could build replicate into model as factor
- Order of replicates unimportant → nested
- Brackets denote which factor it's nested within

$$y_{i,j} = \mu + \tau_i + r_{j(i)}$$

- Replication variability is used as error, $\epsilon_{i,j} = r_{j(i)}$ (note constant variance assumption).
- In SAS, omit lowest level term from `model` statement. Otherwise, all tests must be done using `test` option or statement (i.e., 0 df error)

Subsampling

- In many problems, difficult to measure EU response
- *Subsampling* – sampling EU numerous times
- Done to get more accurate measure of EU response
- Often use average of subsamples for analysis
- What if we include subsamples in analysis?

Treatment	1				2				3			
Replicate	1	2	3	4	5	6	7	8	9	10	11	12
	x	x	x	x	x	x	x	x	x	x	x	x

- No association between subsamples across EU's (although variances constant)
- Numbering of subsample arbitrary
- Subsamples always a nested factor

Analysis of Subsamples

- If subsample added to model, results comparable to using the average of the subsamples.
- Could also look at variance or median as summary
- Helps with design of future experiments
- Can check for consistency of measurements
- Protect against missing values and contamination
- Computational benefit if $\sigma^2_{Sub} > \sigma^2$ (Variance within greater than variance between subsamples.)
- Example
  - Soil samples within plot (e.g., moisture content, acidity)
  - Biochemical analysis of animal tissue
  - Multiple plates of single agar batch

Simple Random Effects Model

$$y_{i,j} = \mu + \tau_i + \epsilon_{i,j} \begin{cases} i = 1, 2, \ldots, a \\ j = 1, 2, \ldots n \end{cases}$$

- In some situations, can consider this as subsampling
- Primarily interested in μ or σ^2_τ
- Two stages of sampling
  - Randomly choose units of interest (σ^2_τ)
  - Obtain measurements on that unit of interest (σ^2)
- Use subsampling variability in test $\mathrm{H}_0 : \sigma^2_\tau = 0$
- $\hat{\mathrm{Var}}(\hat{\mu}) = MS_{Trt}/nk$
- Same variance based on averages of primary units

CRD with Subsampling

- Interested in effect of four methods of spreading mulch on soil moisture content. Have field of 16 plots – 4 for each spreading method.
  - Cannot measure moisture content directly
  - Choose 2 sites within plot to measure moisture
  - Samples averaged to obtain moisture content
  - Can view subsamples *nested* within plot
  - Introduces new source of variability (σ^2_δ), important for estimation

$$y_{i,j,k} = \mu + \tau_i + \epsilon_{j(i)} + \delta_{k(i,j)} \begin{cases} i = 1, 2, \ldots, a \\ j = 1, 2, \ldots, n \\ k = 1, 2, \ldots, s \end{cases}$$

$$\epsilon_{j(i)} \sim N(0, \sigma^2)$$

$$\delta_{k(i,j)} \sim N(0, \sigma^2_\delta)$$

Source	DF	EMS
Trt	$a-1$	$s\sigma^2 + \sigma^2_\delta + ns\sum\tau_i^2/(a-1)$
Plot	$a(n-1)$	$s\sigma^2 + \sigma^2_\delta$
Subsampling	$an(s-1)$	σ^2_δ
Total	$ans-1$	

What is the optimal n if ns is constant?

What happens if s goes to infinity?

SAS Program

```
options nocenter ps=40 ls=72;

data new;
input trt plot sub resp;
cards;
1 1 1 2
1 1 2 3
1 2 1 2
1 2 2 3.5
1 3 1 2.5
1 3 2  3
1 4 1 4.0
1 4 2 2.5
2 1 1 4.5
2 1 2 4.0
```

```
2 2 1 3.5
2 2 2 3.5
2 3 1 5
2 3 2 4.5
2 4 1 4.5
2 4 2 4
3 1 1 3.5
3 1 2 1.5
3 2 1 2.0
3 2 2 2.0
3 3 1 1.5
3 3 2 2.0
3 4 1 2.0
3 4 2 2.5
4 1 1 6.0
4 1 2 6.5
4 2 1 5.5
4 2 2 5.5
4 3 1 5.0
4 3 2 5.5
4 4 1 4.5
4 4 2 5.0
;

/* Plot is nested within trt; sub is nested within plot */

proc sort;
 by trt plot;

proc means noprint;  /* Take means within plot */
 var resp;
 by trt plot;
 output out=new1 mean=respmn;

proc glm;
 class trt;
 model respmn=trt;

proc glm data=new;  /* gives similar results */
 class trt plot sub;
 model resp=trt plot(trt);
 test h=trt e=plot(trt);
```

```
Dependent Variable: respmn
                                    Sum of
Source                    DF       Squares     Mean Square    F Value
Model                      3    26.04296875     8.68098958      40.41
Error                     12     2.57812500     0.21484375
```

```
Corrected Total            15    28.62109375

Source                 Pr > F
Model                  <.0001
Error

/* Percent of variability of moisture explained by
spreading technique (averaged across site within plot) */
R-Square     Coeff Var      Root MSE    respmn Mean
0.909922      12.73167      0.463512       3.640625

Dependent Variable: respmn

Source                     DF    Type III SS    Mean Square   F Value
trt                         3    26.04296875     8.68098958     40.41

Source                 Pr > F
trt                    <.0001

Dependent Variable: resp
                                      Sum of
Source                     DF        Squares    Mean Square   F Value
Model                      15    57.24218750     3.81614583     10.39
Error                      16     5.87500000     0.36718750
Corrected Total            31    63.11718750

Source                 Pr > F
Model                  <.0001
Error

/* Percent of variability of moisture explained by spreading and plot */
R-Square     Coeff Var      Root MSE     resp Mean
0.906919      16.64439      0.605960      3.640625

Dependent Variable: resp

Source                     DF    Type III SS    Mean Square   F Value
trt                         3    52.08593750    17.36197917     47.28
plot(trt)                  12     5.15625000     0.42968750      1.17

Source                 Pr > F
trt                    <.0001
plot(trt)              0.3772

               Tests of Hypotheses Using the Type III
                  MS for plot(trt) as an Error Term
/* same result as first analysis */
Source                     DF    Type III SS    Mean Square   F Value
trt                         3    52.08593750    17.36197917     40.41

Source                 Pr > F
trt                    <.0001
```

RCBD with Subsampling

Interested in studying the tenderizing methods of steak. Three animals are chosen, and the four methods of treatment are applied to like portions of each animal. These portions are then divided up into five smaller portions, and the tenderness is evaluated. Since method of treatment is applied to a larger portion, the EU for tenderness are the larger portions. The individual evaluations relative to the method are subsamples.

Source	DF	EMS
Animal	$b-1$	
Treatment	$a-1$	$s\sigma^2 + \sigma_\delta^2 + bs\sum \tau_i^2/(a-1)$
Animal×Treatment	$(b-1)(a-1)$	$s\sigma^2 + \sigma_\delta^2$
Subsampling	$ab(s-1)$	σ_δ^2
Total	$abs-1$	

Reasoning for Nested Factors

Consider the following two examples

1. Drug company interested in stability of product
   - Two manufacturing sites
   - Three batches from each site
   - Ten tablets from each batch
2. Stratified random sampling procedure
   - Randomly sample five states
   - Randomly select three counties
   - Randomly select two towns
   - Randomly select five households

More manageable experiment than factorial, CRD

- Drug – Batches as non-nested factor?
- Sampling – more concentrated than CRD

Statistical Model

- Consider a two factor problem

$$y_{i,j,k} = \mu + \tau_i + \beta_{j(i)} + \epsilon_{k(i,j)} \begin{cases} i = 1, 2, \ldots, a \\ j = 1, 2, \ldots, b \\ k = 1, 2, \ldots, n \end{cases}$$

- Bracket notation represents nested factor

- Cannot include interaction
  - Not all levels of B appear with all levels of A
  - Cannot separate main effect of B and interaction AB
- Factors may be random or fixed
- Can use EMS algorithm to describe tests

Partitioning the Sum of Squares (Balanced Design)

- Rewrite observation as

$$y_{i,j,k} = \bar{y}_{...} + (\bar{y}_{i..} - \bar{y}_{...}) + (\bar{y}_{i,j.} - \bar{y}_{i..}) + (y_{i,j,k} - \bar{y}_{i,j.})$$

- Can look at $\sum\sum\sum(y_{i,j,k} - \bar{y}_{...})^2$
- Right hand side simplifies to

$$bn\sum_i(\bar{y}_{i..} - \bar{y}_{...})^2 + n\sum_i\sum_j(\bar{y}_{i,j.} - \bar{y}_{i..})^2 + \sum_i\sum_j\sum_k(y_{i,j,k} - \bar{y}_{i,j.})^2$$

- $SS_A + SS_{B(A)} + SS_E$
- as opposed to

$$bn\sum_i(\bar{y}_{i..} - \bar{y}_{...})^2 + an\sum_j(\bar{y}_{.j.} - \bar{y}_{...})^2 + n\sum_i\sum_j(\bar{y}_{ij.} - \bar{y}_{i..} - \bar{y}_{.j.} + \bar{y}_{...})^2 + \sum_i\sum_j\sum_k(y_{i,j,k} - \bar{y}_{i,j.})^2$$

$SS_{B(A)} = SS_B + SS_{AB}$

Under normality, all SS/σ^2 independent

Analysis of Variance Table

Source of Variation	Sum of Squares	Degrees of Freedom	Mean Square	F_0
A	SS_A	$a-1$	MS_A	
$B(A)$	$SS_{B(A)}$	$a(b-1)$	$MS_{B(A)}$	
Error	SS_E	$ab(n-1)$	MS_E	
Total	SS_T	$abn-1$		

$$\begin{aligned}
SS_T &= \sum\sum\sum y_{i,j,k}^2 - y_{...}^2/abn \\
SS_A &= \frac{1}{bn}\sum y_{i..}^2 - y_{...}^2/abn \\
SS_{B(A)} &= \frac{1}{n}\sum\sum y_{i,j.}^2 - \frac{1}{bn}\sum y_{i..}^2 \\
SS_E &= \sum\sum\sum y_{i,j,k}^2 - \frac{1}{n}\sum\sum y_{i,j.}^2
\end{aligned}$$

Use EMS to define tests

Example – 2-Factor Nested Model (Fixed)

	F	F	R	
	a	b	n	
	i	j	k	Expected Mean Square
τ_i	0	b	n	$\sigma^2 + \frac{bn\sum\tau_i^2}{a-1}$
$\beta_{j(i)}$	1	0	n	$\sigma^2 + \frac{n\sum\sum\beta_{j(i)}^2}{a(b-1)}$
$\epsilon_{k(i,j)}$	1	1	1	σ^2

Example – 2-Factor Nested Model (Random)

	R	R	R	
	a	b	n	
	i	j	k	Expected Mean Square
τ_i	1	b	n	$bn\sigma_\tau^2 + n\sigma_\beta^2 + \sigma^2$
$\beta_{j(i)}$	1	1	n	$n\sigma_\beta^2 + \sigma^2$
$\epsilon_{k(i,j)}$	1	1	1	σ^2

Example – 2-Factor Nested Model (Mixed)

	F	R	R	
	a	b	n	
	i	j	k	
τ_i	0	b	n	$\sigma^2 + n\sigma_\beta^2 + \frac{bn\sum\tau_i^2}{a-1}$
$\beta_{j(i)}$	1	1	n	$n\sigma_\beta^2 + \sigma^2$
$\epsilon_{k(i,j)}$	1	1	1	σ^2

Example

A company is interested in testing the uniformity of their film-coated pain tablets. A random sample of three batches were collected from each of their two blending sites. Five tablets were assayed from each batch.

Site	1			2		
Batch	1	2	3	4	5	6
	5.03	4.64	5.10	5.05	5.46	4.90
	5.10	4.73	5.15	4.96	5.15	4.95
	5.25	4.82	5.20	5.12	5.18	4.86
	4.98	4.95	5.08	5.12	5.18	4.86
	5.05	5.06	5.14	5.05	5.11	5.07

- What are the factors?
- Are any nested?
- Which are random and which are fixed?

Source of Variation	Sum of Squares	Degrees of Freedom	Mean Square	F_0
Site	0.01825	1	0.01825	
Batch(Site)	0.45401	4	0.11350	
Error	0.29020	24	0.01209	
Total	0.76246	29		

$$y_{1,1.} = 25.41 \quad y_{1,2.} = 24.20 \quad y_{1,3.} = 25.67$$
$$y_{2,1.} = 25.30 \quad y_{2,2.} = 26.08 \quad y_{2,3.} = 24.64$$

$$\sum\sum\sum y_{i,j,k}^2 = 763.8188$$

- $SS_T = 763.8188 - (25.41 + 24.20 + \ldots + 24.64)^2/2(3)(5) = 763.8188 - 151.3^2/30 = 0.76247$
- $SS_A = ((25.41 + 24.20 + 25.67)^2 + (25.30 + 26.08 + 24.64)^2)/3(5) - (25.41 + 24.20 + \ldots + 24.64)^2/2(3)(5) = (75.28^2 + 76.02^2)/15 - 151.3^2/30 = 0.01825$
- $SS_{B(A)} = (25.41^2 + 24.20^2 + \ldots + 24.64^2)/5 - (75.28^2 + 76.02^2)/15 = 0.4501$
- $SS_E = 763.8188 - 763.5286 = 0.2902$

Results

- *Site:* $F = 0.01825/0.1135 = 0.1608$. There is not enough evidence to suggest that the two coating sites are different.
- *Batch:* $F = 0.1135/0.0121 = 9.39$. Compare to $F_{4,24}$. There is significant batch-to-batch variability.

$$\hat{\sigma}^2 = 0.0121 \quad \hat{\sigma}_\beta^2 = \frac{0.1135-0.0121}{5} = 0.0203$$

- Batch variability is 0.0203/(0.0203+0.0121) = 62.7% of the total variability. It appears that efforts should be made to eliminate the batch-to-batch variability. Investigate what goes into coating a batch and see where the variability could be.

Nested Model as Factorial

- Suppose we treat design as two-factor factorial
- Naively interpret SAS results
  - Significant *batch* $\times$ *site* variability
  - No longer significant batch-to-batch variability

- What does interaction term mean?
- We're assuming batch 1 effect similar across sites
- Can't separate interaction from main effect
- Notice

$$\begin{aligned} SS_{AB} + SS_B &= SS_{B(A)} \\ df_{AB} + df_B &= df_{B(A)} \end{aligned}$$

- Could derive analysis from factorial results

SAS Program

```
options nocenter ls=75;

data new;
infile "h:\System\Desktop\coating.dat";
input site batch tablet resp;

proc glm;  /* Nested Analysis */
class site batch;
model resp=site batch(site);
random batch(site);
test h=site e=batch(site);
output out=new1 p=pred r=res;

symbol1 v=circle;
proc gplot;
plot res*pred;

proc glm data=new;  /* Factorial Analysis */
class site batch;
model resp=site batch site*batch;
random batch site*batch;
test h=site e=batch*site;

proc glm data=new;  /* Factorial Analysis */
class site batch;
model resp=site batch; /* No interaction */
random batch;

run;
```

```
                                       Sum of
Source                       DF       Squares   Mean Square  F Value  Pr > F
Model                         5    0.47226667    0.09445333     7.81  0.0002
```

```
Error                       24    0.29020000    0.01209167
Corrected Total             29    0.76246667

Source                      DF     Type I SS   Mean Square  F Value  Pr > F
site                         1    0.01825333    0.01825333     1.51  0.2311
batch(site)                  4    0.45401333    0.11350333     9.39  0.0001

                 Tests of Hypotheses Using the Type III
                   MS for batch(site) as an Error Term
Source                      DF   Type III SS   Mean Square  F Value  Pr > F
site                         1    0.01825333    0.01825333     0.16  0.7089
-------------------------------------------------------------------------
                                      Sum of
Source                      DF       Squares   Mean Square  F Value  Pr > F
Model                        5    0.47226667    0.09445333     7.81  0.0002
Error                       24    0.29020000    0.01209167
Corrected Total             29    0.76246667

Source                      DF     Type I SS   Mean Square  F Value  Pr > F
site                         1    0.01825333    0.01825333     1.51  0.2311
batch                        2    0.01152667    0.00576333     0.48  0.6266
site*batch                   2    0.44248667    0.22124333    18.30  <.0001

Tests of Hypotheses Using the Type III MS for site*batch as an Error Term
Source                      DF   Type III SS   Mean Square  F Value  Pr > F
site                         1    0.01825333    0.01825333     0.08  0.8010
-------------------------------------------------------------------------
                                      Sum of
Source                      DF       Squares   Mean Square  F Value  Pr > F
Model                        3    0.02978000    0.00992667     0.35  0.7879
Error                       26    0.73268667    0.02818026
Corrected Total             29    0.76246667

Source                      DF     Type I SS   Mean Square  F Value  Pr > F
site                         1    0.01825333    0.01825333     0.65  0.4282
batch                        2    0.01152667    0.00576333     0.20  0.8163
```

Sliding Factors

Factors which appear to be nested, but should be treated as factorials.

Example

Suppose an experiment deals with the formability of body panels. (Formability is the ability to bend a flat panel into an arbitrary shape.) Two different factors, material and thickness, will be considered. Specifically, the materials considered are sheet metal and sheet molded compound, SMC. A thin piece of sheet metal is 0.7 mm thick. A thick piece of metal is 1.2 mm thick. Because SMC is not as strong as sheet metal, a thin piece of SMC is 1.5 mm thick while a thick piece is 5 mm thick.

- Would appear that thickness is nested in material.

- However, if the factor thickness is labeled as thin and thick, thickness appears crossed with material.
- Of course, thickness cannot be both crossed and nested at the same time.
- *Solution:* Recognizing intent of the experimenter.
  - "Does thickness of the panel affect formability?"
  - What does the interaction term mean?

General m-Stage Nested Design

- Consider 3 factor nested design

$$y_{i,j,k,\ell} = \mu + \tau_i + \beta_{j(i)} + \gamma_{k(i,j)} + \epsilon_{\ell(i,j,k)}$$

Source of Variation	Sum of Squares	Degrees of Freedom	Mean Square	F_0
A	SS_A	$a-1$	MS_A	
$B(A)$	$SS_{B(A)}$	$a(b-1)$	$MS_{B(A)}$	
$C(B)$	$SS_{C(B)}$	$ab(c-1)$	$MS_{C(B)}$	
Error	SS_E	$abc(n-1)$	MS_E	
Total	SS_T	$abcn-1$		

- Problem with nested designs
  - Few df for non-nested factor
  - In mixed-random situation, less power for non-nested factor

Staggered Nested Design

- Improve sampling efficiency with unbalanced design
- Consider A fixed, B and C are random
- Staggered Nested Design
  - a samples of non-nested factor (a levels of A)
  - 2 samples of first nested factor
  - 1 sample of second nested factor (except two from one)
  - Continue
- Results in $a-1$ and a degrees of freedom

Crossed and Nested Factors Model

- Can have design with crossed and nested factors
- These factors can be fixed or random
  - Nested-factorial designs
  - Repeated measure designs
- Example: Investigator interested in improving the number of rounds per minute fired from a Navy gun. Believes a new method of loading the gun will increase the number of rounds fired. Needs a team of people to use this gun. Divided teams into groups based on physique (slight, average, and heavy). Selected three teams from each of these groups for the experiment. Each team was presented with both methods of loading and used each method twice in a random order.

  Method (L_i) – Fixed
  Group (G_j) – Fixed
  Team within Group ($T_{k(j)}$) – Random

$$y_{i,j,k,\ell} = \mu + L_i + G_j + LG_{i,j} + T_{k(j)} + LT_{i,k(j)} + \epsilon_{\ell(i,j,k)}$$

Groups	Slight			Normal			Heavy		
Teams	1	2	3	4	5	6	7	8	9
Method 1	x	x	x	x	x	x	x	x	x
	x	x	x	x	x	x	x	x	x
Method 2	x	x	x	x	x	x	x	x	x
	x	x	x	x	x	x	x	x	x

- What are degrees of freedom?

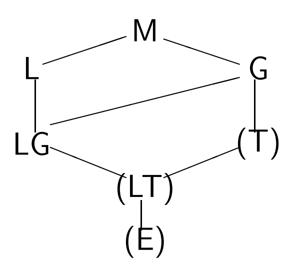
Source of Variation	Degrees of Freedom
L	$(a-1)=1$
G	$(b-1)=2$
LG	$(a-1)(b-1)=2$
$T(G)$	$b(c-1)=6$
$LT(G)$	$(a-1)b(c-1)=6$
Error	$abc(n-1)=18$
Total	35

Computing DF for Nested Effects

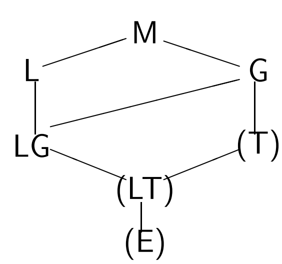
- Treat as factorial and pool df
- $T_{k(j)} = T_k + GT_{k,j}$
- $LT_{i,k(j)} = LT_{i,k} + LGT_{i,j,k}$
- Could pool SS in similar manner

Example - EMS

		F	F	R	R	
		2	3	3	2	Expected Mean Square
		i	j	k	ℓ	
F	L_i	0	3	3	2	$18\sum L_i^2 + 2\sigma_{LT}^2 + \sigma^2$
F	G_j	2	0	3	2	$6\sum G_j^2 + 4\sigma_T^2 + \sigma^2$
F	$LG_{i,j}$	0	0	3	2	$3\sum\sum LG_{i,j}^2 + 2\sigma_{LT}^2 + \sigma^2$
R	$T_{k(j)}$	2	1	1	2	$4\sigma_T^2 + \sigma^2$
R	$LT_{i,k(j)}$	0	1	1	2	$2\sigma_{LT}^2 + \sigma^2$
R	$\epsilon_{\ell(i,j,k)}$	1	1	1	1	σ^2



Restricted Model:
L: Leading term is LT
G: Leading random term is T
LG: Leading term is LT
T: Leading term is E because LT has fixed L
LT: Leading term is E



Unrestricted Model:
L: Leading random term is LT
G: Leading random term is T
LG: Leading term is LT
T: Leading term is LT
LT: Leading term is E

SAS Program

```
options nocenter ls=75;
data new;
infile 'h:\System\Desktop\guns.dat';
input method group team resp;

proc glm;
  class group method team;
  model resp = group|method team(group) method*team(group);
  random team(group) method*team(group);
  test h=group e=team(group);
  test h=method e=method*team(group);
  test h=group*method e=method*team(group);
  means group / duncan lines e=team(group);
  means method / duncan lines e=method*team(group);
  means group*method;

proc mixed;
  class group method team;
  model resp=group|method;
  random team(group) method*team(group);
  lsmeans method group / adjust=duncan tdiff;
run;
```

```
Dependent Variable: resp
                                   Sum of
Source                   DF       Squares   Mean Square  F Value  Pr > F
Model                    17   719.1700000    42.3041176    18.31  <.0001
Error                    18    41.5900000     2.3105556
Corrected Total          35   760.7600000

Source                   DF   Type III SS   Mean Square  F Value  Pr > F
group                     2    16.0516667     8.0258333     3.47  0.0530
method                    1   651.9511111   651.9511111   282.16  <.0001
group*method              2     1.1872222     0.5936111     0.26  0.7762
team(group)               6    39.2583333     6.5430556     2.83  0.0403
method*team(group)        6    10.7216667     1.7869444     0.77  0.6009

Source               Type III Expected Mean Square
group                Var(Error) + 2 Var(method*team(group)) + 4
                     Var(team(group)) + Q(group,group*method)
method               Var(Error) + 2 Var(method*team(group)) +
                     Q(method,group*method)
group*method         Var(Error) + 2 Var(method*team(group)) +
                     Q(group*method)
team(group)          Var(Error) + 2 Var(method*team(group)) + 4
                     Var(team(group))
method*team(group)   Var(Error) + 2 Var(method*team(group))
```

$$\hat{\sigma}_T^2 = \frac{6.543 - 1.789}{4} = 1.19 \quad \hat{\sigma}_{LT}^2 = \frac{1.787 - 2.31}{2} = -0.262$$

$$\hat{\sigma}^2 = \frac{41.59}{18} = 2.31$$

```
                  Tests of Hypotheses Using the Type III
                    MS for team(group) as an Error Term

Source                    DF   Type III SS   Mean Square  F Value  Pr > F
group                      2   16.05166667    8.02583333     1.23  0.3576

                 Tests of Hypotheses Using the Type III MS
                  for method*team(group) as an Error Term

Source                    DF   Type III SS   Mean Square  F Value  Pr > F
method                     1   651.9511111   651.9511111   364.84  <.0001
group*method               2     1.1872222     0.5936111     0.33  0.7297


Duncan's Multiple Range Test across group
NOTE: This test controls the type I comparison error rate, not the
experimentwise error rate.

Alpha                        0.05
Error Degrees of Freedom        6
Error Mean Square        6.543056

Number of Means          2          3
Critical Range       2.555      2.648

          Mean      N    group
A       20.125     12    1
A
A       19.383     12    2
A
A       18.492     12    3


The Mixed Procedure

                     Iteration History
Iteration    Evaluations    -2 Res Log Like       Criterion
        0              1       129.36405857
        1              2       125.85726953      0.00000003
        2              1       125.85726852      0.00000000
                   Convergence criteria met.


Covariance Parameter Estimates

Cov Parm                Estimate
team(group)               1.0908
```

method*team(group)	0
Residual	2.1797

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
group	2	6	1.23	0.3576
method	1	6	299.11	<.0001
group*method	2	6	0.27	0.7705

Least Squares Means

Effect	group	method	Estimate	Standard Error	DF	t Value	Pr > |t|
method		1	23.5889	0.4922	6	47.92	<.0001
method		2	15.0778	0.4922	6	30.63	<.0001
group	1		20.1250	0.7384	6	27.25	<.0001
group	2		19.3833	0.7384	6	26.25	<.0001
group	3		18.4917	0.7384	6	25.04	<.0001

Differences of Least Squares Means

Effect	group	method	_group	_method	Estimate	Standard Error	DF	t Value
method		1		2	8.5111	0.4921	6	17.29
group	1		2		0.7417	1.0443	6	0.71
group	1		3		1.6333	1.0443	6	1.56
group	2		3		0.8917	1.0443	6	0.85

Differences of Least Squares Means

Effect	group	method	_group	_method	Pr > |t|	Adjustment	Adj P
method		1		2	<.0001	Tukey-Kramer	<.0001
group	1		2		0.5042	Tukey	0.7667
group	1		3		0.1688	Tukey	0.3297
group	2		3		0.4260	Tukey	0.6862

Improving Power

- What if we're interested in G?
  - Since tested over $T_{k(j)}$, increase number of teams
- What if interested in L?
  - Since tested over $LT_{i,k(j)}$, increase number of teams
- What if interested in LT, T?
  - Since tested over error, increase number of replications

Split-Plot Design

Consider an experiment to study the effect of oven temperature (three levels) and amount of baking soda (4 levels) on the consistency of a chocolate chip cookie.

Method 1: *Factorial Model.* Each combination of temperature and baking soda are replicated three times. Combination randomly assigned to each of thirty-six cookies. Total of 36 cooking periods.

Method 2: Oven is heated to specific temperature and four cookies put in oven. Each cookie contains a different amount of baking soda. Do this three times for each oven temperature: a total of nine cooking periods.

Method 2 is different from Method 1 because of a randomization restriction. Instead of randomly assigning oven temperature to each cookie, oven temperature is randomly assigned to a group of four cookies. In other words, the experimental unit for oven temperature is the sheet of four cookies. Since the four cookies within a sheet are randomly assigned an amount of baking soda, the experimental unit for baking soda is still an individual cookie.

- Whole plot: Batch of four cookies
- Subplot: Individual cookies
- Whole plot divided into smaller regions known as *subplot*

Split-plot Design

- Arose in agriculture
  - Whole plot – Large field
  - Subplot – Smaller sections of field

    Four fertilizers and six corn varieties
    Spreader covers 15 foot wide section
    Planter covers 5 foot wide section
    Spread fertilizer on 15 $\times$ 10 foot section (whole plot)
    Plant seed in 5 $\times$ 5 foot section (subplot)
    Six subplots per whole plot

- Very useful in other areas
  - Many situations where EU's of factors varies
  - Repeated measures – subject "split" into time sections
  - Engineering – machine set once of a group of runs

Split Plot Structure

- Different from nested because factors are crossed
- Different from factorial because of randomization
- Information on factors from two levels or strata
- Whole plot – replications for first factor/block for second factor
- Practical problem: Can the subplots be matched/crossed? If EU's are serially correlated within whole plot block, then inference on subplot could be less valid. (Danger of constrained randomization opens up to confounding with block effects.)
- Could consider split-plot as consisting of

  2 randomized block designs (whole plots are blocks with replicates for subplots; whole plots are nested within whole plot factor)
  CRD and RCBD (whole plots are crossed with first factor; whole plots are blocks for subplots)

- For larger units, subdivision to smaller units ignored
- For smaller units, larger units considered blocks
- More power for main subplot effect and interaction
- Should use design only for practical reasons
- Factorial design more powerful if feasible

First Statistical Model

A: whole plot factor (a levels of τ_i)
B: split plot factor (b levels of β_j)
n whole plots per level of A

$$y_{i,j,k} = \mu + \alpha_i + \eta_{k(i)} + \beta_j + (\alpha\beta)_{i,j} + \epsilon_{k(i,j)} \begin{cases} i = 1, \ldots, a \\ k(i) = 1, \ldots, n \\ j = 1, \ldots, b \end{cases}$$

$\eta_{k(i)}$ – whole plot level random error (given by replication of whole plot)
$\epsilon_{k(i,j)}$ – split plot level random error

On subplot level, $\eta_{k(i)}$ are block effects.

EMS

- Fixed A and B (n replicates, given as whole plots, of level A)

  Whole plots are replicates of A (CRD in whole plot)

Source of Variation	Degrees of Freedom	Expected Mean Square
A	$a-1$	$nb\phi_A + b\sigma_R^2 + \sigma^2$
$R(A)$	$a(n-1)$	$b\sigma_R^2 + \sigma^2$
B	$b-1$	$an\phi_B + \sigma^2$
AB	$(a-1)(b-1)$	$n\phi_{AB} + \sigma^2$
Error	$a(b-1)(n-1)$	σ^2

Note assumptions of additivity here.

Soybean Yields

Interested in the effect of soybean varieties and fertilizers on the yield (bushels per subplot unit). Fertilizers were randomly applied to acres within each farm, varieties then randomly applied to subunits of each acres. Consider fertilizers and varieties as fixed. Farm, as a block, is considered random. Whole plot testing similar if block random or fixed. In subplot, if block fixed, all interactions with block are pooled into error. If it is random, this may or may not be done. If it is not done, there are other tests that may be of interest (page 495)

Farm 1			Farm 2			Farm 3		
	Fertilizer			Fertilizer			Fertilizer	
Variety	1	2	Variety	2	1	Variety	1	2
1	10.6	10.9	2	11.9	11.5	3	9.5	9.8
2	11.4	11.7	3	12.6	12.1	1	8.1	8.2
3	11.8	12.4	1	11.6	10.8	2	8.7	9.3

SAS Program

```
option nocenter ps=50 ls=72;

data new;
infile "h:/System/Desktop/soy.dat";
input farm fert var resp;

/* Second analysis */
proc glm;
class farm fert var;
model resp=farm fert farm*fert var farm*var fert*var;
test h=fert e=farm*fert;
```

```
test h=var e=farm*var;
output out=subplot r=res p=pred;

proc gplot;
 plot res*pred;

proc sort data=new;
 by farm fert;
proc means NOPRINT;
 var resp;
 by farm fert;
 output out=new1 mean=resp1;

proc glm;
 class farm fert;
 model resp1=farm fert;
 output out=wholeplot r=res p=pred;

proc gplot;
 plot res*pred;

/* First analysis */
proc glm data=new;
class farm fert var;
model resp=farm|fert var fert*var;
test h=fert e=farm*fert;
run;
```

```
Dependent Variable: resp

                                         Sum of
Source                      DF          Squares    Mean Square   F Value
Model                       13      35.19166667     2.70705128     81.21
Error                        4       0.13333333     0.03333333
Corrected Total             17      35.32500000

Source                  Pr > F
Model                   0.0003


R-Square     Coeff Var      Root MSE     resp Mean
0.996226      1.703647      0.182574      10.71667

Source                      DF      Type I SS    Mean Square   F Value   Pr > F
farm                         2    28.86333333    14.43166667    432.95   <.0001
fert                         1     0.84500000     0.84500000     25.35   0.0073
farm*fert                    2     0.04333333     0.02166667      0.65   0.5696
var                          2     5.34333333     2.67166667     80.15   0.0006
farm*var                     4     0.09333333     0.02333333      0.70   0.6310
fert*var                     2     0.00333333     0.00166667      0.05   0.9518
```

```
               Tests of Hypotheses Using the Type III
                  MS for farm*fert as an Error Term
Source                     DF    Type III SS    Mean Square   F Value
fert                        1     0.84500000     0.84500000     39.00

Source                 Pr > F
fert                   0.0247

               Tests of Hypotheses Using the Type III
                  MS for farm*var as an Error Term
Source                     DF    Type III SS    Mean Square   F Value
var                         2     5.34333333     2.67166667    114.50

Source                 Pr > F
var                   0.0003


Dependent Variable: resp
                                       Sum of
Source                     DF        Squares    Mean Square   F Value
Model                       9    35.09833333     3.89981481    137.64
Error                       8     0.22666667     0.02833333
Corrected Total            17    35.32500000

Source                 Pr > F
Model                  <.0001

Source             DF      Type I SS    Mean Square   F Value    Pr > F
farm                2    28.86333333    14.43166667    509.35    <.0001
fert                1     0.84500000     0.84500000     29.82    0.0006
farm*fert           2     0.04333333     0.02166667      0.76    0.4967
var                 2     5.34333333     2.67166667     94.29    <.0001
fert*var            2     0.00333333     0.00166667      0.06    0.9433

               Tests of Hypotheses Using the Type III
                  MS for farm*fert as an Error Term

Source                     DF    Type III SS    Mean Square   F Value
fert                        1     0.84500000     0.84500000     39.00

Source                 Pr > F
fert                   0.0247
```

Using proc mixed

```
proc mixed;
class fert var farm;
model resp = fert|var;
random farm farm*fert farm*var;
```

```
Cov Parm      Estimate
```

```
farm              2.4007
fert*farm              0
var*farm               0
Residual         0.02700

        Type 3 Tests of Fixed Effects

              Num     Den
Effect         DF      DF    F Value    Pr > F
fert            1       2      31.30    0.0305
var             2       4      98.95    0.0004
fert*var        2       4       0.06    0.9410
```

Whole Plot/Subplot Experiment

- Can have > one factor in whole plot/subplot
- Whole Plot
  - CRD
  - RCBD
  - Factorial (k factors)
  - BIB
- Subplot
  - RCBD
  - BIB
  - Factorial in Blocking Design
- Analysis of Covariance
  - Covariate linear with response in subplot and whole plot

EMS Caution: Fixed Effects in Whole Plot

Whole plot factors: A and B; Subplot factor: C

- Must include within plot (WP) factor in EMS table ($n = 1$)
- Else: everything appears tested over subplot error

Source of Variation	Degrees of Freedom	Expected Mean Square
A	$a-1$	$bc\phi_A + c\sigma^2_{WP} + \sigma^2$
B	$b-1$	$ac\phi_B + c\sigma^2_{WP} + \sigma^2$
AB	$(a-1)(b-1)$	$c\phi_{AB} + c\sigma^2_{WP} + \sigma^2$
$\text{Rep}_1(AB)$	0	$c\sigma^2_{WP} + \sigma^2$
C	$c-1$	$ab\phi_C + \sigma^2$
AC	$(a-1)(c-1)$	$b\phi_{AC} + \sigma^2$
BC	$(b-1)(c-1)$	$a\phi_{BC} + \sigma^2$
ABC	$(a-1)(b-1)(c-1)$	$\sigma^2_{ABC} + \sigma^2$
$\text{Rep}_2(ABC)$	0	σ^2

Pooling in Split Plot

- Have two layers so we can't simply pool all errors
- If we did, result in
  - Overstating significance of whole plot factor
  - If $\sigma^2_{WP} > \sigma^2_{SP}$, understate subplot factor
- Should pool errors separately
- Consider 2 mixed factors in whole plot, 1 fixed factor in subplot

Source of Variation	Degrees of Freedom	Expected Mean Square
A	$a-1$	$bcn\phi_A + nc\sigma^2_{AB} + c\sigma^2_{WP} + \sigma^2$
B	$b-1$	$acn\sigma^2_B + c\sigma^2_{WP} + \sigma^2$
AB	$(a-1)(b-1)$	$cn\sigma^2_{AB} + c\sigma^2_{WP} + \sigma^2$
$\text{Rep}(AB)$	$ab(n-1)$	$c\sigma^2_{WP} + \sigma^2$
C	$c-1$	$abn\phi_C + an\sigma^2_{BC} + \sigma^2$
AC	$(a-1)(c-1)$	$bn\phi_{AC} + n\sigma^2_{ABC} + \sigma^2$
BC	$(b-1)(c-1)$	$an\phi_{BC} + \sigma^2$
ABC	$(a-1)(b-1)(c-1)$	$n\sigma^2_{ABC} + \sigma^2$
Error	$ab(c-1)(n-1)$	σ^2

Extensions of Split Plot Design

- Can further split subplot units into sub-subplots
- Known as Split-split Plot Design
  - CRD with 2 RCBD's
  - Three RCBD's

Source of Variation	Degrees of Freedom	Expected Mean Square
D	$d-1$	$abc\sigma^2_D + \sigma^2$
A	$a-1$	$bcd\phi_A + bc\sigma^2_{AD} + \sigma^2$
AD	$(a-1)(d-1)$	$bc\sigma^2_{AD} + \sigma^2$
B	$b-1$	$acd\phi_B + ac\sigma^2_{BD} + \sigma^2$
BD	$(b-1)(d-1)$	$ac\sigma^2_{BD} + \sigma^2$
AB	$(a-1)(b-1)$	$cd\phi_{AB} + c\sigma^2_{ABD} + \sigma^2$
ABD	$(a-1)(b-1)(d-1)$	$c\sigma^2_{ABD} + \sigma^2$
C	$c-1$	$abd\phi_C + ab\sigma^2_{CD} + \sigma^2$
CD	$(c-1)(d-1)$	$ab\sigma^2_{CD} + \sigma^2$
AC	$(a-1)(c-1)$	$bd\phi_{AC} + b\sigma^2_{ACD} + \sigma^2$
ACD	$(a-1)(c-1)(d-1)$	$b\sigma^2_{ACD} + \sigma^2$
BC	$(b-1)(c-1)$	$ad\phi_{BC} + a\sigma^2_{BCD} + \sigma^2$
BCD	$(b-1)(c-1)(d-1)$	$a\sigma^2_{BCD} + \sigma^2$
ABC	$(a-1)(b-1)(c-1)$	$d\phi_{ABC} + \sigma^2_{ABCD} + \sigma^2$
$ABCD$	$(a-1)(b-1)(c-1)(d-1)$	$\sigma^2_{ABCD} + \sigma^2$

Example of Strip Plot/Split Plot

Investigating the long-term effects of pasture composition for different patterns of grazing. Response is the percent of area covered by principal grass. Consider three factors:

- Length of time grazing (3, 9, 18 days)
- (SP)ring grazing cycles (2 with long gap or 4 with short gap)
- (S)ummer grazing cycles (2 with long gap or 4 with short gap)

Experiment set up in a 3×3 Latin Square design. Each of the nine whole plots split twice in a criss-cross design for the two grazing cycle factors.

		S				SP				SP	
	2		4		2		4		2		4
4	12.5		26.2	4	59.2		49.9	4	55.0		27.3
SP		18		S		9		S		3	
2	33.4		44.2	2	47.6		15.8	2	35.9		18.3
		S				S				S	
	4		2		2		4		2		4
2	56.2		52.3	2	67.7		62.2	2	28.0		29.4
SP		9		SP		3		SP		18	
4	27.5		25.1	4	24.1		27.5	4	19.5		29.9
		S				S				SP	
	2		4		2		4		2		4
4	57.2		69.5	4	30.3		26.6	4	61.9		26.2
SP		3		SP		18		S		9	
2	16.9		19.5	2	11.0		17.6	2	46.5		15.4

What are the whole plot effects? Subplot effects?

Strip Plot/Criss Cross Design

- Criss-cross or Strip-Plot Design
- Two factor treatment structure
- Both treatments require large number of EU's
- Arrange EU's in rectangles ($a \times b$)
- Each rectangle – whole plot rows and whole plot columns
- Three levels of information
  - Rows
  - Columns
  - Rows $\times$ Column (cell)

Source of Variation	Degrees of Freedom	Expected Mean Square
D (Blocks)	$d-1$	$ab\sigma_D^2 + \sigma^2$
A	$a-1$	$bd\phi_A + b\sigma_{AD}^2 + \sigma^2$
AD (WP error)	$(a-1)(d-1)$	$b\sigma_{AD}^2 + \sigma^2$
B	$b-1$	$ab\phi_B + a\sigma_{BD}^2 + \sigma^2$
BD (WP error)	$(b-1)(d-1)$	$a\sigma_{BD}^2 + \sigma^2$
AB	$(a-1)(b-1)$	$d\sigma_{AB}^2 + \sigma_{ABD}^2 + \sigma^2$
ABD (Subplot error)	$(a-1)(b-1)(d-1)$	$\sigma_{ABD}^2 + \sigma^2$

In the pasture example, interested in effect of length of grazing time (`period`), number of spring grazing cycles (`sp`), and the number of summer grazing cycles (`sum`).

- Period – whole plot; cells are replicates (cells nested within Period)
- Two grazing cycle effects – subplots; crossed with cells (cells acting as blocks)
- Need to take out row and column block effect (which compose cell effect)

Breaking Down the Error

- Looks like replicated Latin Square (with *period* as whole plot factor)
- Grazing cycles (the two subplot factors) crossed within cells; treat as separate split-plots

$y = row + col + per + sp + sum + per \times sp + per \times sum + sp \times sum + per \times sp \times sum + error$

Sources of error:

- Replication of *period* (after *row* and *column* taken out): `period(row column)`
- Replication of *period* $\times$ *spring* (after *row* and *column* taken out): `sp*period(row column)`
- Replication of *period* $\times$ *summer* (after *row* and *column* taken out): `sum*period(row column)`
- Replication of *period*$\times$*summer*$\times$*spring* (after *row* and *column* taken out): `sum*spr*period(row column)` (not included in `model` statement)

```
options nocenter ls=75;
data new;
input row column period sp sum resp;
cards;
1 1 18 4 2 12.5
1 1 18 4 4 26.2
1 1 18 2 2 33.4
1 1 18 2 4 44.2
1 2  9 2 4 59.2
1 2  9 4 4 49.9
1 2  9 2 2 47.6
1 2  9 4 2 15.8
1 3  3 2 4 55.0
1 3  3 4 4 27.3
1 3  3 2 2 35.9
1 3  3 4 2 18.3
2 1  9 2 4 56.2
2 1  9 2 2 52.3
2 1  9 4 4 27.5
2 1  9 4 2 25.1
2 2  3 2 2 67.7
2 2  3 2 4 62.2
2 2  3 4 2 24.1
2 2  3 4 4 27.5
2 3 18 2 2 28.0
2 3 18 2 4 29.4
2 3 18 4 2 19.5
2 3 18 4 4 29.9
3 1  3 2 2 57.2
3 1  3 2 4 69.5
3 1  3 4 2 16.9
3 1  3 4 4 19.5
3 2 18 2 2 30.3
```

```
3 2 18 2 4 26.6
3 2 18 4 2 11.0
3 2 18 4 4 17.6
3 3  9 2 4 61.9
3 3  9 4 4 26.2
3 3  9 2 2 46.5
3 3  9 4 2 15.4
;

proc glm;
class row column period sp sum;
model resp=row column period period(row column) sp period*sp
sp*period(row column) sum period*sum sum*period(row column)
sp*sum period*sp*sum;
test h=period e=period(row column);
test h=sp e=sp*period(row column);
test h=sum e=sum*period(row column);
test h=sp*period e=sp*period(row column);
test h=sum*period e=sum*period(row column);
means sum sp|period;
run;
```

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	29	10336.90306	356.44493	12.10	0.0025
Error	6	176.73333	29.45556		
Corrected Total	35	10513.63639			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
row	2	107.620556	53.810278	1.83	0.2401
column	2	121.202222	60.601111	2.06	0.2087
period	2	1677.430556	838.715278	28.47	0.0009
period(row*column)	2	214.770556	107.385278	3.65	0.0920
sp	1	5697.733611	5697.733611	193.43	<.0001
period*sp	2	822.157222	411.078611	13.96	0.0055
perio*sp(row*column)	6	477.966667	79.661111	2.70	0.1257
sum	1	696.080278	696.080278	23.63	0.0028
period*sum	2	80.977222	40.488611	1.37	0.3225
perio*sum(row*colum)	6	367.580000	61.263333	2.08	0.1972
sp*sum	1	21.313611	21.313611	0.72	0.4276
period*sp*sum	2	52.070556	26.035278	0.88	0.4609

Tests of Hypotheses Using the Type III MS
for period(row*column) as an Error Term

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	2	1677.430556	838.715278	7.81	0.1135

Tests of Hypotheses Using the Type III MS
for perio*sp(row*column) as an Error Term

```
Source                     DF   Type III SS   Mean Square  F Value  Pr > F
sp                          1   5697.733611   5697.733611    71.52  0.0001
period*sp                   2    822.157222    411.078611     5.16  0.0497

                Tests of Hypotheses Using the Type III MS
                for perio*sum(row*colum) as an Error Term

Source                     DF   Type III SS   Mean Square  F Value  Pr > F
sum                         1   696.0802778   696.0802778    11.36  0.0150
period*sum                  2    80.9772222    40.4886111     0.66  0.5503


/* proc means for significant effects */
Level of            -------------resp------------
sum            N            Mean          Std Dev
2             18      30.9722222       16.8618890
4             18      39.7666667       17.1224998

Level of            -------------resp------------
sp             N            Mean          Std Dev
2             18      47.9500000       14.3149141
4             18      22.7888889        8.8527755

Level of            -------------resp------------
period         N            Mean          Std Dev
3             12      40.0916667       20.5891171
9             12      40.3000000       17.1050763
18            12      25.7166667        9.3164403

Level of     Level of            -------------resp------------
period       sp            N            Mean          Std Dev
3            2             6      57.9166667       12.1818581
3            4             6      22.2666667        4.6534575
9            2             6      53.9500000        6.2349820
9            4             6      26.6500000       12.5552778
18           2             6      31.9833333        6.4126178
18           4             6      19.4500000        7.4551325
```

Computing Standard Errors: Simple Random Effects

$$y_{i,j} = \mu + \tau_i + \epsilon_{i,j} \begin{cases} i = 1, 2, \ldots, a \\ j = 1, 2, \ldots, n \end{cases}$$

$\tau_i \sim N(0, \sigma_\tau^2)$ and $\epsilon_{i,j} \sim N(0, \sigma^2)$
$\{\tau_i\}$ and $\{\epsilon_{i,j}\}$ independent

$$\begin{aligned} \mathrm{Var}(\bar{y}_{..}) &= \mathrm{Var}(\mu) + \mathrm{Var}(\bar{\tau}_{.}) + \mathrm{Var}(\bar{\epsilon}_{..}) \\ &= 0 + \sigma_\tau^2/a + \sigma^2/an \\ &= (n\sigma_\tau^2 + \sigma^2)/an \end{aligned}$$

Since $\mathrm{E}(MS_A) = n\sigma_\tau^2 + \sigma^2$, we use this mean square and the associated degrees of freedom when constructing a confidence interval or performing a hypothesis test.

Two Factor Random Effects Model

$$y_{i,j,k} = \mu + \tau_i + \beta_j + (\tau\beta)_{i,j} + \epsilon_{i,j,k} \begin{cases} i = 1, 2, \ldots, a \\ j = 1, 2, \ldots, b \\ k = 1, 2, \ldots n \end{cases}$$

$\tau_i \sim N(0, \sigma_\tau^2)$ and $\beta_j \sim N(0, \sigma_\beta^2)$
$(\tau\beta)_{i,j} \sim N(0, \sigma_{\tau\beta}^2)$ and $\epsilon_{i,j,k} \sim N(0, \sigma^2)$
$\{\tau_i\}$, $\{\beta_j\}$, $\{(\tau\beta)_{i,j}\}$ and $\{\epsilon_{i,j,k}\}$ independent

$$\begin{aligned} \mathrm{Var}(\bar{y}_{...}) &= \mathrm{Var}(\mu + \bar{\tau}_. + \bar{\beta}_. + (\bar{\tau\beta})_{..} + \bar{\epsilon}_{...}) \\ &= 0 + \sigma_\tau^2/a + \sigma_\beta^2/b + \sigma_{\tau\beta}^2/ab + \sigma^2/abn \\ &= (bn\sigma_\tau^2 + an\sigma_\beta^2 + n\sigma_{\tau\beta}^2 + \sigma^2)/abn \end{aligned}$$

In this case, there is no expected mean square equal to the numerator. As a result, the combination $MS_A + MS_B - MS_{AB}$ is used to estimate the variance and Satterthwaite's degrees of freedom formula is used to approximate the degrees of freedom.

Two-Factor Mixed Effects Model

$$y_{i,j,k} = \mu + \tau_i + \beta_j + (\tau\beta)_{i,j} + \epsilon_{i,j,k} \begin{cases} i = 1, 2, \ldots, a \\ j = 1, 2, \ldots, b \\ k = 1, 2, \ldots n \end{cases}$$

$$\begin{array}{rcl} \sum \tau_i = 0 & \text{and} & \beta \sim N(0, \sigma_\beta^2) \\ (\tau\beta)_{i,j} \sim N(0, (a-1)\sigma_{\tau\beta}^2/a) & \text{and} & \sum_i (\tau\beta)_{i,j} = 0 \text{ for } \beta \text{ level } j \end{array}$$

$$\epsilon_{i,j,k} \sim N(0, \sigma^2)$$

$$\begin{aligned} \mathrm{Var}(\bar{y}_{i..}) &= \mathrm{Var}(\mu + \tau_i + \bar{\beta}_. + (\bar{\tau\beta})_{i.} + \bar{\epsilon}_{i..}) \\ &= 0 + \sigma_\beta^2/b + (a-1)\sigma_{\tau\beta}^2/ab + \sigma^2/bn \end{aligned}$$

The unrestricted model would not have this $\frac{a-1}{a}$ coefficient in front of the $\sigma_{\tau\beta}^2$. In either case, the estimate of the variance can only be written in the form $p_1 MS_1 + p_2 MS_2 + \ldots + p_k MS_k$, where some of the p_i are different from ± 1. The formula on page 512 can be generalized to approximate this situation. It is simply

$$df = \frac{(\sum p_i MS_i)^2}{\sum p_i^2 MS_i^2 / df_i}$$

$$
\begin{aligned}
\text{Var}(\bar{y}_{i..} - \bar{y}_{i'..}) &= \text{Var}(\tau_i - \tau_{i'} + (\bar{\tau\beta})_{i.} - (\bar{\tau\beta})_{i'.} + \bar{\epsilon}_{i..} - \bar{\epsilon}_{i'..}) \\
&= 2\sigma^2_{\tau\beta}/b + 2\sigma^2/bn
\end{aligned}
$$

In both the restricted and unrestricted models, the variance of the difference between two treatment means is the same. Here we would use MS_{AB} and its degrees of freedom when performing hypothesis tests.

Split Plot Design

Will use unrestricted mixed model and look at both pooled and unpooled subplot error. Will also focus on RCBD in whole plot with no replication.

There are several comparisons that may be of interest.

1. Main effect in whole plot (i)
2. Main effect in subplot (k)
3. Interaction with i fixed
4. Interaction with k fixed

Pooled

$$
y_{i,j,k} = \mu + B_j + A_i + AB_{i,j} + C_k + AC_{i,k} + \epsilon_{i,j,k}
\begin{cases}
i = 1, 2, \ldots, a \\
j = 1, 2, \ldots, b \\
k = 1, 2, \ldots, c
\end{cases}
$$

$$
\begin{aligned}
\sum A_i = 0 \quad &\text{and} \quad B \sim N(0, \sigma^2_B) \\
AB_{i,j} \sim N(0, \sigma^2_{AB}) \quad &\text{and} \quad \epsilon_{i,j,k} \sim N(0, \sigma^2) \\
\sum C_k = 0 \quad &\text{and} \quad \sum\sum AC_{i,k} = 0
\end{aligned}
$$

$$
\begin{aligned}
\bar{y}_{i..} &= \mu + \bar{B}_{.} + A_i + \bar{AB}_{i.} + \bar{C}_{.} + \bar{AC}_{i.} + \bar{\epsilon}_{i..} \\
\bar{y}_{..k} &= \mu + \bar{B}_{.} + \bar{A}_{.} + \bar{AB}_{i.} + C_k + \bar{AC}_{.k} + \bar{\epsilon}_{..k} \\
\bar{y}_{i.k} &= \mu + \bar{B}_{.} + A_i + \bar{AB}_{i.} + C_k + AC_{ik} + \bar{\epsilon}_{i.k}
\end{aligned}
$$

1. Use MS_{AB} in calculations

$$
\begin{aligned}
\text{Var}(\bar{y}_{i..} - \bar{y}_{i'..}) &= \text{Var}(A_i + A_{i'} + \bar{AB}_{i.} + \bar{AB}_{i'.} + \bar{\epsilon}_{i..} - \bar{\epsilon}_{i'..}) \\
&= 2(\sigma^2_{AB}/b + \sigma^2/bc)
\end{aligned}
$$

2. Use MS_E in calculations

$$
\begin{aligned}
\text{Var}(\bar{y}_{..k} - \bar{y}_{..k'}) &= \text{Var}(C_k - C_{k'} + \bar{\epsilon}_{..k} - \bar{\epsilon}_{..k'}) \\
&= 2\sigma^2/ab
\end{aligned}
$$

3. Use MS_E in calculations

$$\begin{aligned}\text{Var}(\bar{y}_{i.k} - \bar{y}_{i.k'}) &= \text{Var}(C_k - C_{k'} + AC_{ik} - AC_{ik'} + \bar{\epsilon}_{i.k} - \bar{\epsilon}_{i.k'}) \\ &= 2\sigma^2/b\end{aligned}$$

4. Use linear combination $(c-1)MS_E + MS_{AB}$

$$\begin{aligned}\text{Var}(\bar{y}_{i.k} - \bar{y}_{i'.k}) &= \text{Var}(A_i - A_{i'} + \bar{AB}_{i.} - \bar{AB}_{i'.} + AC_{ik} - AC_{i'k} + \bar{\epsilon}_{i.k} - \bar{\epsilon}_{i'.k}) \\ &= 2(\sigma^2_{AB}/b + \sigma^2/b)\end{aligned}$$

Unpooled

$$y_{i,j,k} = \mu + B_j + A_i + AB_{i,j} + C_k + AC_{i,k} + BC_{j,k} + \epsilon_{u,j,k}$$

1. Same: Use MS_{AB} in calculations
2. Use MS_{BC} in calculations

$$\begin{aligned}\text{Var}(\bar{y}_{..k} - \bar{y}_{..k'}) &= \text{Var}(C_k + C_{k'} + \bar{BC}_{.k} - \bar{BC}_{.k'} + \bar{\epsilon}_{..k} - \bar{\epsilon}_{..k'}) \\ &= 2(\sigma^2_{BC}/b + \sigma^2/ab)\end{aligned}$$

3. Use linear combination $(a-1)MS_E + MS_{BC}$

$$\begin{aligned}\text{Var}(\bar{y}_{i.k} - \bar{y}_{i.k'}) &= \text{Var}(C_k - C_{k'} + AC_{i,k} - AC_{i,k'} + \bar{BC}_{.k} - \bar{BC}_{.k'} + \bar{\epsilon}_{i.k} - \epsilon_{i.k'}) \\ &= 2(\sigma^2_{BC}/b + \sigma^2/b)\end{aligned}$$

4. Same as before

Repeated Measures Analysis

- Often take measurements on EU over time
  1. Single summary of time points
     - Peak response or total concentration in body
     - Response mean or orthogonal polynomials (shape summary)
     - Typically RCBD or CRD on summary statistic
  2. Interested in time as a factor
     - Interaction of treatments with time
     - Shape of response curve over time
- Common to take Split Plot approach

  - Subject is whole plot
  - Time units are subplot

- Problems
  - Assumptions: With large changes in response over time, may have problems with constant variance assumption.
  - non-randomness of time: Not randomly applying time to subplot EU. Observations at adjacent times more correlated than times further away.

- Other approaches (when time a factor)
  - Multivariate analysis (takes correlation into account)
  - `proc mixed` to model correlation structure

Example

- Consider pretest/posttest problem
- Subject assigned to treatment group
- Measurements taken pre and 2 post treatment
- Use pre-test score to standardize post

Subject	Treatment	Pretest	Post 1	Post 2	Average Post	Diff
1	1	100	125	135	130.0	30.0
2	2	110	125	125	125.0	15.0
3	2	90	105	104	104.5	14.5
4	1	110	130	139	134.5	24.5
5	1	105	130	141	135.5	30.5
6	2	125	135	136	135.5	10.5

- Perform t-test of diffs (remove time as factor)

$$\frac{28.33 - 13.33}{\sqrt{8.583(\frac{1}{3} + \frac{1}{3})}} = 6.17$$

$$p = 0.0033$$

- Treat as split-plot design
  - Use only post-test scores (adjusted for pre-test)

Source	df	SS	MS	F	p
Trt	1	675.00	675.00	39.32	0.0033
Subj(Trt)	4	68.67	17.17		
Time	1	75.00	75.00	150.00	0.0003
Time × Trt	1	75.00	75.00	150.00	0.0003
Error	4	2.00	0.50		

Split-Plot Approach

- Split plot compares trts by averaging over time
- If other summary of obs desired, use CRD/RCBD
- Provides info on time and time×trt interaction
- Are these p-values correct?
- Not properly randomized (time only moves forward)
- Recall single factor CRD split-plot model

$$\begin{aligned}\text{Var}(y_{i,j,k}) &= \sigma_R^2 + \sigma^2 \\ \text{Cor}(y_{i,j,k}, y_{i,j',k}) &= \sigma_R^2/(\sigma_R^2 + \sigma^2)\end{aligned}$$

Any two observations in same whole plot have same correlation
Known as assumption of *compound symmetry*
Split plot approach appropriate when repeated measures have compound symmetry

Huyhn-Feldt Conditions

(JASA, 1970)

- Split-plot analysis valid under these conditions
- Less restrictive than compound symmetry
- Also known as *sphericity condition*
- Instead of constant correlation

$$\text{Var}(y_{i,j,k} - y_{i,j',k}) = c$$

- In SAS, tests for sphericity assumptions
- Adjusts F for deviations from these conditions
  - H-F and G-G adjust F-values (multiply F by number 0-1)

Example

Studying different methods (two methods and control) to increase speed of throwing a baseball. Assume seven subjects were assigned to each group and followed a specific training method for one month. Each subject's throwing velocity (km/hr) was observed at the end of two and four weeks (adjusted for initial throwing velocity).

Repeated measures problem. Subjects nested within method. While the EU for method is the subject, we're interested in relationship over time so we want to include time in the model.

$$y_{i,j,k,\ell} = \mu + M_i + S_{j(i)} + T_k + MT_{i,k} + ST_{j,k(i)} + \epsilon_{\ell(i,j,k)}$$

SAS Program using `glm`

```
options nocenter ls=75;

data new;
input meth subj time1 time2;
cards;
1    1 25.4 30.6
1    2 27.4 29.3
1    3 25.5 30.0
1    4 25.8 29.7
1    5 26.2 31.3
1    6 24.6 26.6
1    7 25.6 28.0
2    1 27.6 27.1
2    2 24.7 29.0
2    3 26.3 27.3
2    4 25.0 29.7
2    5 25.7 29.5
2    6 28.5 29.7
2    7 22.9 27.2
3    1 22.8 25.1
3    2 24.2 24.0
3    3 25.3 25.2
3    4 25.4 24.7
3    5 24.5 26.2
3    6 25.6 26.9
3    7 25.6 24.8
;

data new1;
 set new;
 resp=time1; time=1; output;
 resp=time2; time=2; output;
```

```
proc glm data=new1;
 class meth subj time;
 model resp=meth subj(meth) time meth*time;
 test h=meth e=subj(meth);
 means meth|time;
```

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	23	161.4569048	7.0198654	5.31	0.0003
Error	18	23.8014286	1.3223016		
Corrected Total	41	185.2583333			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
meth	2	52.43190476	26.21595238	19.83	<.0001
subj(meth)	18	38.26142857	2.12563492	1.61	0.1614
time	1	53.26880952	53.26880952	40.28	<.0001
meth*time	2	17.49476190	8.74738095	6.62	0.0070

Tests of Hypotheses Using the Type III MS for subj(meth) as an Error Term

Source	DF	Type III SS	Mean Square	F Value	Pr > F
meth	2	52.43190476	26.21595238	12.33	0.0004

Level of meth	N	resp Mean	resp Std Dev
1	14	27.5714286	2.22552624
2	14	27.1571429	2.06647760
3	14	25.0214286	0.99705611

Level of time	N	resp Mean	resp Std Dev
1	21	25.4571429	1.35593932
2	21	27.7095238	2.18194976

Level of meth	Level of time	N	resp Mean	resp Std Dev
1	1	7	25.7857143	0.86106247
1	2	7	29.3571429	1.59672283
2	1	7	25.8142857	1.87299099
2	2	7	28.5000000	1.23962360
3	1	7	24.7714286	1.02747958
3	2	7	25.2714286	0.97590007

Using `repeated` in `proc glm`

- `repeated` command does several analyses
  - Multivariate Analysis
  - Split Plot (with HF and GG df corrections)
  - Orthogonal polynomials (single df summaries)

```
proc glm data=new;
class meth subj;
model time1 time2 = meth;
repeated time 2 (1 2) polynomial / summary;
run;
```

```
The GLM Procedure

Dependent Variable: time1
                                       Sum of
Source                    DF          Squares    Mean Square  F Value  Pr > F
Model                      2       4.94000000     2.47000000     1.40  0.2730
Error                     18      31.83142857     1.76841270
Corrected Total           20      36.77142857

Source                    DF      Type I SS      Mean Square  F Value  Pr > F
meth                       2       4.94000000     2.47000000     1.40  0.2730


Dependent Variable: time2
                                       Sum of
Source                    DF          Squares    Mean Square  F Value  Pr > F
Model                      2      64.98666667    32.49333333    19.35  <.0001
Error                     18      30.23142857     1.67952381
Corrected Total           20      95.21809524

Source                    DF      Type I SS      Mean Square  F Value  Pr > F
meth                       2      64.98666667    32.49333333    19.35  <.0001

Repeated Measures Analysis of Variance

  Repeated Measures Level Information
Dependent Variable       time1    time2
     Level of time           1        2

              Manova Test Criteria and Exact F Statistics
                 for the Hypothesis of no time Effect
                   H = Type III SSCP Matrix for time
                         E = Error SSCP Matrix
                         S=1    M=-0.5    N=8

Statistic                     Value    F Value   Num DF   Den DF   Pr > F
Wilks' Lambda            0.30882775      40.28        1       18   <.0001
Pillai's Trace           0.69117225      40.28        1       18   <.0001
Hotelling-Lawley Trace   2.23805094      40.28        1       18   <.0001
Roy's Greatest Root      2.23805094      40.28        1       18   <.0001

              Manova Test Criteria and Exact F Statistics
               for the Hypothesis of no time*meth Effect
                H = Type III SSCP Matrix for time*meth
                         E = Error SSCP Matrix
                           S=1    M=0    N=8
```

```
Statistic                        Value   F Value   Num DF   Den DF   Pr > F
Wilks' Lambda               0.57635894      6.62        2       18   0.0070
Pillai's Trace              0.42364106      6.62        2       18   0.0070
Hotelling-Lawley Trace      0.73502991      6.62        2       18   0.0070
Roy's Greatest Root         0.73502991      6.62        2       18   0.0070

Repeated Measures Analysis of Variance
Tests of Hypotheses for Between Subjects Effects

Source                     DF   Type III SS   Mean Square  F Value  Pr > F
meth                        2   52.43190476   26.21595238    12.33  0.0004
Error                      18   38.26142857    2.12563492

Repeated Measures Analysis of Variance
Univariate Tests of Hypotheses for Within Subject Effects

Source                     DF   Type III SS   Mean Square  F Value  Pr > F
time                        1   53.26880952   53.26880952    40.28  <.0001
time*meth                   2   17.49476190    8.74738095     6.62  0.0070
Error(time)                18   23.80142857    1.32230159
```

Example with 3 time pts

- Consider another test given after additional 2 weeks. No training

```
options nocenter ls=75;

data new;
input meth subj time1 time2 time3;
cards;
1    1 25.4 30.6 29.1
1    2 27.4 29.3 28.0
1    3 25.5 30.0 27.0
1    4 25.8 29.7 27.9
1    5 26.2 31.3 29.2
1    6 24.6 26.6 26.6
1    7 25.6 28.0 28.3
2    1 27.6 27.1 27.8
2    2 24.7 29.0 26.2
2    3 26.3 27.3 28.4
2    4 25.0 29.7 29.9
2    5 25.7 29.5 29.4
2    6 28.5 29.7 30.4
2    7 22.9 27.2 26.4
3    1 22.8 25.1 27.2
3    2 24.2 24.0 26.2
3    3 25.3 25.2 28.1
3    4 25.4 24.7 31.0
3    5 24.5 26.2 29.4
```

```
3    6 25.6 26.9 29.2
3    7 25.6 24.8 28.9
;

data new1;
 set new;
 resp=time1; time=1; output;
 resp=time2; time=2; output;
 resp=time3; time=3; output;
proc glm data=new1;
class meth subj time;
model resp = meth subj(meth) time meth*time;
test h=meth e= subj(meth);
means meth*time;

proc glm data=new;
 class meth;
 model time1 time2 time3=meth / nouni;
 repeated time (0 1 2) polynomial / summary;

proc sort;
 by meth;
proc means;
 var time1-time3; by meth;
run;
```

```
meth=1

The MEANS Procedure

Variable    N           Mean        Std Dev        Minimum        Maximum
-------------------------------------------------------------------------
time1      21     25.7857143      0.8168756     24.6000000     27.4000000
time2      21     29.3571429      1.5147843     26.6000000     31.3000000
time3      21     28.0142857      0.9253571     26.6000000     29.2000000
-------------------------------------------------------------------------


meth=2

Variable    N           Mean        Std Dev        Minimum        Maximum
-------------------------------------------------------------------------
time1      21     25.8142857      1.7768753     22.9000000     28.5000000
time2      21     28.5000000      1.1760102     27.1000000     29.7000000
time3      21     28.3571429      1.5702138     26.2000000     30.4000000
-------------------------------------------------------------------------

meth=3

Variable    N           Mean        Std Dev        Minimum        Maximum
```

```
---------------------------------------------------------------------------
time1      21     24.7714286       0.9747527      22.8000000      25.6000000
time2      21     25.2714286       0.9258201      24.0000000      26.9000000
time3      21     28.5714286       1.4906854      26.2000000      31.0000000
---------------------------------------------------------------------------


                Manova Test Criteria and Exact F Statistics
                   for the Hypothesis of no time Effect
                     H = Type III SSCP Matrix for time
                           E = Error SSCP Matrix

                            S=1    M=0    N=7.5

Statistic                        Value    F Value    Num DF    Den DF    Pr > F
Wilks' Lambda               0.15118762      47.72         2        17    <.0001
Pillai's Trace              0.84881238      47.72         2        17    <.0001
Hotelling-Lawley Trace      5.61429826      47.72         2        17    <.0001
Roy's Greatest Root         5.61429826      47.72         2        17    <.0001


                 Manova Test Criteria and F Approximations
                 for the Hypothesis of no time*meth Effect
                  H = Type III SSCP Matrix for time*meth
                           E = Error SSCP Matrix

                          S=2    M=-0.5    N=7.5

Statistic                        Value    F Value    Num DF    Den DF    Pr > F
Wilks' Lambda               0.27994760       7.56         4        34    0.0002
Pillai's Trace              0.72095225       5.07         4        36    0.0024
Hotelling-Lawley Trace      2.56888265      10.74         4    19.407    <.0001
Roy's Greatest Root         2.56763078      23.11         2        18    <.0001

NOTE: F Statistic for Roy's Greatest Root is an upper bound.
NOTE: F Statistic for Wilks' Lambda is exact.

Repeated Measures Analysis of Variance
Tests of Hypotheses for Between Subjects Effects

Source                    DF   Type III SS   Mean Square  F Value  Pr > F

meth                       2   29.03746032   14.51873016     4.20  0.0319
Error                     18   62.26666667    3.45925926

Source                    DF   Type III SS   Mean Square  F Value  Pr > F
time                       2   95.21555556   47.60777778    46.63  <.0001
time*meth                  4   41.99492063   10.49873016    10.28  <.0001
Error(time)               36   36.75619048    1.02100529

                         Adj Pr > F
Source                 G - G    H - F
time                  <.0001   <.0001
```

```
time*meth             <.0001    <.0001
Error(time)

Greenhouse-Geisser Epsilon    0.9194
Huynh-Feldt Epsilon           1.1328

Contrast Variable: time_1

Source                    DF   Type III SS   Mean Square  F Value  Pr > F
Mean                       1   85.71428571   85.71428571   100.93  <.0001
meth                       2    4.84000000    2.42000000     2.85  0.0841
Error                     18   15.28571429    0.84920635

Contrast Variable: time_2

Source                    DF   Type III SS   Mean Square  F Value  Pr > F
Mean                       1    9.50126984    9.50126984     7.97  0.0113
meth                       2   37.15492063   18.57746032    15.57  0.0001
Error                     18   21.47047619    1.19280423
```

Split Plot Analysis

```
data new1;
 set new;
 resp=time1; time=1; output;
 resp=time2; time=2; output;
 resp=time3; time=3; output;
proc glm data=new1;
class meth subj time;
model resp = meth subj(meth) time meth*time;
test h=meth e= subj(meth);
means meth*time;
```

```
Dependent Variable: resp
                                   Sum of
Source                    DF      Squares   Mean Square  F Value  Pr > F
Model                     26   228.5146032    8.7890232     8.61  <.0001
Error                     36    36.7561905    1.0210053
Corrected Total           62   265.2707937

Source                    DF   Type III SS   Mean Square  F Value  Pr > F
meth                       2   29.03746032   14.51873016    14.22  <.0001
subj(meth)                18   62.26666667    3.45925926     3.39  0.0009
time                       2   95.21555556   47.60777778    46.63  <.0001
meth*time                  4   41.99492063   10.49873016    10.28  <.0001

Tests of Hypotheses Using the Type III MS for subj(meth) as an Error Term

Source                    DF   Type III SS   Mean Square  F Value  Pr > F
meth                       2   29.03746032   14.51873016     4.20  0.0319
```

Analysis Using `proc mixed`

- Consider covariance of observations within subject
- `mixed` allows for different covariance structures
- Recall Latin Square as repeated measures problem
- Use simple ($\sigma^2 I$) as default (independence)

Assume three time points per subject

$$\sigma^2 I = \begin{bmatrix} \sigma^2 & 0 & 0 \\ 0 & \sigma^2 & 0 \\ 0 & 0 & \sigma^2 \end{bmatrix}$$

  - Use one of various provided
  - Create your own

Covariance Structures

Consider three time points per subject

- Compound Symmetry

$$\begin{bmatrix} \sigma^2 + \sigma_1^2 & \sigma_1^2 & \sigma_1^2 \\ \sigma_1^2 & \sigma^2 + \sigma_1^2 & \sigma_1^2 \\ \sigma_1^2 & \sigma_1^2 & \sigma^2 + \sigma_1^2 \end{bmatrix}$$

- Unstructured

$$\begin{bmatrix} \sigma_{11}^2 & \sigma_{21} & \sigma_{31} \\ \sigma_{21} & \sigma_{22}^2 & \sigma_{32} \\ \sigma_{31} & \sigma_{32}^2 & \sigma_{33}^2 \end{bmatrix}$$

- First order autoregressive

$$\sigma^2 \begin{bmatrix} 1 & \rho & \rho^2 \\ \rho & 1 & \rho \\ \rho^2 & \rho & 1 \end{bmatrix}$$

Example

```
options nocenter ls=75;

data new;
input meth subj time1 time2 time3;
resp=time1; time=1; person=7*(meth-1)+subj;output;
resp=time2; time=2; person=7*(meth-1)+subj;output;
resp=time3; time=3; person=7*(meth-1)+subj;output;

cards;
1    1 25.4 30.6 29.1
1    2 27.4 29.3 28.0
1    3 25.5 30.0 27.0
1    4 25.8 29.7 27.9
1    5 26.2 31.3 29.2
1    6 24.6 26.6 26.6
1    7 25.6 28.0 28.3
2    1 27.6 27.1 27.8
2    2 24.7 29.0 26.2
2    3 26.3 27.3 28.4
2    4 25.0 29.7 29.9
2    5 25.7 29.5 29.4
2    6 28.5 29.7 30.4
2    7 22.9 27.2 26.4
3    1 22.8 25.1 27.2
3    2 24.2 24.0 26.2
3    3 25.3 25.2 28.1
3    4 25.4 24.7 31.0
3    5 24.5 26.2 29.4
3    6 25.6 26.9 29.2
3    7 25.6 24.8 28.9
;

proc mixed;
class meth subj time;
model resp = meth time meth*time / solution;
random subj(meth);
lsmeans meth*time / diff;
```

Other Correlation Structures

```
proc mixed;
class meth subj time;
model resp = meth time meth*time;
random subj(meth);
repeated / subject=person type=un r;
```

```
lsmeans meth*time / diff;

proc mixed;
class meth subj time;
model resp = meth time meth*time;
random subj(meth);
repeated / subject=person type=cs r;
lsmeans meth*time /diff;

proc mixed;
class meth subj time;
model resp = meth time meth*time;
random subj(meth);
repeated / subject=person type=ar(1) r;
lsmeans meth*time / diff;
```

```
 Covariance Parameter
       Estimates

Cov Parm       Estimate
subj(meth)       0.8128
Residual         1.0210

        Type 3 Tests of Fixed Effects
             Num     Den
Effect        DF      DF    F Value    Pr > F
meth           2      18       4.20    0.0319
time           2      36      46.63    <.0001
meth*time      4      36      10.28    <.0001
------------------------------------------------------
  Covariance Parameter Estimates

Cov Parm       Subject    Estimate
subj(meth)                  0.8128
CS             person            0
Residual                    1.0210

        Type 3 Tests of Fixed Effects

             Num     Den
Effect        DF      DF    F Value    Pr > F
meth           2      18       4.20    0.0319
time           2      36      46.63    <.0001
meth*time      4      36      10.28    <.0001
    Estimated R Matrix for Subject 1

 Row        Col1        Col2        Col3
   1      0.7935     -0.5733     0.08675
   2     -0.5733      0.7046
   3     0.08675                  1.0784

        Type 3 Tests of Fixed Effects
```

Effect	Num DF	Den DF	F Value	Pr > F
meth	2	18	4.20	0.0319
time	2	36	50.53	<.0001
meth*time	4	36	11.56	<.0001

Estimated R Matrix for Subject 1

Row	Col1	Col2	Col3
1	0.8912	-0.2308	0.05976
2	-0.2308	0.8912	-0.2308
3	0.05976	-0.2308	0.8912

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
subj(meth)		0.9341
AR(1)	person	-0.2590
Residual		0.8912

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
meth	2	18	4.24	0.0310
time	2	36	55.44	<.0001
meth*time	4	36	9.08	<.0001