Repeated Measures

- **Two-Factor Experiments with Repeated Measures on Both Factors**

$$Y_{ijk} = \mu_{...} + \rho_i + \alpha_j + \beta_k + (\alpha\beta)_{jk} + (\rho\alpha)_{ij} + (\rho\beta)_{ik} + \epsilon_{ijk}$$

where:

1. $\mu_{...}$ is a constant.

2. $\rho_{i(j)}$ are independent $N(0, \sigma_\rho^2)$.

3. α_j are constants subject to $\sum_j \alpha_j = 0$.

4. β_k are constants subject to $\sum_k \beta_k = 0$.

5. $(\alpha\beta)_{jk}$ are constants subject to $\sum_j (\alpha\beta)_{jk} = 0$ for all k and $\sum_k (\alpha\beta)_{jk} = 0$ for all j.

6. $(\rho\beta)_{ik}$ are $N(0, \frac{b-1}{b}\sigma_{\rho\beta}^2)$ subject to $\sum_k (\rho\beta)_{ik} = 0$ for all i.

7. $(\rho\alpha)_{ij}$ are $N(0, \frac{a-1}{a}\sigma_{\rho\alpha}^2)$ subject to $\sum_j (\rho\alpha)_{ij} = 0$ for all i.

8. ρ_i, $(\rho\alpha)_{ij}$, and $(\rho\beta)_{ik}$ are pairwise independent.

9. ϵ_{ij} are independent $N(0, \sigma^2)$ and independent of ρ_i, $(\rho\alpha)_{ij}$, and $(\rho\beta)_{ik}$.

10. $i = 1, \ldots, s; j = 1, \ldots, a; k = 1, \ldots, b$

- **Example: Blood Flow.** A clinician studied the effects of two drugs used either alone or together on the blood flow in human subjects. Twelve healthy middle-aged males participated in the study and they are viewed as a random sample from a relevant population of middle-aged males. The four treatments used in the study are defined as follows

A_0B_0	Placebo (no drug)
A_0B_1	Drug B alone
A_1B_0	Drug A alone
A_1B_1	Both drugs A and B

The 12 subjects received each of the four treatments in independently randomized orders. The response variable is the increase in blood flow from before to shortly after the administration of the treatment. The treatments were administered on successive days. This wash-out period prevented any carryover effects because the effect of each drug is short-lived. The experiment was conducted in a double-blind fashion so that neither the physician nor the subjects knew which treatment was administered when the chance in blood flow was measured. The data are stored in the data file "BloodFlow.csv".

- **ANOVA Table for Two-Factor Experiment with Repeated Measures on Both Factors**

Source of Variation	DF	SS*	Mean Square	E(MS)
Subjects	$s-1$	SSS	$MSS = \frac{SSS}{a-1}$	$\sigma^2 + ab\sigma_\rho^2$
Factor A	$a-1$	SSA	$MSA = \frac{SSA}{a-1}$	$\sigma^2 + b\sigma_{\rho\alpha}^2 + bs\frac{\sum_j \alpha_j^2}{a-1}$
Factor B	$b-1$	SSB	$MSB = \frac{SSB}{b-1}$	$\sigma^2 + a\sigma_{\rho\beta}^2 + as\frac{\sum_k \beta_k^2}{b-1}$
AB interactions	$(a-1)(b-1)$	$SSAB$	$MSAB = \frac{SSAB}{(a-1)(b-1)}$	$\sigma^2 + s\frac{\sum_j \sum_k (\alpha\beta)_{jk}}{(a-1)(b-1)}$
AS interactions	$(a-1)(s-1)$	$SSAS$	$MSAS = \frac{SSAS}{(a-1)(s-1)}$	$\sigma^2 + b\sigma_{\rho\alpha}^2$
BS interactions	$(b-1)(s-1)$	$SSBS$	$MSBS = \frac{SSBS}{(b-1)(s-1)}$	$\sigma^2 + a\sigma_{\rho\beta}^2$
Error	$(a-1)(b-1)(s-1)$	SSE	$MSE = \frac{SSE}{(a-1)(b-1)(s-1)}$	σ^2
Total	$abs-1$	$SSTO$		

*The formulas for SS are listed on page 1156.

- **R commands:**

```
data=read.csv("BloodFlow.csv",header=T)
attach(data)
A=factor(drugA)
B=factor(drugB)
S=factor(subject)

result=aov(aov(flow~A*B*S))
anova(result)
Response: flow
          Df Sum Sq Mean Sq F value Pr(>F)
A          1 1587.0 1587.00
B          1 2028.0 2028.00
S         11  258.5   23.50
A:B        1  147.0  147.00
A:S       11   22.5    2.05
B:S       11   42.5    3.86
A:B:S     11   12.5    1.14
Residuals  0    0.0

F_A=1587/2.05          #F_A=MSA/MSAS=774.1463
p_value_A=1-pf(774.1463,1,11) #p_value_A=1.511502e-11

F_AB=147/1.14          #F_AB=MSAB/MSABS=128.9474

tapply(flow,A:B,mean)
 0:0  0:1  1:0  1:1
 0.5 10.0  8.5 25.0
```

- **Estimation of Contrasts.** In the Blood Flow example, we found out that there are a substantial interaction effects between the two drugs. To study the nature of the interaction effects, the clinician wished to compare the joint use of the two drugs with the use of each drug along, drug A and drug B, and each drug with no drug. That is, the following contrasts are to be estimated:

  1. $L_1 = \mu_{\cdot 11} - \mu_{\cdot 10}$

  2. $L_2 = \mu_{\cdot 11} - \mu_{\cdot 01}$

  3. $L_3 = \mu_{\cdot 10} - \mu_{\cdot 01}$

  4. $L_4 = \mu_{\cdot 10} - \mu_{\cdot 00}$

  5. $L_5 = \mu_{\cdot 01} - \mu_{\cdot 00}$