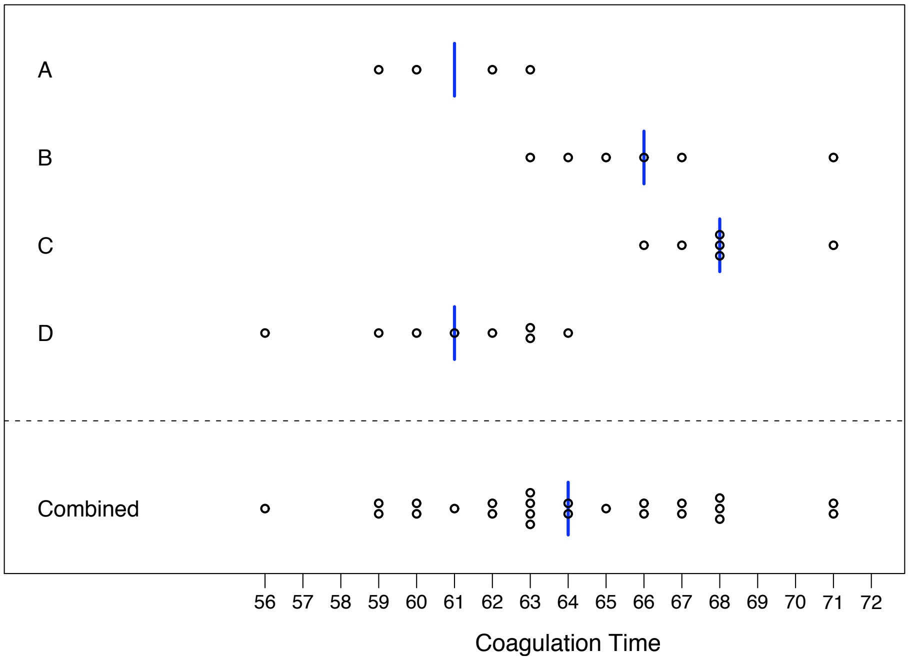
Analysis of Variance

Blood coagulation time

T		avg
A	62 60 63 59	61
B	63 67 71 64 65 66	66
C	68 66 71 67 68 68	68
D	56 62 60 61 63 64 63 59	61
		64

Blood coagulation time



Notation

Assume we have k treatment groups.

n_t	number of subjects in treatment group t
N	number of subjects (overall)
Y_{ti}	response i in treatment group t
$\bar{Y}_{t\cdot}$	average response in treatment group t
$\bar{Y}$	average response (overall)

Variance contributions

$$\sum_t \sum_i (Y_{ti} - \bar{Y})^2 = \sum_t n_t(\bar{Y}_{t\cdot} - \bar{Y})^2 + \sum_t \sum_i (Y_{ti} - \bar{Y}_{t\cdot})^2$$

$$S_T \quad = \quad S_B \quad + \quad S_W$$

$$N - 1 \quad = \quad k - 1 \quad + \quad N - k$$

Estimating the variability

We assume that the data are random samples from four normal distributions having the same variance σ^2, differing only (if at all) in their means.

We can estimate the variance σ^2 for each treatment t, using the sum of squared differences from the averages within each group.

Define, for treatment group t,

$$S_t = \sum_{i=1}^{n_t} (Y_{ti} - \bar{Y}_{t\cdot})^2.$$

Then

$$E(S_t) = (n_t - 1) \times \sigma^2.$$

Within group variability

The within-group sum of squares is the sum of all treatment sum of squares:

$$S_W = S_1 + \cdots + S_k = \sum_t \sum_i (Y_{ti} - \bar{Y}_{t\cdot})^2$$

The within-group mean square is defined as

$$M_W = \frac{S_1 + \cdots + S_k}{(n_1 - 1) + \cdots + (n_k - 1)} = \frac{S_W}{N - k} = \frac{\sum_t \sum_i (Y_{ti} - \bar{Y}_{t\cdot})^2}{N - k}$$

It is our first estimate of σ^2.

Between group variability

The between-group sum of squares is

$$S_B = \sum_{t=1}^{k} n_t (\bar{Y}_{t\cdot} - \bar{Y})^2$$

The between-group mean square is defined as

$$M_B = \frac{S_B}{k - 1} = \frac{\sum_t n_t (\bar{Y}_{t\cdot} - \bar{Y})^2}{k - 1}$$

It is our second estimate of σ^2.

That is, if there is no treatment effect!

Important facts

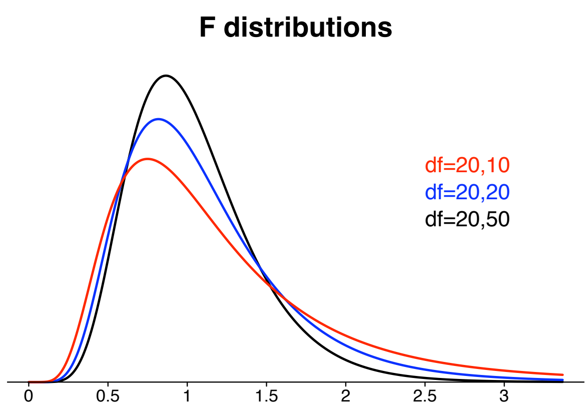
The following are facts that we will exploit later for some formal hypothesis testing:

- The distribution of S_W/σ^2 is χ^2(df=N-k)
- The distribution of S_B/σ^2 is χ^2(df=k-1)   if there is no treatment effect!
- S_W and S_B are independent

The F distribution

Let $Z_1 \sim \chi^2_m$, and $Z_2 \sim \chi^2_n$. Assume Z_1 and Z_2 are independent.

$\longrightarrow$ Then $\dfrac{Z_1/m}{Z_2/n} \sim F_{m,n}$



ANOVA table

source	sum of squares	df	mean square
between treatments	$S_B = \sum_t n_t(\bar{Y}_{t\cdot} - \bar{Y})^2$	$k - 1$	$M_B = S_B/(k - 1)$
within treatments	$S_W = \sum_t \sum_i (Y_{ti} - \bar{Y}_{t\cdot})^2$	$N - k$	$M_W = S_W/(N - k)$
total	$S_T = \sum_t \sum_i (Y_{ti} - \bar{Y})^2$	$N - 1$	

Example

source	sum of squares	df	mean square
between treatments	228	3	76.0
within treatments	112	20	5.6
total	340	23	

The ANOVA model

We write $\quad Y_{ti} = \mu_t + \epsilon_{ti} \quad$ with $\quad \epsilon_{ti} \sim$ iid N(0,σ^2).

Using $\quad \tau_t = \mu_t - \mu \quad$ we can also write

$$Y_{ti} = \mu + \tau_t + \epsilon_{ti}.$$

The corresponding analysis of the data is

$$y_{ti} = \bar{y}_{..} + (\bar{y}_{t.} - \bar{y}_{..}) + (y_{ti} - \bar{y}_{t.})$$

The ANOVA model

Three different ways to describe the model:

A. Y_{ti} independent with $Y_{ti} \sim N(\mu_t, \sigma^2)$

B. $Y_{ti} = \mu_t + \epsilon_{ti}$ where $\epsilon_{ti} \sim$ iid $N(0, \sigma^2)$

C. $Y_{ti} = \mu + \tau_t + \epsilon_{ti}$ where $\epsilon_{ti} \sim$ iid $N(0, \sigma^2)$ and $\sum_t \tau_t = 0$

Now what did we do...?

$$
\begin{pmatrix}
62 & 63 & 68 & 56 \\
60 & 67 & 66 & 62 \\
63 & 71 & 71 & 60 \\
59 & 64 & 67 & 61 \\
 & 65 & 68 & 63 \\
 & 66 & 68 & 64 \\
 & & & 63 \\
 & & & 59
\end{pmatrix}
=
\begin{pmatrix}
64 & 64 & 64 & 64 \\
64 & 64 & 64 & 64 \\
64 & 64 & 64 & 64 \\
64 & 64 & 64 & 64 \\
 & 64 & 64 & 64 \\
 & 64 & 64 & 64 \\
 & & & 64 \\
 & & & 64
\end{pmatrix}
+
\begin{pmatrix}
-3 & 2 & 4 & -3 \\
-3 & 2 & 4 & -3 \\
-3 & 2 & 4 & -3 \\
-3 & 2 & 4 & -3 \\
 & 2 & 4 & -3 \\
 & 2 & 4 & -3 \\
 & & & -3 \\
 & & & -3
\end{pmatrix}
+
\begin{pmatrix}
1 & -3 & 0 & -5 \\
-1 & 1 & -2 & 1 \\
2 & 5 & 3 & -1 \\
-2 & -2 & -1 & 0 \\
 & -1 & 0 & 2 \\
 & 0 & 0 & 3 \\
 & & & 2 \\
 & & & -2
\end{pmatrix}
$$

	observations		grand average		treatment deviations		residuals
	y_{ti}	=	$\bar{y}_{..}$	+	$\bar{y}_{t.} - \bar{y}_{..}$	+	$y_{ti} - \bar{y}_{t.}$
Vector	**Y**	=	**A**	+	**T**	+	**R**
Sum of Squares	98,644	=	98,304	+	228	+	112
D's of Freedom	24	=	1	+	3	+	20

Hypothesis testing

We assume

$$Y_{ti} = \mu + \tau_t + \epsilon_{ti} \qquad \text{with} \qquad \epsilon_{ti} \sim \text{iid } N(0,\sigma^2).$$

Equivalently, $Y_{ti} \sim$ independent $N(\mu_t, \sigma^2)$

We want to test

$$H_0 : \tau_1 = \cdots = \tau_k = 0 \qquad \text{versus} \qquad H_a : H_0 \text{ is false.}$$

Equivalently, $H_0 : \mu_1 = \ldots = \mu_k$

For this, we use a one-sided F test.

Another fact

It can be shown that

$$E(M_B) = \sigma^2 + \frac{\sum_t n_t \tau_t^2}{k - 1}$$

Therefore

$$E(M_B) = \sigma^2 \quad \text{if } H_0 \text{ is true}$$

$$E(M_B) > \sigma^2 \quad \text{if } H_0 \text{ is false}$$

Recipe for the hypothesis test

Under H_0 we have

$$\frac{M_B}{M_W} \sim F_{k-1,\, N-k}.$$

Therefore

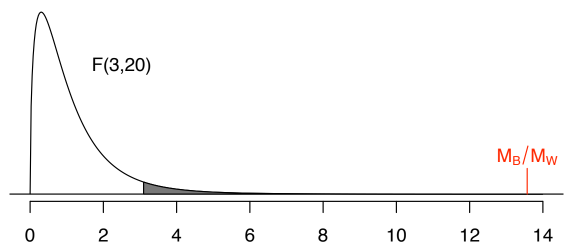
- Calculate M_B and M_W.
- Calculate M_B/M_W.
- Calculate a p-value using M_B/M_W as test statistic, using the right tail of an F distribution with $k - 1$ and $N - k$ degrees of freedom.

Example (cont)

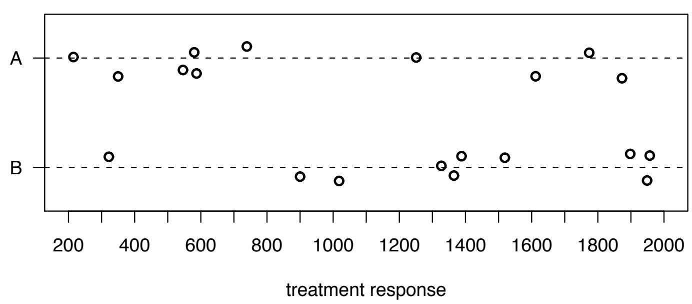
$H_0 : \tau_1 = \tau_2 = \tau_3 = \tau_4 = 0$ versus $H_a : H_0$ is false.

$M_B = 76$, $M_W = 5.6$, therefore $M_B/M_W = 13.57$.

Using an F distribution with 3 and 20 degrees of freedom, we get a pretty darn low p-value. Therefore, we reject the null hypothesis.



Another example



Are the population means the same?

By now, we know two ways of testing that:

Two-sample t-test, and ANOVA with two treatments.

$\longrightarrow$ But do they give similar results?

ANOVA table

source	sum of squares	df	mean square
between treatments	$S_B = \sum_t n_t (\bar{Y}_{t\cdot} - \bar{Y})^2$	$k - 1$	$M_B = S_B/(k-1)$
within treatments	$S_W = \sum_t \sum_i (Y_{ti} - \bar{Y}_{t\cdot})^2$	$N - k$	$M_W = S_W/(N-k)$
total	$S_T = \sum_t \sum_i (Y_{ti} - \bar{Y})^2$	$(N - 1)$	

ANOVA for two groups

The ANOVA test statistic is M_B/M_W, with

$$M_B = n_1(\bar{Y}_1 - \bar{Y})^2 + n_2(\bar{Y}_2 - \bar{Y})^2$$

and

$$M_W = \frac{\sum_{i=1}^{n_1} (Y_{1i} - \bar{Y}_1)^2 + \sum_{i=1}^{n_2} (Y_{2i} - \bar{Y}_2)^2}{n_1 + n_2 - 2}$$

Two-sample t-test

The test statistic for the two sample t-test is

$$t = \frac{\bar{Y}_1 - \bar{Y}_2}{s\sqrt{1/n_1 + 1/n_2}}$$

with

$$s^2 = \frac{\sum_{i=1}^{n_1} (Y_{1i} - \bar{Y}_1)^2 + \sum_{i=1}^{n_2} (Y_{2i} - \bar{Y}_2)^2}{n_1 + n_2 - 2}$$

This also assumes equal variance within the groups!

Reference distributions

$\longrightarrow$ Result: $\frac{M_B}{M_W} = t^2$

If there was no difference in means, then

$$\frac{M_B}{M_W} \sim F_{1,n_1+n_2-2}$$

$$t \sim t_{n_1+n_2-2}$$

Now does this mean $F_{1,n_1+n_2-2} = (t_{n_1+n_2-2})^2$?

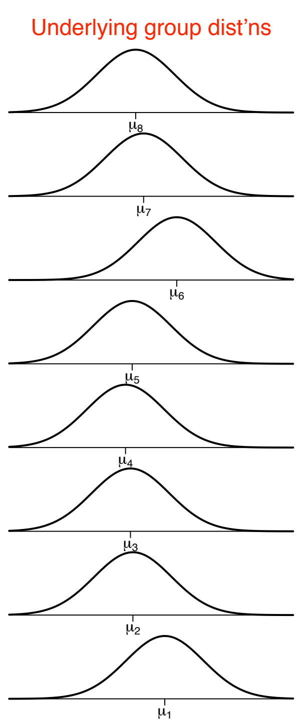
A few facts

$$F_{1,k} = t_k^2$$

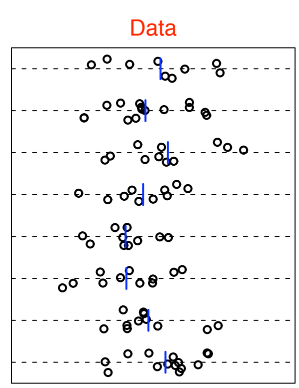
$$F_{k,\infty} = \frac{\chi_k^2}{k}$$

$$N(0,1)^2 = \chi_1^2 = F_{1,\infty} = t_\infty^2$$

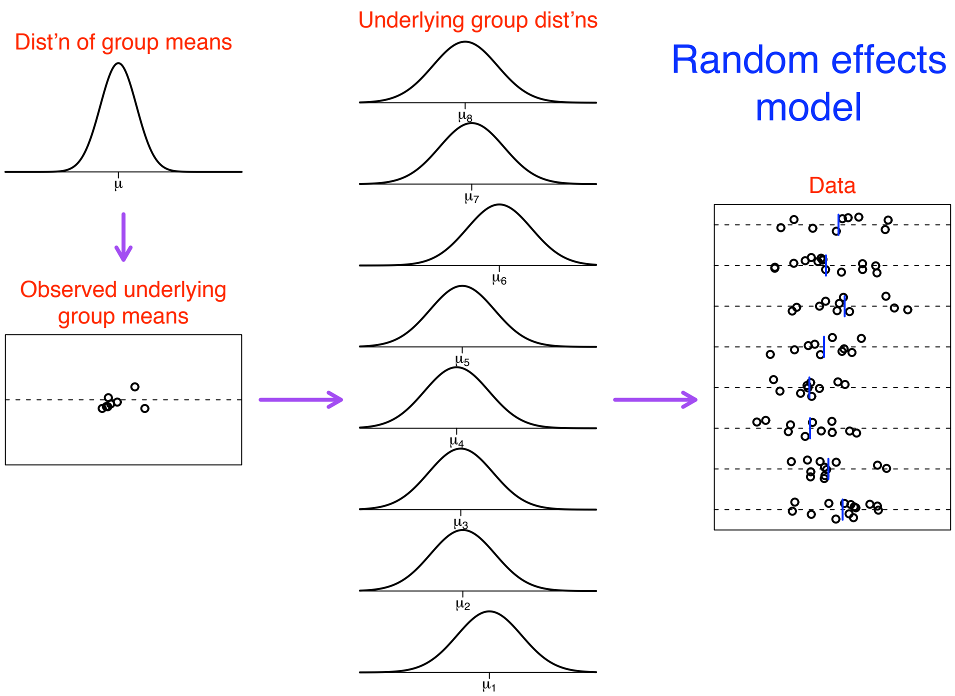
Fixed effects



Standard ANOVA model



Random effects



The random effects model

Two different ways to describe the model:

A. $\mu_t \sim$ iid $N(\mu, \sigma_A^2)$

$Y_{ti} = \mu_t + \epsilon_{ti}$ where $\epsilon_{ti} \sim$ iid $N(0, \sigma^2)$

B. $\tau_t \sim$ iid $N(0, \sigma_A^2)$

$Y_{ti} = \mu + \tau_t + \epsilon_{ti}$ where $\epsilon_{ti} \sim$ iid $N(0, \sigma^2)$

$\longrightarrow$ We add another layer of sampling.

Hypothesis testing

→ In the standard ANOVA model, we considered the μ_t as fixed but unknown quantities.

We test the hypothesis $H_0 : \mu_1 = \cdots = \mu_k$ (versus H_0 is false) using the statistic M_B/M_W from the ANOVA table and the comparing this to an $F(k-1, N-k)$ distribution.

→ In the random effects model, we consider the μ_t as random draws from a normal distribution with mean μ and variance σ_A^2.

We seek to test the hypothesis $H_0 : \sigma_A^2 = 0$ versus $H_a : \sigma_A^2 > 0$.

As it turns out, we end up with the same test statistic and same null distribution. For one-way ANOVA, that is!

Estimation

For the random effects model it can be shown that

$$E(M_B)=\sigma^2 + n_0 \times \sigma_A^2$$

where

$$n_0=\frac{1}{k-1}\left(N - \frac{\sum_t n_t^2}{\sum_t n_t}\right)$$

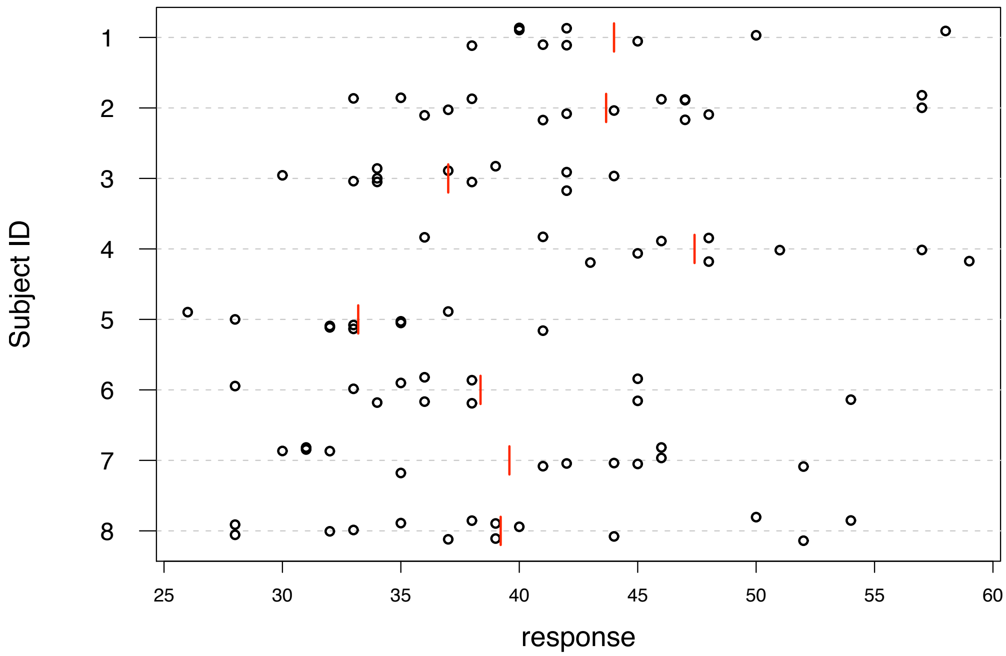
Recall also that $E(M_W) = \sigma^2$.

Thus, we may estimate σ^2 by $\hat{\sigma}^2 = M_W$.

And we may estimate σ_A^2 by $\hat{\sigma}_A^2 = (M_B - M_W)/n_0$

(provided that this is ≥ 0).

Random effects example



Random effects example

The samples sizes for the 8 subjects were (14, 12, 11, 10, 10, 11, 15, 9), for a total sample size of 92. Thus, $n_0 \approx 11.45$.

source	SS	df	MS	F	P-value
between subjects	1485	7	212	4.60	0.0002
within subjects	3873	84	46		
total	5358	91			

We have $M_B = 212$ and $M_W = 46$. Thus

$$\hat{\sigma} = \sqrt{46} = 6.8$$

$\longrightarrow$ overall sample mean = 40.3

$$\hat{\sigma}_A = \sqrt{(212 - 46)/11.45} = 3.81.$$

ANOVA assumptions

- Data in each group are a random sample from some population.
- Observations within groups are independent.
- Samples are independent.
- Underlying populations normally distributed.
- Underlying populations have the same variance.

⟶ The Kruskal-Wallis test is a non-parametric rank-based approach to assess differences in means.

⟶ In the case of two groups, the Kruskal-Wallis test reduces exactly to the Wilcoxon rank-sum test.

⟶ This is just like how ANOVA with two groups is equivalent to the two-sample t test.

Multiple comparisons

When we carry out an ANOVA on k treatments, we test

$$H_0 : \mu_1 = \cdots = \mu_k \quad \text{versus} \quad H_a : H_0 \text{ is false}$$

Assume we reject the null hypothesis, i.e. we have some evidence that not all treatment means are equal. Then we could for example be interested in which ones are the same, and which ones differ. For this, we might have to carry out some more hypothesis tests.

⟶ This procedure is referred to as multiple comparisons.

Key issue

We will be conducting, say, **T** different tests, and we become concerned about the overall error rate (sometimes called the *family-wise error rate*).

Overall error rate=Pr(reject at least one H_0 | all H_0 are true)

$$\begin{cases} =1 - \{1 - \text{Pr(reject first} \mid \text{first } H_0 \text{ is true)}\}^T & \text{if independent} \\ \leq T \times \text{Pr(reject first} \mid \text{first } H_0 \text{ is true)} & \text{generally} \end{cases}$$

Types of multiple comparisons

There are two different types of multiple comparisons procedures:

Sometimes we already know in advance what questions we want to answer. Those comparisons are called planned (or a priori) comparisons.

Sometimes we do not know in advance what questions we want to answer, and the judgement about which group means will be studied the same depends on the ANOVA outcome. Those comparisons are called unplanned (or a posteriori) comparisons.

Former example

We previously investigated whether the mean blood coagulation times for subjects receiving different treatments (A, B, C or D) were the same.

Imagine A is the standard treatment, and we wish to compare each of treatments B, C, D to treatment A.

$\longrightarrow$ planned comparisons!

After inspecting the treatment means, we find that A and D look similar, and B and C look similar, but A and D are quite different from B and C. We might want to formally test the hypothesis $\mu_A = \mu_D \neq \mu_B = \mu_C$.

$\longrightarrow$ unplanned comparisons!

Adjusting the significance level

Assume the investigator plans to make T independent significance tests, all at the significance level α'. If all the null hypothesis are true, the probability of making no Type I error is $(1 - \alpha')^T$. Hence the overall significance level is

$$\alpha = 1 - (1 - \alpha')^T$$

Solving the above equation for α' yields

$$\alpha' = 1 - (1 - \alpha)^{\frac{1}{T}}$$

The above adjustment is called the Dunn – Sidak method.

An alternative method

In the literature, investigators often use

$$\alpha'' = \frac{\alpha}{T}$$

where T is the number of planned comparisons.

This adjustment is called the Bonferroni method.

"Unplanned" comparisons

Suppose we are comparing k treatment groups.

Suppose ANOVA indicates that you reject $H_0 : \mu_1 = \cdots = \mu_k$

What next?

Which of the μ's are different from which others?

Consider testing $H_0 : \mu_i = \mu_j$ for all pairs i,j.

There are $\binom{k}{2} = \frac{k\,(k-1)}{2}$ such pairs.

k = 5 $\longrightarrow$ $\binom{k}{2} = 10.$

k = 10 $\longrightarrow$ $\binom{k}{2} = 45.$

Bonferroni correction

Suppose we have 10 treatment groups, and so 45 pairs.

If we perform 45 t-tests at the significance level α = 0.05, we would expect to reject 5% $\times$ 45 $\approx$ 2 of them, even if all of the means were the same.

Let α = Pr(reject at least one pairwise test | all μ's the same)

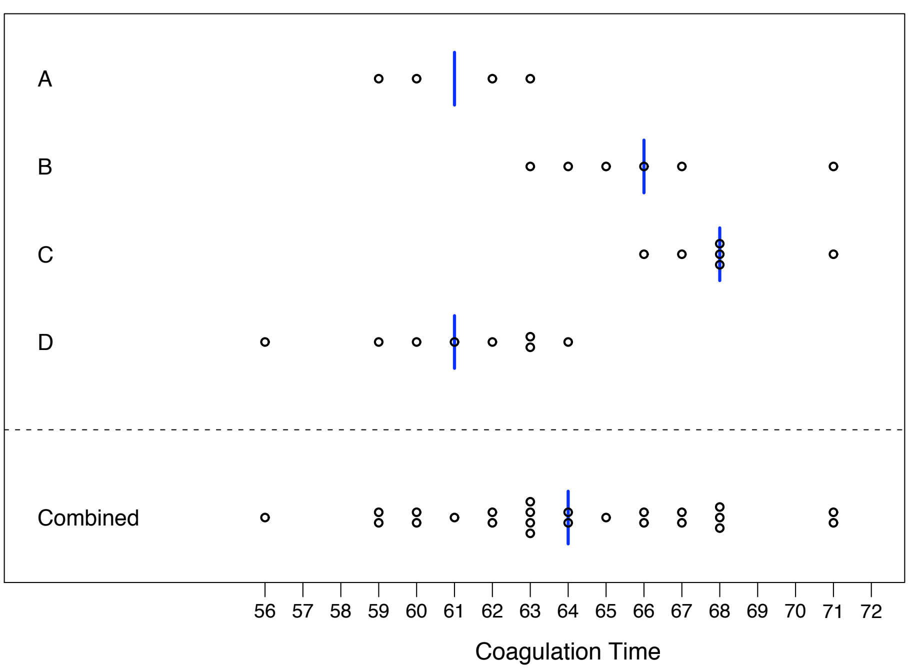
$\leq$ (no. tests) $\times$ Pr(reject test #1 | μ's the same)

The Bonferroni correction:

Use $\alpha' = \alpha/(\text{no. tests})$ as the significance level for each test.

For example, with 10 groups and so 45 pairwise tests, we would use α' = 0.05 / 45 $\approx$ 0.0011 for each test.

Blood coagulation time

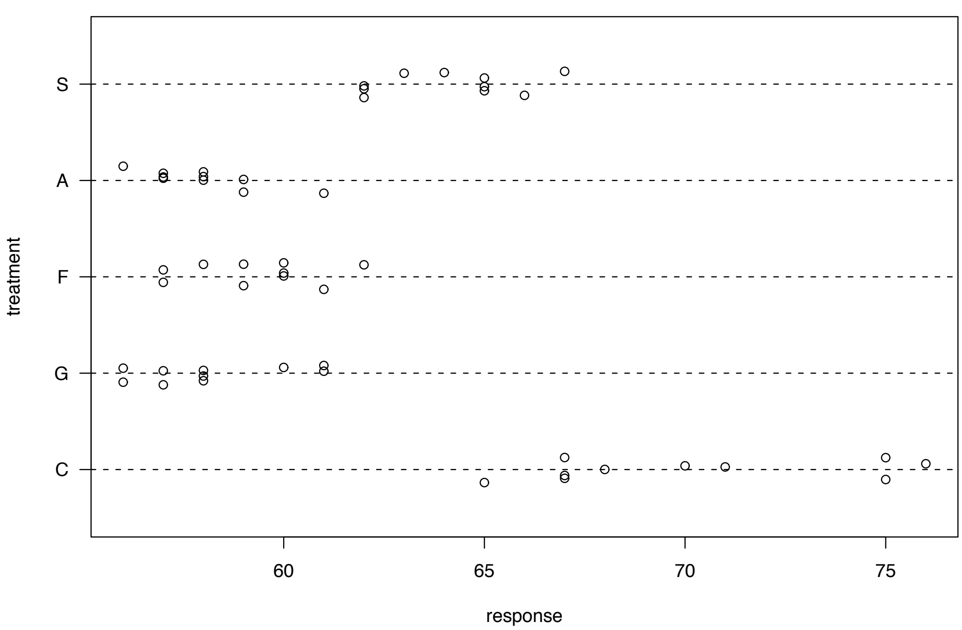


Pairwise comparisons

Comparison	p-value
A vs B	0.004
A vs C	< 0.001
A vs D	1.000
B vs C	0.159
B vs D	< 0.001
C vs D	< 0.001

$$\alpha'' = \frac{\alpha}{k} = \frac{0.05}{6} = 0.0083$$

Another example



ANOVA table

Source	SS	Df	MS	F-value	p-value
Between treatment	1077.3	4	269.3	49.4	< 0.001
Within treatment	245.5	45	5.5		

$\binom{5}{2}$ = 10 pairwise comparisons $\longrightarrow$ α' = 0.05/10 = 0.005

For each pair, consider $T_{i,j} = (\bar{Y}_{i\cdot} - \bar{Y}_{j\cdot}) \,/\, \left(\hat{\sigma}\sqrt{\frac{1}{n_i} + \frac{1}{n_j}}\right)$

Use $\hat{\sigma} = \sqrt{M_W}$ (M_W = within-group mean square)
and refer to a t distribution with df = 45.

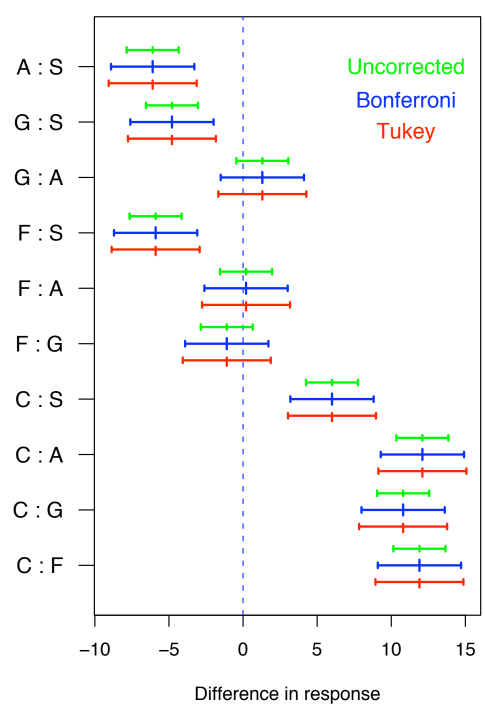
A comparison

Uncorrected:

Each interval, individually, had (in advance) a 95% chance of covering the true mean difference.

Corrected:

(In advance) there was a greater than 95% chance that all of the intervals would cover their respective parameters.



Newman-Keuls procedure

Goal: Identify sets of treatments whose mean responses are not significantly different.
(Assuming equal sample sizes for the treatment groups.)

Procedure:

1. Calculate the group sample means.
2. Order the sample means from smallest to largest.
3. Calculate a triangular table of all pairwise sample means.
4. Calculate $q_i = Q_\alpha(i, df)$ for i = 2, 3, . . . , k.
   The Q is called the studentized range distribution!
5. Calculate $R_i = q_i \times \sqrt{M_W/n}$.

Newman-Keuls procedure (continued)

Procedure:

6. If the difference between the biggest and the smallest means is less than R_k, draw a line under all of the means and stop.
7. Compare the second biggest and the smallest (and the second-smallest and the biggest) to R_{k-1}. If observed difference is smaller than the critical value, draw a line between these means.
8. Continue to look at means for which a line connecting them has not yet been drawn, comparing the difference to R_i with progressively smaller i's.

Example

Sorted sample means:

A	F	G	S	C
58.0	58.2	59.3	64.1	70.1

Table of differences:

	F	G	S	C
A	0.2	1.3	6.1	12.1
F		1.1	5.9	11.9
G			4.8	10.0
S				6.0

Example (continued)

From the ANOVA table:

$M_W = 5.46$ $\quad$ n = 10 for each group $\quad$ $\sqrt{M_W/10} = 0.739$ $\quad$ df = 45

The q_i (using df=45 and $\alpha = 0.05$):

q_2	q_3	q_4	q_5
2.85	3.43	3.77	4.02

$R_i = q_i \times \sqrt{M_W/10}$:

R_2	R_3	R_4	R_5
2.10	2.53	2.79	2.97

Example (continued)

Table of differences:

	F	G	S	C
A	0.2	1.3	6.1	12.1
F		1.1	5.9	11.9
G			4.8	10.0
S				6.0

$R_i = q_i \times \sqrt{M_W/10}$:

R_2	R_3	R_4	R_5
2.10	2.53	2.79	2.97

Results

Sorted sample means:

A	F	G	S	C
58.0	58.2	59.3	64.1	70.1

Interpretation:

$$A \approx F \approx G < S < C$$

Another example

Sorted sample means:

D	C	A	B	E
29.6	32.9	40.0	40.7	48.8

Interpretation:

$$\{\text{D, C, A, B}\} < \text{E} \qquad \text{and} \qquad \text{D} < \{\text{A, B}\}$$

Nested ANOVA: Example

We have:

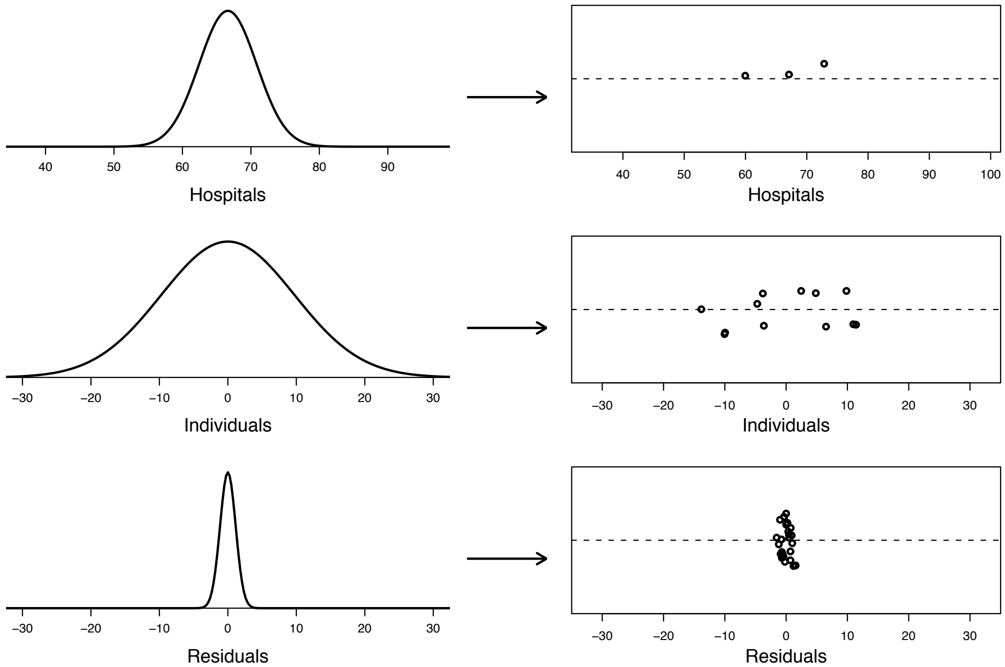
$\longrightarrow$ 3 hospitals

$\longrightarrow$ 4 subjects within each hospital

$\longrightarrow$ 2 independent measurements per subject

Hospital I				Hospital II				Hospital III			
1	2	3	4	1	2	3	4	1	2	3	4
58.5	77.8	84.0	70.1	69.8	56.0	50.7	63.8	56.6	77.8	69.9	62.1
59.5	80.9	83.6	68.3	69.8	54.5	49.3	65.8	57.5	79.2	69.2	64.5

The model



Nested ANOVA: models

$$Y_{ijk} = \mu + \alpha_i + \beta_{ij} + \epsilon_{ijk}$$

μ = overall mean

α_i = "effect" for ith hospital

β_{ij} = "effect" for jth subject within ith hospital

ϵ_{ijk} = random error

Random effects model	Mixed effects model
$\alpha_i \sim \text{Normal}(0, \sigma^2_A)$	α_i fixed; $\sum \alpha_i = 0$
$\beta_{ij} \sim \text{Normal}(0, \sigma^2_{B\mid A})$	$\beta_{ij} \sim \text{Normal}(0, \sigma^2_{B\mid A})$
$\epsilon_{ijk} \sim \text{Normal}(0, \sigma^2)$	$\epsilon_{ijk} \sim \text{Normal}(0, \sigma^2)$

Example: sample means

	Hospital I				Hospital II				Hospital III			
	1	2	3	4	1	2	3	4	1	2	3	4
	58.5	77.8	84.0	70.1	69.8	56.0	50.7	63.8	56.6	77.8	69.9	62.1
	59.5	80.9	83.6	68.3	69.8	54.5	49.3	65.8	57.5	79.2	69.2	64.5
$\bar{Y}_{ij.}$	59.00	79.35	83.80	69.20	69.80	55.25	50.00	64.80	57.05	78.50	69.55	63.30
$\bar{Y}_{i..}$	72.84				59.96				67.10			
$\bar{Y}_{...}$					66.63							

Calculations (equal sample sizes)

Source	**Sum of squares**	**df**
among groups	$SS_{among}=bn \sum_i (\bar{Y}_{i..} - \bar{Y}_{...})^2$	$a-1$
subgroups within groups	$SS_{subgr}=n \sum_i \sum_j (\bar{Y}_{ij.} - \bar{Y}_{i..})^2$	$a\,(b-1)$
within subgroups	$SS_{within}= \sum_i \sum_j \sum_k (Y_{ijk} - \bar{Y}_{ij.})^2$	$a\,b\,(n-1)$
TOTAL	$\sum_i \sum_j \sum_k (Y_{ijk} - \bar{Y}_{...})^2$	$a\,b\,n-1$

ANOVA table

SS	df	MS	F	expected MS
SS_{among}	$a - 1$	$\frac{SS_{among}}{a - 1}$	$\frac{MS_{among}}{MS_{subgr}}$	$\sigma^2 + n\,\sigma^2_{B\mid A} + n\,b\,\sigma^2_A$
SS_{subgr}	$a\,(b - 1)$	$\frac{SS_{subgr}}{a(b - 1)}$	$\frac{MS_{subgr}}{MS_{within}}$	$\sigma^2 + n\,\sigma^2_{B\mid A}$
SS_{within}	$a\,b\,(n - 1)$	$\frac{SS_{within}}{ab(n - 1)}$		σ^2
SS_{total}	$a\,b\,n - 1$			

Example

source	df	SS	MS	F	P-value
among groups	2	665.68	332.84	1.74	0.23
among subgroups within groups	9	1720.68	191.19	146.88	< 0.001
within subgroups	12	15.62	1.30		
TOTAL	23	2401.97			

Variance components

Within subgroups (error; between measurements on each subject)

$s^2 = MS_{within} = 1.30$ $\qquad s = \sqrt{1.30} = 1.14$

Among subgroups within groups (among subjects within hospitals)

$$s^2_{B|A} = \frac{MS_{subgr} - MS_{within}}{n} = \frac{191.19 - 1.30}{2} = 94.94 \qquad s_{B|A} = \sqrt{94.94} = 9.74$$

Among groups (among hospitals)

$$s^2_{A} = \frac{MS_{among} - MS_{subgr}}{nb} = \frac{332.84 - 191.19}{8} = 17.71 \qquad s_{A} = \sqrt{17.71} = 4.21$$

Variance components (2)

$s^2 + s^2_{B|A} + s^2_A = 1.30 + 94.94 + 17.71 = 113.95.$

$$\begin{array}{lll} s^2 & \text{represents } \dfrac{1.30}{113.95} & = \ 1.1\% \\ s^2_{B|A} & \text{represents } \dfrac{94.94}{113.95} & = \ 83.3\% \\ s^2_{A} & \text{represents } \dfrac{17.71}{113.95} & = \ 15.6\% \end{array}$$

Note:

$\longrightarrow$ $\text{var}(Y) = \sigma^2 + \sigma^2_{B|A} + \sigma^2_A$

$\longrightarrow$ $\text{var}(Y \mid A) = \sigma^2 + \sigma^2_{B|A}$

$\longrightarrow$ $\text{var}(Y \mid A, B) = \sigma^2$

Subject averages

	I-1	I-2	I-3	I-4	II-1	II-2	II-3	II-4	III-1	III-2	III-3	III-4
	58.5	77.8	84.0	70.1	69.8	56.0	50.7	63.8	56.6	77.8	69.9	62.1
	59.5	80.9	83.6	68.3	69.8	54.5	49.3	65.8	57.5	79.2	69.2	64.5
ave	59.0	79.4	83.8	69.2	69.8	55.2	50.0	64.8	57.0	78.5	69.6	63.3

ANOVA table

source	df	SS	MS	F	P-value
between	2	332.8	166.4	1.74	0.23
within	9	860.3	95.6		

Higher-level nested ANOVA models

You can have as many levels as you like. For example, here is a three-level nested mixed ANOVA model:

$$Y_{ijkl} = \mu + \alpha_i + B_{ij} + C_{ijk} + \epsilon_{ijkl}$$

Assumptions: $B_{ij} \sim N(0, \sigma^2_{B|A})$, $C_{ijk} \sim N(0, \sigma^2_{C|B})$, $\epsilon_{ijkl} \sim N(0, \sigma^2)$.

Calculations

Source	Sum of squares	df
among groups	$SS_{among} = b\,c\,n \sum_i (\bar{Y}_{i...} - \bar{Y}_{....})^2$	$a - 1$
among subgroups	$SS_{subgr} = c\,n \sum_i \sum_j (\bar{Y}_{ij..} - \bar{Y}_{i...})^2$	$a\,(b - 1)$
among subsubgroups	$SS_{subsubgr} = n \sum_i \sum_j \sum_k (\bar{Y}_{ijk.} - \bar{Y}_{ij..})^2$	$a\,b\,(c - 1)$
within subsubgroups	$SS_{subsubgr} = \sum_i \sum_j \sum_k \sum_l (Y_{ijkl} - \bar{Y}_{ijk.})^2$	$a\,b\,c\,(n - 1)$

ANOVA table

SS	MS	F	expected MS
SS_{among}	$\frac{bcn \sum_a (\bar{Y}_A - \bar{Y})^2}{a - 1}$	$\frac{MS_{among}}{MS_{subgr}}$	$\sigma^2 + n\sigma^2_{C \subset B} + nc\sigma^2_{B \subset A} + ncb\frac{\sum \alpha^2}{a - 1}$
SS_{subgr}	$\frac{cn \sum_a \sum_b (\bar{Y}_B - \bar{Y}_A)^2}{a(b - 1)}$	$\frac{MS_{subgr}}{MS_{subsubgr}}$	$\sigma^2 + n\sigma^2_{C \subset B} + nc\sigma^2_{B \subset A}$
$SS_{subsubgr}$	$\frac{n \sum_a \sum_b \sum_c (\bar{Y}_C - \bar{Y}_B)^2}{ab(c - 1)}$	$\frac{MS_{subsubgr}}{MS_{within}}$	$\sigma^2 + n\sigma^2_{C \subset B}$
SS_{within}	$\frac{\sum_a \sum_b \sum_c \sum_n (Y - \bar{Y}_C)^2}{abc(n - 1)}$		σ^2

Unequal sample size

It is best to design your studies such that you have equal sample sizes in each cell. However, once in a while this is not possible.

In the case of unequal sample sizes, the calculations become really painful (though a computer can do all of the calculations for you).

Even worse, the F tests for the upper levels in the ANOVA table no longer have a clear null distribution.

$\longrightarrow$ Maximum likelihood methods are more complicated, but can solve this problem.

Two-way ANOVA

	Treatment	
Gender	1	2
Male	709	592
	679	538
	699	476
Female	657	508
	594	505
	677	539

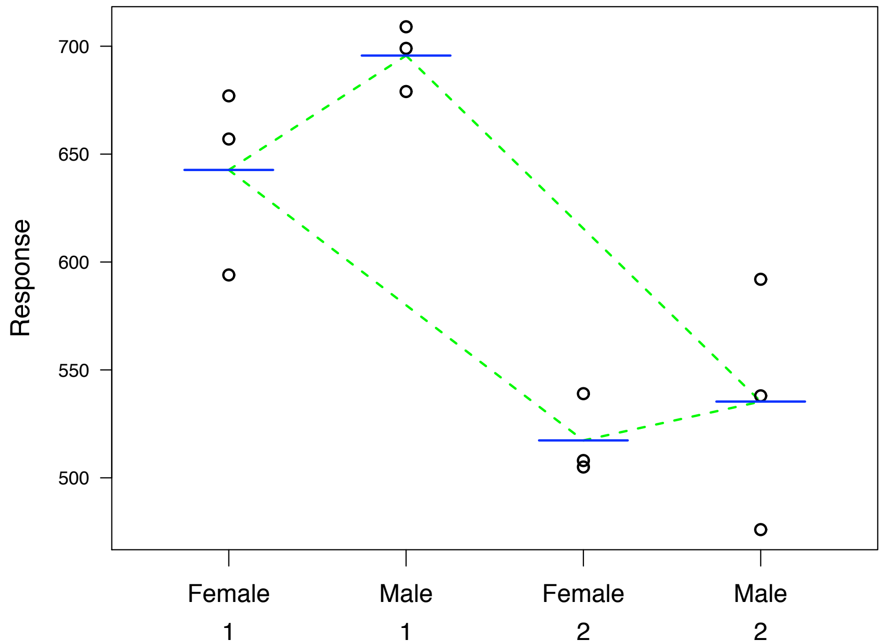
Let

r be the number of rows in the two-way ANOVA,

c be the number of columns in the two-way ANOVA,

n be the number of observations within each of those $r \times c$ groups.

A picture



All sorts of means

	Treatment		
Gender	1	2	
Male	695.67	535.33	615.50
Female	642.67	517.33	580.00
	669.17	526.33	597.75

⟶ This table shows the cell, row, and column means, plus the overall mean.

Two-way ANOVA table

source	sum of squares	df
between rows	$SS_{rows} = c\,n \sum_i (\bar{Y}_{i..} - \bar{Y}_{...})^2$	$r - 1$
between columns	$SS_{columns} = r\,n \sum_j (\bar{Y}_{.j.} - \bar{Y}_{...})^2$	$c - 1$
interaction	$SS_{interaction}$	$(r - 1)(c - 1)$
error	$SS_{within} = \sum_i \sum_j \sum_k (Y_{ijk} - \bar{Y}_{ij.})^2$	$rc(n - 1)$
total	$SS_{total} = \sum_i \sum_j \sum_k (Y_{ijk} - \bar{Y}_{...})^2$	$rcn - 1$

Example

source	sum of squares	df	mean squares
sex	3781	1	3781
treatment	61204	1	61204
interaction	919	1	919
error	11667	8	1458

The ANOVA model

Let Y_{ijk} be the k^{th} item in the subgroup representing the i^{th} group of factor A (r levels) and the j^{th} group of factor B (c levels). We write

$$Y_{ijk} = \mu + \alpha_i + \beta_j + \gamma_{ij} + \epsilon_{ijk}$$

The corresponding analysis of the data is

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

Towards hypothesis testing

source	mean squares	expected mean squares
between rows	$\frac{c\,n \sum_i (\bar{Y}_{i..} - \bar{Y}_{...})^2}{r-1}$	$\sigma^2 + \frac{c\,n}{r-1} \sum_i \alpha_i^2$
between columns	$\frac{r\,n \sum_j (\bar{Y}_{.j.} - \bar{Y}_{...})^2}{c-1}$	$\sigma^2 + \frac{r\,n}{c-1} \sum_j \beta_j^2$
interaction	$\frac{n \sum_i \sum_j (\bar{Y}_{ij.} - \bar{Y}_{i..} - \bar{Y}_{.j.} + \bar{Y}_{...})^2}{(r-1)(c-1)}$	$\sigma^2 + \frac{n}{(r-1)(c-1)} \sum_i \sum_j \gamma_{ij}^2$
error	$\frac{\sum_i \sum_j \sum_k (Y_{ijk} - \bar{Y}_{ij.})^2}{r\,c\,(n-1)}$	σ^2

This is for fixed effects, and equal number of observations per cell!

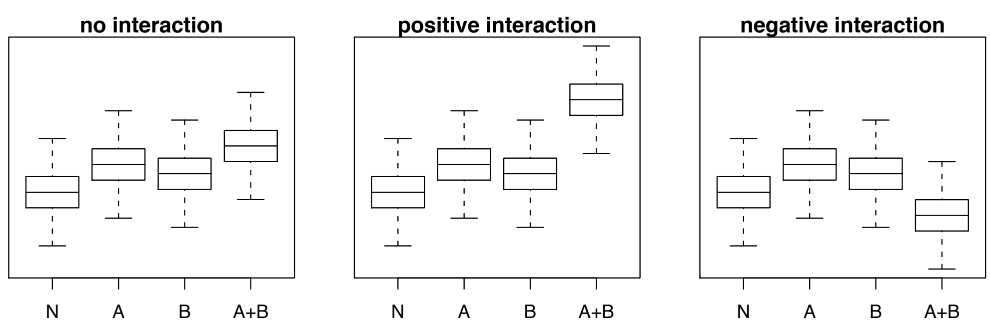
Example (continued)

source	SS	df	MS	F	p-value
sex	3781	1	3781	2.6	0.1460
treatment	61204	1	61204	42.0	0.0002
interaction	919	1	919	0.6	0.4503
error	11667	8	1458		

Interaction in a 2-way ANOVA model

Let Y_{ijk} be the k^{th} item in the subgroup representing the i^{th} group of factor A (r levels) and the j^{th} group of factor B (c levels). We write

$$Y_{ijk} = \mu + \alpha_i + \beta_j + \gamma_{ij} + \epsilon_{ijk}$$



Expected mean squares

source	fixed effects	random effects	mixed effects
between rows	$\sigma^2 + \frac{c\,n}{r-1}\sum_i \alpha_i^2$	$\sigma^2 + n\,\sigma^2_{R\times C} + c\,n\,\sigma^2_R$	$\sigma^2 + n\,\sigma^2_{R\times C} + \frac{c\,n}{r-1}\sum_i \alpha_i^2$
between columns	$\sigma^2 + \frac{r\,n}{c-1}\sum_j \beta_j^2$	$\sigma^2 + n\,\sigma^2_{R\times C} + r\,n\,\sigma^2_C$	$\sigma^2 \quad + r\,n\,\sigma^2_C$
interaction	$\sigma^2 + \frac{n}{(r-1)(c-1)}\sum_i\sum_j \gamma_{ij}^2$	$\sigma^2 + n\,\sigma^2_{R\times C}$	$\sigma^2 + n\,\sigma^2_{R\times C}$
error	σ^2	σ^2	σ^2

Two-way ANOVA without replicates

	Physician		
Concentration	A	B	C
60	9.6	9.3	9.3
80	10.6	9.1	9.2
160	9.8	9.3	9.5
320	10.7	9.1	10.0
640	11.1	11.1	10.4
1280	10.9	11.8	10.8
2560	12.8	10.6	10.7

ANOVA table

source	**df**	**SS**	**MS**
physician	2	2.79	1.39
concentration	6	12.54	2.09
interaction	12	4.11	0.34
total	20		

We have 21 observations. That means we have no degrees of freedom left to estimate an error!

Expected mean squares

In general, we have:

source	fixed effects	random effects	mixed effects
between rows	$\sigma^2 + \frac{c\,n}{r-1}\sum_i \alpha_i^2$	$\sigma^2 + n\,\sigma^2_{R\times C} + c\,n\,\sigma^2_R$	$\sigma^2 + n\,\sigma^2_{R\times C} + \frac{c\,n}{r-1}\sum_i \alpha_i^2$
between columns	$\sigma^2 + \frac{r\,n}{c-1}\sum_j \beta_j^2$	$\sigma^2 + n\,\sigma^2_{R\times C} + r\,n\,\sigma^2_C$	$\sigma^2 \qquad + r\,n\,\sigma^2_C$
interaction	$\sigma^2 + \frac{n}{(r-1)(c-1)}\sum_i\sum_j \gamma_{ij}^2$	$\sigma^2 + n\,\sigma^2_{R\times C}$	$\sigma^2 + n\,\sigma^2_{R\times C}$
error	σ^2	σ^2	σ^2

Expected mean squares

If n=1 and there is no interaction in truth, we have:

source	fixed effects	random effects	mixed effects
between rows	$\sigma^2 + \frac{c}{r-1}\sum_i \alpha_i^2$	$\sigma^2 + c\,\sigma_R^2$	$\sigma^2 + \frac{c}{r-1}\sum_i \alpha_i^2$
between columns	$\sigma^2 + \frac{r}{c-1}\sum_j \beta_j^2$	$\sigma^2 + r\,\sigma_C^2$	$\sigma^2 + r\,\sigma_C^2$
error	σ^2	σ^2	σ^2

Expected mean squares

If n=1 but there is an interaction, we have:

source	fixed effects	random effects	mixed effects
between rows	$\sigma^2 + \frac{c}{r-1}\sum_i \alpha_i^2$	$\sigma^2 + \sigma_{R\times C}^2 + c\,\sigma_R^2$	$\sigma^2 + \sigma_{R\times C}^2 + \frac{c}{r-1}\sum_i \alpha_i^2$
between columns	$\sigma^2 + \frac{r}{c-1}\sum_j \beta_j^2$	$\sigma^2 + \sigma_{R\times C}^2 + r\,\sigma_C^2$	$\sigma^2 \qquad + r\,\sigma_C^2$
interaction	$\sigma^2 + \frac{1}{(r-1)(c-1)}\sum_i\sum_j \gamma_{ij}^2$	$\sigma^2 + \sigma_{R\times C}^2$	$\sigma^2 + \sigma_{R\times C}^2$
error	σ^2	σ^2	σ^2