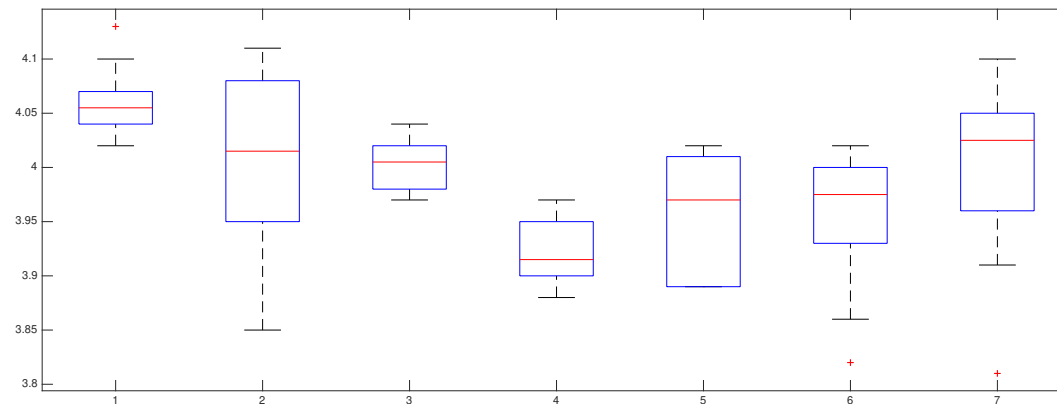


## Slides 12: ANOVA one-way layout

- Normal theory model
- Maximum likelihood estimates
- F-tests
- Simultaneous confidence interval
- Bonferroni and Tukey



## Normal theory model

Suppose the expectation of the response variable is a function of a single main factor having  $I$  different levels so that

$$Y(i) = \mu_i + \epsilon, \quad \epsilon \sim N(0, \sigma), \quad i = 1, \dots, I.$$

We will use a representation  $\mu_i = \mu + \alpha_i$ , where  $\alpha_1 + \dots + \alpha_I = 0$ ,

$\mu = \frac{\mu_1 + \dots + \mu_I}{I}$  is the overall mean

$\alpha_i = \mu_i - \mu$  is the effect of the main factor at the level  $i$

Given  $I$  independent random samples of the same size  $n$

$$(y_{i1}, \dots, y_{in}), \quad i = 1, \dots, I$$

we want to develop a test of

$$H_0 : \mu_1 = \dots = \mu_I, \text{ against } H_1 : \mu_u \neq \mu_v \text{ for some } (u, v).$$

In terms of  $I$  different treatments in a comparison study, this null hypothesis claims that the compared treatments have the same effect .

## Example: seven labs

Data: each of  $I = 7$  labs made  $n = 10$  measurements of chlorpheniramine maleate in tablets with a nominal dosage of 4 mg. See seven boxplots on the first slide.

Lab 1	Lab 2	Lab 3	Lab 4	Lab 5	Lab 6	Lab 7
4.13	3.86	4.00	3.88	4.02	4.02	4.00
4.07	3.85	4.02	3.88	3.95	3.86	4.02
4.04	4.08	4.01	3.91	4.02	3.96	4.03
4.07	4.11	4.01	3.95	3.89	3.97	4.04
4.05	4.08	4.04	3.92	3.91	4.00	4.10
4.04	4.01	3.99	3.97	4.01	3.82	3.81
4.02	4.02	4.03	3.92	3.89	3.98	3.91
4.06	4.04	3.97	3.9	3.89	3.99	3.96
4.10	3.97	3.98	3.97	3.99	4.02	4.05
4.04	3.95	3.98	3.90	4.00	3.93	4.06

Ordered means

Lab $i$	1	3	7	2	5	6	4
Mean $\hat{\mu}_i$	4.062	4.003	3.998	3.997	3.957	3.955	3.920

**Question.** Are the observed differences between sample means statistically significant?

## Maximum likelihood estimates

With  $N = I \cdot n$  independent random variables

$$Y_{ik} = \mu + \alpha_i + \epsilon_{ik}, \quad \epsilon_{ik} \sim N(0, \sigma),$$

the maximum likelihood approach gives the following point estimates

$$\hat{\mu} = \bar{y}_{..}, \quad \hat{\mu}_i = \bar{y}_{i.}, \quad \hat{\alpha}_i = \bar{y}_{i.} - \bar{y}_{..},$$

expressed in terms of the sample means

$$\bar{y}_{i.} = \frac{1}{n} \sum_k y_{ik}, \quad \bar{y}_{..} = \frac{1}{I} \sum_i \bar{y}_{i.} = \frac{1}{N} \sum_i \sum_k y_{ik}.$$

The observed responses can be represented as

$$y_{ik} = \hat{\mu} + \hat{\alpha}_i + \hat{\epsilon}_{ik}, \quad \hat{\epsilon}_{ik} = y_{ik} - \bar{y}_{i.},$$

where  $\hat{\epsilon}_{ik}$  are the so-called residuals.

**Question.** What is the sum of all  $\hat{\alpha}_i$ ? What is the total sum of residuals?

## Sums of squares

The ANOVA tests are built around the following observation:

$$\text{Decomposition of the total sum of squares: } SS_T = SS_A + SS_E$$

saying that the total variation in response values is the sum of the between-group variation and the within-group variation.

$SS_T = \sum_i \sum_k (y_{ik} - \bar{y}_{..})^2$  is the total sum of squares,

$SS_A = n \sum_i \hat{\alpha}_i^2$  is the factor A sum of squares,  $df_A = I - 1$ ,

$SS_E = \sum_i \sum_k \hat{\epsilon}_{ik}^2$  is the error sum of squares,  $df_E = I \cdot (n - 1)$ .

Define two mean squares

$$MS_A = \frac{SS_A}{df_A}, \quad MS_E = \frac{SS_E}{df_E}.$$

where  $df_A = I - 1$  is the number of degrees of freedom in  $SS_A$ , and  $df_E = I \cdot (n - 1)$  is the number of degrees of freedom in  $SS_E$ .

**Question.** What is the number of degrees of freedom  $df_T$  in  $SS_T$ ?

If treated as random variables, the mean squares lead the following formulas for the expected values

$$E(MS_A) = \sigma^2 + \frac{n}{I-1} \sum_i \alpha_i^2, \quad E(MS_E) = \sigma^2,$$

which suggest looking for the ratio between the two mean squares

$$F = \frac{MS_A}{MS_E}$$

to find an evidence against the null hypothesis

$$H_0 : \alpha_1 = \dots = \alpha_I = 0.$$

F-test: reject  $H_0$  for large values of  $F$  based on the null distribution

$$F \stackrel{H_0}{\sim} F_{n_1, n_2}, \text{ where } n_1 = I - 1, \ n_2 = I(n - 1).$$

$F_{n_1, n_2}$  is called F-distribution with degrees of freedom  $(n_1, n_2)$ .

It is the distribution for the ratio  $\frac{X_1/n_1}{X_2/n_2} \sim F_{n_1, n_2}$ ,

where  $X_1 \sim \chi_{n_1}^2$  and  $X_2 \sim \chi_{n_2}^2$  are independent random variables.

## ANOVA 1 table

The pooled sample variance is an unbiased estimate of  $\sigma^2$ .

$$s_p^2 = MS_E = \frac{1}{I} \sum_{i=1}^I \left( \frac{1}{n-1} \sum_{k=1}^n (y_{ik} - \bar{y}_{i.})^2 \right)$$

### Example: seven labs

The normal probability plot of residuals  $\hat{\epsilon}_{ik}$  supports the normality assumption. Noise size  $\sigma$  is estimated by  $s_p = \sqrt{0.0037} = 0.061$ . One-way Anova table

Source	df	SS	MS	F	P
Labs	6	.125	.0210	5.66	.0001
Error	63	.231	.0037		
Total	69	.356			

Conclusion: the largest pairwise difference (1 – 4) is significant.

**Question.** Which of the  $\binom{7}{2} = 21$  pairwise differences are significant?

## The multiple comparison problem

A naive approach to find significant pairwise differences is to apply a 95% confidence interval for two independent samples  $(u, v)$

$$I_{\mu_u - \mu_v} = (\bar{y}_{u.} - \bar{y}_{v.}) \pm t_{63}(0.025) \cdot \frac{s_p}{\sqrt{5}} = (\bar{y}_{u.} - \bar{y}_{v.}) \pm 0.055,$$

where  $t_{63}(0.025) = 2.00$ .

This confidence interval formula detects 9 significant differences:

$u-v$	1-4	1-6	1-5	3-4	7-4	2-4	1-2	1-7	1-3
$\hat{\mu}_u - \hat{\mu}_v$	0.142	0.107	0.105	0.083	0.078	0.077	0.065	0.064	0.059

For all other pairs,  $|\hat{\mu}_u - \hat{\mu}_v| < 0.055$  and zero is covered by  $I_{\mu_u - \mu_v}$ .

However, there exists the so called multiple comparison problem.

The above confidence interval formula is aimed at a single difference, and may produce false discoveries. What we need instead, is a simultaneous confidence interval formula taking care of all  $c = 21$  pairwise comparisons.

**Question.** Why do we use  $df = 63$  for the pairwise confidence interval  $I_{\mu_u - \mu_v}$ ?



## Bonferroni's method

Think of a statistical test repeatedly applied to  $c$  independent samples of size  $n$ . The overall result is positive if we get at least one positive result among these  $c$  tests.

Bonferroni's correction: to ensure the overall significance level  $\alpha$ , each single test is performed at significance level  $\alpha_c = \frac{\alpha}{c}$ .

Indeed, assuming  $H_0$  is true, the number of positive results among  $c$  tests is  $X \sim \text{Bin}(c, \alpha_c)$ . Thus for small values of  $\alpha_c$ ,

$$P(X \geq 1|H_0) = 1 - (1 - \alpha_c)^c \approx c\alpha_c = \alpha.$$

Bonferroni's  $100(1 - \alpha)\%$  simultaneous confidence interval for  $c = \binom{I}{2}$  pairwise differences

$$B_{\mu_u - \mu_v} = \bar{y}_{u.} - \bar{y}_{v.} \pm t_{\text{df}}\left(\frac{\alpha_c}{2}\right) \cdot s_p \sqrt{\frac{2}{n}}, \quad 1 \leq u < v \leq I.$$

where  $\text{df} = I(n - 1)$  and  $\alpha_c = \frac{2\alpha}{I(I-1)}$ .

**Question.** Are pairwise differences  $\mu_u - \mu_v$  independent ?

## Studentised range distribution

Pairwise differences  $\delta_{u,v} = \mu_u - \mu_v$  are not independent. For example

$$\delta_{1,2} + \delta_{2,3} = \delta_{1,3}$$

To take account of linear dependence between  $\delta_{u,v}$ , consider

$$Z_i = \bar{Y}_{i.} - \mu_i \sim N(0, \frac{\sigma}{\sqrt{n}}), \quad i = 1, \dots, I$$

independent and identically distributed random variables. The range

$$R = \max\{Z_1, \dots, Z_I\} - \min\{Z_1, \dots, Z_I\}$$

gives the largest pairwise difference between the components of the vector  $(Z_1, \dots, Z_I)$ . The corresponding normalised range has a distribution that is free from the parameter  $\sigma$

$$\frac{R}{S_p/\sqrt{n}} \sim \text{SR}(I, \text{df}), \quad \text{df} = I(n-1).$$

The so-called studentised range distribution SR has two parameters: the number of samples and the number of df used in the variance estimate  $s_p^2$ .

## Tukey's method

Tukey's  $100(1 - \alpha)\%$  simultaneous confidence interval is built using an appropriate quantile  $q_{I,df}(\alpha)$  of the studentised range distribution

$$T_{\mu_u - \mu_v} = \bar{y}_{u.} - \bar{y}_{v.} \pm q_{I,df}(\alpha) \cdot \frac{s_p}{\sqrt{n}}$$

Bonferroni method gives slightly wider intervals compared to the Tukey method.

### Example: seven labs

Bonferroni's 95% (using  $t_{63}(0.0012) = 3.17$ )

$$B_{\mu_u - \mu_v} = (\bar{y}_{u.} - \bar{y}_{v.}) \pm t_{63}(\frac{.025}{21}) \cdot \frac{s_p}{\sqrt{5}} = (\bar{y}_{u.} - \bar{y}_{v.}) \pm 0.086,$$

detects 3 significant differences between labs (1,4), (1,5), (1,6).

Tukey's 95%

$$T_{\mu_u - \mu_v} = \bar{y}_{u.} - \bar{y}_{v.} \pm q_{7,63}(0.05) \cdot \frac{0.061}{\sqrt{10}} = \bar{y}_{u.} - \bar{y}_{v.} \pm 0.083,$$

brings four significant pairwise differences: (1,4), (1,5), (1,6), (3,4).