ST4241: Design and Analysis of Clinical Trials

2009/2010: Semester I

Tutorial 4

1. In the table below, each block represents a different subject, the units within blocks are four blood samples from each subject, and four treatments were randomly assigned to the blood samples within each set. The values are the clotting times of plasm, in minutes.

	Treatment				
Subject	1	2	3	4	Mean
1	8.4	9.4	9.8	12.2	9.950
2	12.8	15.2	12.9	14.4	13.825
3	9.6	9.1	11.2	9.8	9.925
4	9.8	8.8	9.9	12.0	10.125
5	8.4	8.2	8.5	8.5	8.400
6	8.6	9.9	9.8	10.9	9.800
7	8.9	9.0	9.2	10.4	9.375
8	7.9	8.1	8.2	10.0	8.550
Mean	9.300	9.713	9.938	11.025	9.994
sd	1.550	2.294	1.514	1.815	

(i) Suppose we are only interested in investigating the following three differences: (a) $\mu_1 - \mu_4$, (b) $\mu_2 - \mu_4$ and (c) $\mu_3 - \mu_4$, where μ_j is the mean effect of treatment j. Test the significance of these differences at level 0.05 by using an appropriate multiple comparison criterion.

(ii) Give the critical values controlling the overall error rate at 0.05 of Scheff's, Tukey's, Dunnett's and Bonferroni's criterion respectively.

(iii) Test the three differences in part (i) using each of the criteria in part (ii). Comment on the results.

2. The following is the results of a factorial study:

Block	Preparation 1		Preparation 2	
	Dose A	Dose B	Dose A	Dose B
1	3.0	5.5	5.0	6.0
2	2.0	4.0	4.5	5.5
3	2.5	5.0	4.0	5.0
4	3.0	4.5	4.5	6.0
5	3.0	4.0	2.5	5.5
6	3.5	4.5	4.5	5.5

(i) Complete the following table:

Source of variation	df	SS
Preparations		
Doses		
Interaction		
Blocks		
Residual		

(ii) Test whether the interaction effect is significant at level 0.05. If not, test the significance of the effects of the two factors: preparation and dose.

3. The following concerns the nonparametric tests for CRBD data.

(i) Prove that the numerator of the Signed rank test statistic Z is equal to

$$\frac{n_+ n_-}{n.}(\bar{R}_+ - \bar{R}_-) + \frac{(n. + 1)(n_+ - n_-)}{4}.$$

The statistic Z is given by

$$Z = \frac{R_+ - \frac{n.(n.+1)}{4}}{\sqrt{\frac{n.(n.+1)(2n.+1)f}{24}}},$$

where f is the factor for adjusting ties.

(ii) Prove that, when $g = 2$, the Friedman's test statistic is equal to

$$\chi^2 = \frac{(n_+ - n_-)^2}{n.}.$$

4. The following table is the layout of the data from a complete random blocks design:

	Treatment					
Block	1	$\cdots$	j	$\cdots$	g	Mean
1	X_{11}	$\cdots$	X_{1j}	$\cdots$	X_{1g}	$\bar{X}_{1\cdot}$
$\vdots$						
i	X_{i1}	$\cdots$	X_{ij}	$\cdots$	X_{ig}	$\bar{X}_{i\cdot}$
$\vdots$						
n	X_{n1}	$\cdots$	X_{nj}	$\cdots$	X_{ng}	$\bar{X}_{n\cdot}$
Mean	$X_{\cdot 1}$	$\cdots$	$X_{\cdot j}$	$\cdots$	$X_{\cdot g}$	$X_{\cdot\cdot}$
sd	s_1	$\cdots$	s_j	$\cdots$	s_g	

A linear model for the data is as follows:

$$X_{ij} = \mu_j + b_i + \epsilon_{ij},$$

where μ_j is the underlying mean response to Treatment j, b_i is the effect on the response due to the particular characteristics of the experimental units constituting Block i, and ϵ_{ij} is a random variable representing chance measurement errors and other random perturbations in the data. Assume that b_i's are random variables with mean zero and variance σ_b^2 and are independent of ϵ_{ij}'s.

(i) Prove that the expected value of the mean square for blocks is $\sigma_\epsilon^2 + g\sigma_b^2$.

(ii) Prove that the expected value of the residual mean squares is σ_ϵ^2.

Note: for those who are required to submit the assignment, please submit the solutions to Question 1 and 3 only.