

Exercise 25: Repeated measurements

Five persons were tested on two different drugs A and B. After taking the drug each person was followed for six hours and the antibiotic serum level was recorded after 1, 2, 3, and 6 hours. Assume that there is no carry-over effect from one drug to another. The data are given below.

Subject	Drug A				Drug B			
	Time (hours)				Time (hours)			
	1	2	3	6	1	2	3	6
1	1.08	1.99	1.46	1.21	1.48	2.50	2.62	1.95
2	1.19	2.10	1.21	0.96	0.62	0.88	0.68	0.48
3	1.22	1.91	1.36	0.90	0.65	1.52	1.32	0.95
4	0.60	1.10	1.03	0.61	0.32	2.12	1.48	1.09
5	0.55	1.00	0.82	0.52	1.48	0.90	0.75	0.44

- a) Read the data into R and plot the antibiotic serum levels versus time for persons and drugs (Multiple plotting is a good idea). Discuss what you may learn from the plot.

The main objective of the study was to investigate if the two drugs had a different effect on the antibiotic serum level. A simple approach to the analysis is to work with suitable "derived variables" for each person; cf. page 261 in the text book. A useful "derived variable" is the "area under the curve", usually denoted AUC.

- b) Explain that here AUC may be given as

$$\begin{aligned} AUC &= 0.5 \cdot s_1 + 0.5 \cdot (s_1 + s_2) + 0.5 \cdot (s_2 + s_3) + 0.5 \cdot (s_3 + s_6) \cdot 3 \\ &= s_1 + s_2 + 2s_3 + 1.5s_6 \end{aligned}$$

where s_t is the serum level at time t . (When computing AUC we assume that the serum level at time zero is 0.)

- c) Compute the AUC for each person for each of the two drugs, and use a paired t-test to test the hypothesis that there is no effect of drug. What do you conclude from the test?

In order to study the effect of both time and drugs, we will use a random components model with drugs and time as fixed factors and person as a random effect.

- d) Fit a random effects model as described above. Discuss what you may learn from the fitted model.
- e) Test the hypothesis that there is no effect of drug. Also test the hypothesis that there is no effect of time. What do you conclude from these tests? Which model would you use to describe the data?
- f) Use the model you end up with in question e to give an estimate of the correlation between two serum level measurements for the same person.