Crossover designs and Latin Squares

- Persons as blocks
- More than one block factor
- Carry-over effect

Crossover designs

Each person gets several treatments. block = person, plot = person×time

Example: Wine-tasting

		Judge						
Tasting	1	2	3	4	5	6	7	8
1	2	4	4	2	1	2	4	4
2	1	3	1	4	4	4	2	3
3	3	2	2	3	3	1	1	1
4	4	1	3	1	2	3	3	2

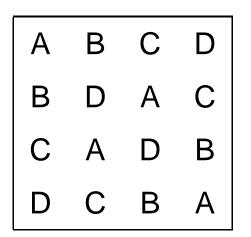
Randomisation: Tasting order of wines

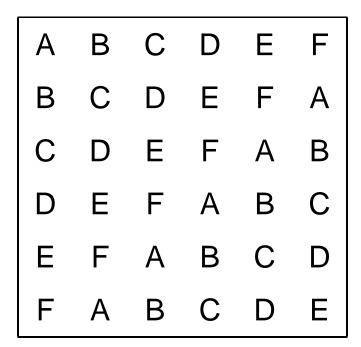
Row-Column-Design

- Each judge tastes each wine equally often (1×), person=block
- Each wine gets equally often tasted first, second, third, fourth (2×). position in tasting order=block

 \implies 2 systems of blocks persons (columns), position (rows)

A Latin square of order n is an arrangement of n symbols in a $n \times n$ square array in such a way that each symbol occurs once in each row and once in each column.





Construction of Latin Squares

Cyclic method:

- Write the letters in the top row in any order.
- In the second row, shift the letters one place to the right.
- Continue like this ...

Use of Latin squares

Interpretation: n^2 plots

- 2 system of blocks, 1 factor
- 1 system of blocks, 2 factors
- 3 factors

Take a Latin square of order n and superimpose upon it a second square with treatments denoted by greek letters. The two squares are orthogonal if each Latin letter occurs with each greek letter exactly once. The resulting design is a Graeco-Latin Square.

Construction Row-Column-Design

Take two Latin squares of size 4.

			Judge 1 2 3 4 5 6 7 8						
		1	2	3	4	5	6	7	8
	1	А	В	С	D	А	В	С	D
Tasting	2	В	С	D	А	С	D	А	В
	3	С	D	А	В	В	А	D	С
Tasting	4	D	А	В	С	D	С	В	А

Randomly permute the rows

Permutation 3241

						Juc	dge			
			1	2	3	4	5	6	7	8
	3	1	С	D	А	В	В	А	D	С
Tasting	2	2	В	С	D	А	С	D	А	В
	4	3	D	А	В	С	D	С	В	А
	1	4	A	В	С	D	А	В	С	C B A D

Randomly permute the columns

Permutation 52134687

			Judge						
		5	2	1	3	4	6	8 7	7
		1	2	3	4	5	6	7	8
	1	В	D	С	А	В	А	С	D
Tasting	2	С	С	В	D	А	D	В	А
	3	D	А	D	В	С	С	А	В
	4	А	В	А	С	D	В	7 C B A D	С

$$Y_{ij} = \mu + p_i + z_j + T_{k(ij)} + \epsilon_{ij}$$

 p_i and z_j are person and position effect (both random).

A unit (i, j) gets exactly one treatment (wine) k(ij). $T_{k(ij)}$ is the effect of wine k(ij).

Anova Table

Sum of squares partition:

$$SS_{tot} = SS_{persons} + SS_{position} + SS_{treat} + SS_{res}$$

Source	df	MS	F
Persons	7		
Tasting	3		
Wine	3	MS_{Wine}	MS_{Wine}/MS_{res}
Residual	18	MS_{res}	
Total	31		

- + more efficient than parallel designs, lower costs
- no treatment should leave a subject in a very different state at the end of the period (cure, death)
- drop-out more likely
- $\begin{array}{ll} \mbox{ experimental situation} \neq \mbox{ real situation} \\ \mbox{ sequence} & \mbox{ one treatment} \end{array}$
- carry-over effect: treatment effect lasts into subsequent time-period

Α effect of B + lasting effect of A

36 subjects with chronic pain take three different drugs response: hours without pain

T_1	T_2	T_3	T_1	T_3	T_2	T_2	T_1	T_3
6	8	7	6	6	5	2	8	7
4	4	3	7	3	3	0	8	11
13	0	8	6	0	2	3	14	13
5	5	4	8	11	10	3	11	12
8	12	5	12	13	11	0	6	6
4		3	4	13	5	2	11	8

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T_2	T_3	T_1	T_3	T_1	T_2	T_3	T_2	T_1
8	7	12	6	14	4	12	11	7
2	12	10	4	13	0	5	12	8
2	0	9	0	9	3	2	3	14
3	5		1			4	5	6
1	10	11	8	12	5	6	6	5

Anova Table

Source	SS	df	MS	F	P-Wert
Persons	503.6	35	14.4		
Time-period	192.1	2	96.0		
Medication	268.7	2	134.3	14.4	0.0000
Residual	632.6	68	9.3		
Total	1596.9	107			

Treatment comparison (se = $\sqrt{2MS_{res}/36} = 0.72$): $T_1 - T_2 = 3.84$ $T_1 - T_3 = 2.34$ $T_2 - T_3 = -1.50$ Carry-over effect = Interaction treatment \times time-period

	time-period 1	time-period 2
group 1	T_1	T_2
group 2	T_2	T_1

Approaches:

- wash-out period
- model carry-over effects:

