## 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** 

				Juc	dge			
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

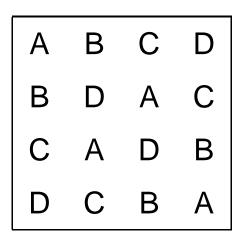
Randomisation: Tasting order of wines

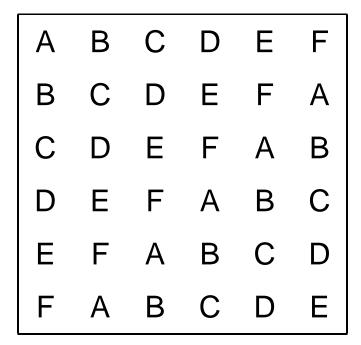
## Row-Column-Design

- Each judge tastes each wine equally often (1x), person=block
- Each wine gets equally often tasted first, second, third, fourth (2×). position in tasting order=block
- ⇒ 2 systems of blocks persons (columns), position (rows)

## Definition of Latin Squares

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

## Graeco-Latin Square

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.

$A\alpha$	Beta	$C\gamma$	$D\delta$	$E\epsilon$
$oldsymbol{B}\gamma$	$C\delta$	$D\epsilon$	E lpha	Aeta
$C\epsilon$	D lpha	Eeta	$A\gamma$	$B\delta$
$oldsymbol{D}eta$	$E\gamma$	$A\delta$	$B\epsilon$	$\mathbf{C}\alpha$
$E\delta$	$A\epsilon$	$\mathbf{B}\alpha$	$\mathbf{C}eta$	$D\gamma$

# Construction Row-Column-Design

Take two Latin squares of size 4.

					Juc	dge			
		1						7	
	1	Α	В	С	D	Α	В	С	D
Tasting	2	В	С	D	Α	C	D	Α	В
	3		U	А	D	D	А	D	
	4	D	Α	В	С	D	С	В	Α

# Randomly permute the rows

#### Permutation 3241

							dge			
			1				5			
	3	1	С	D	Α	В	ВС	Α	D	С
Tasting	2	2	В	С	D	Α	С	D	Α	В
	4	3	D	Α	В	С	D	С	В	Α
	1	4	Α	В	С	D	D A	В	С	D

## Randomly permute the columns

#### Permutation 52134687

					Juc	_			
		5	2	1	3	4	6	8 <b>7</b>	7
		1	2	3	4	5	6	7	8
	1	В	D	С	Α	В	Α	С	D
Tasting	2	С	С	C B D	D	Α	D	В	Α
	3	D	Α	D	В	С	С	Α	В
	4	Α	В	Α	С	D	В	D	С

#### Model

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

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

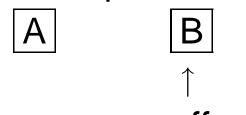
A unit (i, j) gets exactly one treatment (wine) k(ij).  $T_{k(ij)}$  is the effect of wine k(ij).

#### Anova Table

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

#### **Properties of Crossovers**

- + 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
- experimental situation \( \neq \) real situation sequenceone treatment
- carry-over effect: treatment effect lasts into subsequent time-period



effect of B + lasting effect of A

#### Pain Medication

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	
4	4						8	
13							14	
5	5	4	8	11	10	3	11	12
8	12	5	12	13	11	0	6	6
4	4	3	4	13	5	2	11	8

## more data

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

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:

ABB

ABBA

or

BAA

BAAB