

Split Plot Designs

- Large and small units
- Confounding main effects
- Repeated measures anova

Study in Dental Medicine

- Can measurement of electric resistance help in detecting tooth decay?
- 40 measurements on teeth with and without inflamed gums, with and without special treatment.
- 2^2 factorial with factor A (inflammation) and factor B (special treatment).

Correct anova table?

Source	df	MS	F
A	1	MS_A	MS_A/MS_{res}
B	1	MS_B	MS_B/MS_{res}
AB	1	MS_{AB}	MS_{AB}/MS_{res}
Residual	36		
Total	39		

Depends on design structure. How many subjects, how many teeth?

8 subjects, one tooth each

One treatment per person, 5 repeated measurements

Stratum	Source	df	F
Person	A	1	$MS_A/MS_{res-person}$
	B	1	$MS_B/MS_{res-person}$
	AB	1	$MS_{AB}/MS_{res-person}$
	Residual	4	
	Total	7	
Measurement	Residual	32	
	Total	39	

5 subjects, 4 teeth each

Each person has 2 inflamed and 2 not inflamed teeth. Each tooth was measured once with special treatment and once without special treatment.

Stratum	Source	df	F
Person	Person	4	
Tooth	A	1	$MS_A / MS_{res-tooth}$
	Residual	14	
	Total	15	
Measurement	B	1	$MS_B / MS_{res-meas}$
	AB	1	$MS_{AB} / MS_{res-meas}$
	Residual	18	
	Total	20	
Total	Total	39	

Special properties of this design

- Replication on three stages: persons, teeth and measurements.
- One factor varies between teeth, the other between measurements.
- **main plot**= tooth, **sub-plot** = measurement

Split-plot design

- A first factor needs to be applied to large plots, called main plots.
- Main plots are split into smaller plots, called subplots. These are assigned to different levels of a second factor.
- Two different levels for comparing factor levels: effects of the first factor must be examined relative to main plot variation, effects of the second factor must be examined relative to subplot variation.

Rice experiment

4 irrigation methods I1-I4 on main plots, 3 fertilizer mixtures X,Y, Z on sub-plots, 2 complete replicates.

Layout:

Block I				Block II			
z	x	y	z	x	y	z	x
x	z	z	y	z	x	x	y
y	y	x	x	y	z	y	z
I4	I2	I3	I1	I2	I1	I4	I3

Irrigation is confounded with main plots.

Model

$$Y_{ijk} = \mu + b_i + Irrr_j + \epsilon_{ij} + Fert_k + (Irr : Fert)_{jk} + \delta_{ijk}$$

$$i = 1, \dots, I; j = 1, \dots, J; k = 1, \dots, n.$$

b_i : i th block effect

$Irrr_j$: j th effect of irrigation

ϵ_{ij} : main plot error

$Fert_k$: k th effect of fertilizer

$(Irr : Fert)_{ij}$: jk th interaction

δ_{ijk} : sub-plot error

Skeleton Anova

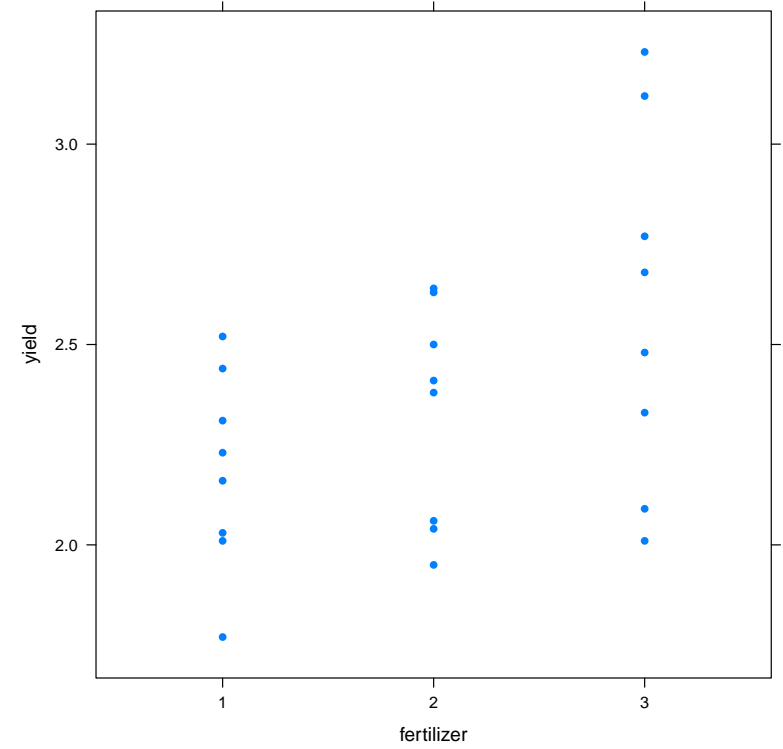
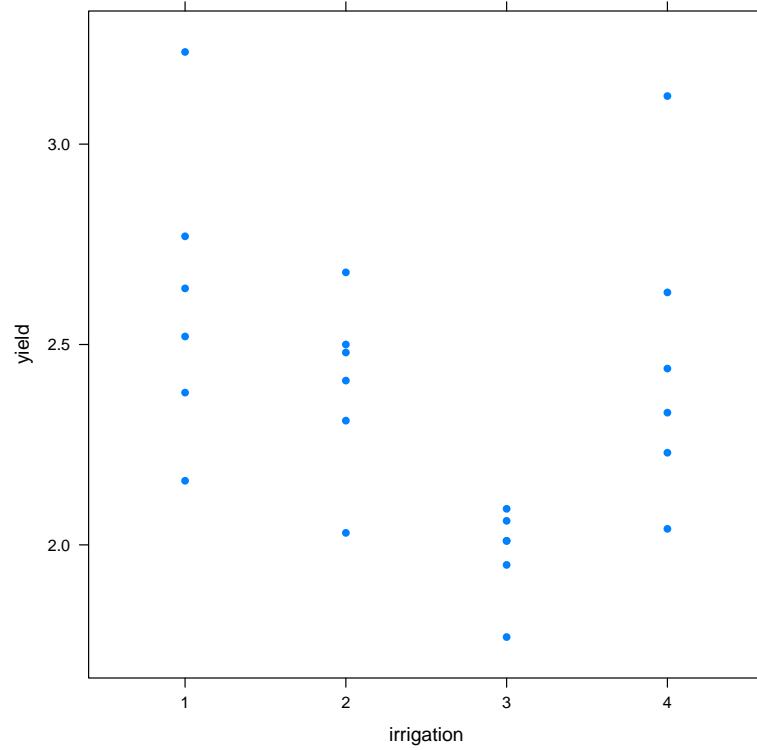
Stratum	Source	df	F
Blocks	Blocks	1	
Main plots	Irr	3	$MS_{Irr}/MS_{res-main}$
	Residual	3	
	Total	7	
Sub-plots	Fert	2	$MS_{Fert}/MS_{res-sub}$
	Irr:Fert	6	
	Residual	8	$MS_{Irr:Fert}/MS_{res-sub}$
	Total	16	
	Total	23	

Data on crop yield (tonnes/hectare)

	Irrigation			
Block I	I1	I2	I3	I4
Fertilizer x	2.16	2.03	1.77	2.44
y	2.38	2.41	1.95	2.63
z	2.77	2.68	2.01	3.12

	Irrigation			
Block I	I1	I2	I3	I4
Fertilizer x	2.52	2.31	2.01	2.23
y	2.64	2.50	2.06	2.04
z	3.23	2.48	2.09	2.33

Graphical display



Anova Table

```
> mod2=aov(yield~irrigation*fertilizer+Error(block/irrigation))
> summary(mod2)
```

Error: block

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
Residuals	1	0.0003375	0.0003375		

Error: block:irrigation

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
irrigation	3	1.32971	0.44324	2.0424	0.2862
Residuals	3	0.65105	0.21702		

Error: Within

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
fertilizer	2	0.67530	0.33765	16.6262	0.001414 **
irrigation:fertilizer	6	0.20110	0.03352	1.6504	0.250110
Residuals	8	0.16247	0.02031		

Repeated measures, Longitudinal data

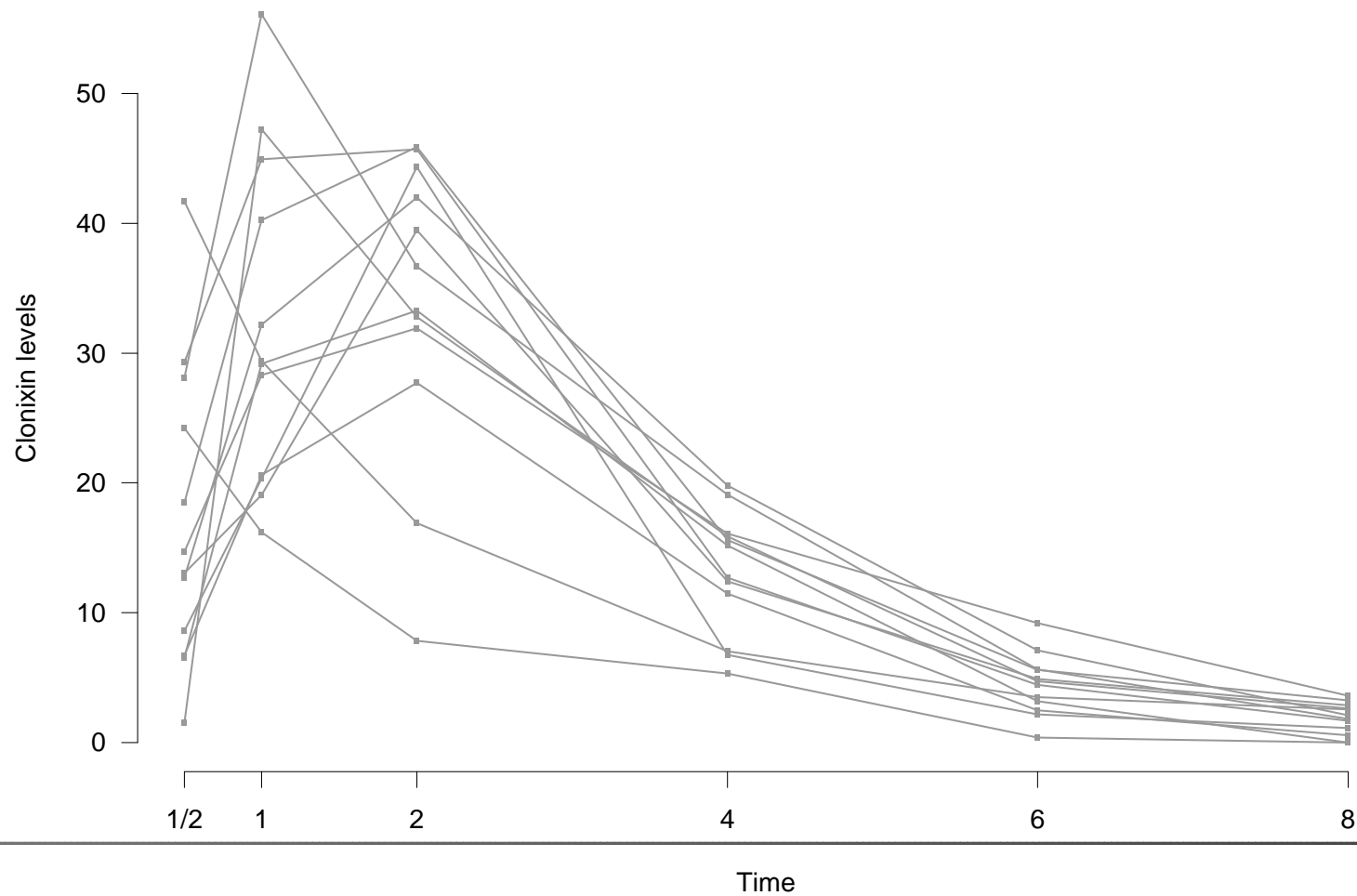
- Subjects are measured more than once
 - Compare values of an outcome variable before and after a treatment
 - Look at changes over time in an outcome variable
- Measurements at the same unit are correlated with each other

Rheumatoid arthritis

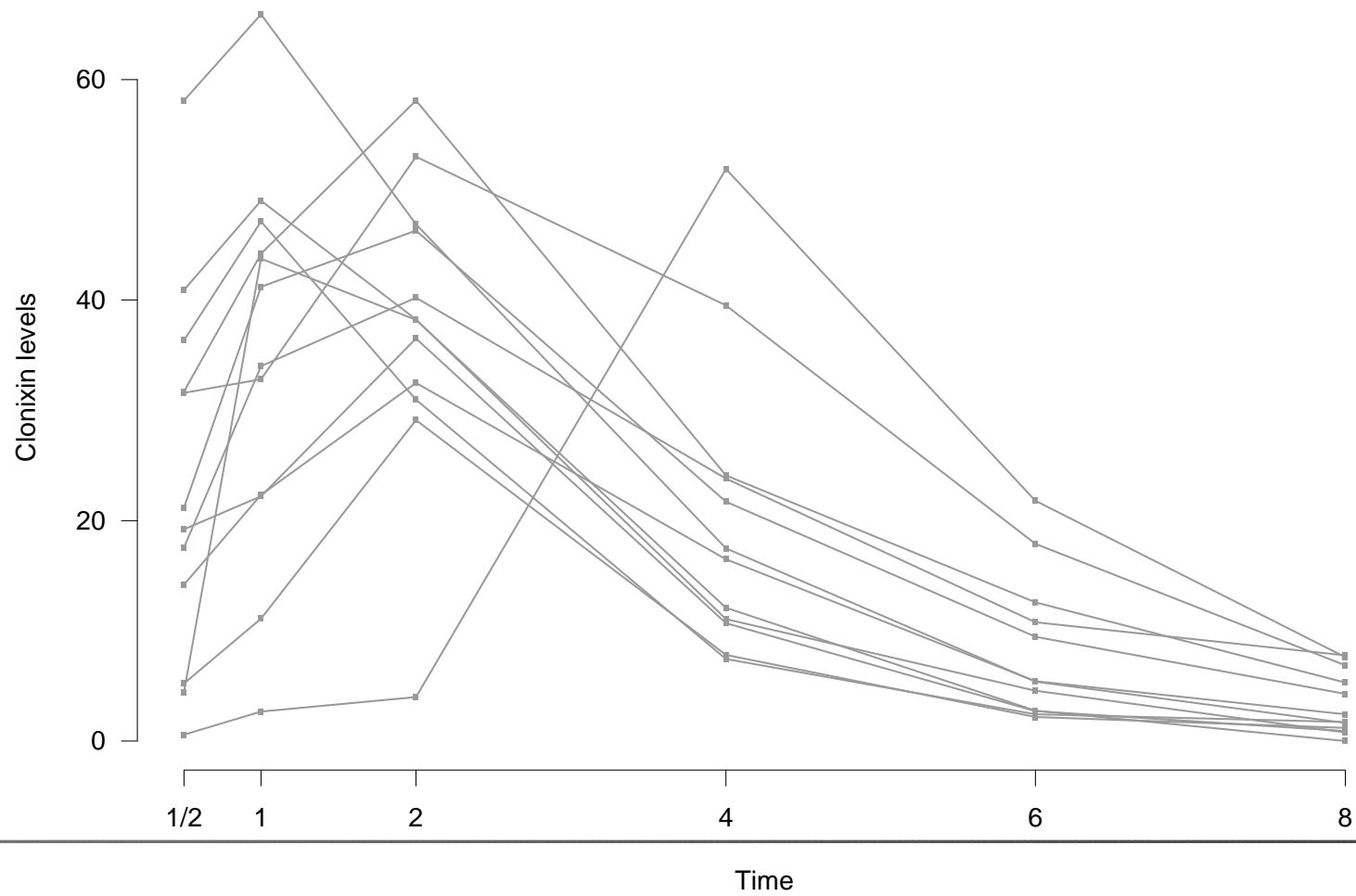
Patients with rheumatoid arthritis and normal controls obtained an anti-inflammatory analgesic. Serum clonixin levels (in mg/ml) were measured 1/2, 1, 2, 4, 6 and 8 hours after administration of a single dose of three 250 mg tablets of clonixin.

Subject	Time (in hours)					
	1/2	1	2	4	6	8
1	12.70	32.20	42.00	19.80	7.09	2.10
2	18.48	40.24	45.87	15.61	5.58	3.25
3	6.70	20.60	27.70	11.49	2.48	0.56
4	24.20	16.20	7.84	5.30	0.38	0.00
⋮	⋮					

Patients with arthritis



Controls



How to analyze the data?

- Separate analysis at each time point
- Summary measure: mean, maximal value, time until maximal value, steepest slope, area under curve (AUC)
- Repeated measures anova, split-plot approach: subjects=main plots, subject \times time=subplot. Critical assumption is **sphericity**: same variance of measurements at each time point and the same correlation between measurements taken at different times.
- Correction for deviation from sphericity: Greenhouse-Geisser, Huynh-Feldt

Anova table

Stratum	Source	df	F
Person	Treatment	1	$MS_{treat}/MS_{res-Person}$
	Residual	22	
	Total	23	
Person \times Time	Time	5	$MS_{time}/MS_{res-Person \times time}$
	Treatment \times Time	5	
	Residual	110	
	Total	120	
	Total	143	

R Output

```
> mod1 = aov(clonixin ~ time*group + Error(id),data=rheuma.long)
> summary(mod1)
```

Error: id

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
group	1	658.4	658.44	3.0483	0.09477 .
Residuals	22	4752.0	216.00		

Error: Within

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
time	5	22152.8	4430.6	42.0703	<2e-16 ***
time:group	5	138.2	27.6	0.2624	0.9326
Residuals	110	11584.5	105.3		

Other types of split-plot designs

- Repeated splitting: a third factor may be applied to sub-subplots
- Confounding interactions of sub-plot factors in split-plot designs
- Other designs for main plots, e.g. Latin squares
- Strip-plot design

