Index of Lecture 5–L:
Repeated measures ANOVA + first example of linear mixed modelling

— in addition to overheads by Davis (2002):
161,163–67,170–75,196–99,209–10,227,229–246,254–259

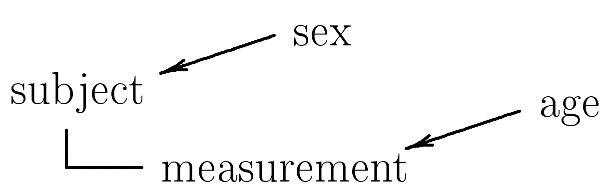
Repeated Measures ANOVA Methods

Classical ANOVA $\sim$ hierarchical/split-plot model
— for Dental study data:

$$y_{ij} = \mu + \alpha_{\text{sex}(i)} + \beta_j + (\alpha\beta)_{\text{sex}(i),j} + \pi_i + \varepsilon_{ij},$$
$$i = 1, \ldots, 27 \sim \text{ subjects}, \; j = 1, \ldots, 4 \sim \text{ ages},$$

where α's $\sim$ group (sex) effects, β's $\sim$ age effects (age as categorical), $\alpha\beta$'s $\sim$ their interaction, π_i's $\sim$ subject random effects (from $\mathrm{N}(0, \sigma_\pi^2)$), and ε_{ij}'s $\sim$ errors.

Hierarchical (2-level) data structure:



Repeated measures ANOVA methods
= amendments to split-plot ANOVA when it is inadequate:

- test for necessary assumption for validity of ANOVA table: Mauchly's test, with reference χ^2-distrib.,
- estimate seriousness of violation of the assumption by "ϵ-statistics" ($\epsilon \geq 1 \sim$ split-plot model ok),
  - $\hat{\epsilon}$ — Greenhouse-Geisser statistic,
  - $\tilde{\epsilon}$ — Huynh-Feldt statistic,
- correct F-tests in split-plot ANOVA for violation of the assumption using the ϵ-statistics,
- available in SAS and SPSS (partly in Stata).

Repeated Measures ANOVA for Dental Study

- split-plot ANOVA table:

Source	DF	SS	MS	F	P
Sex	1	140.5	140.5	9.29	.0054
Subjects	25	377.9	15.1	–	–
Age	3	237.2	79.1	40.0	<.0001
Sex × Age	3	14.0	4.66	2.36	.078
Error	75	148.1	1.98		
Total	107	917.7			

note: F for Sex based on MS(Subjects), and always ok!,

- Mauchly's test: statistic=7.29, df=5, P=0.20 — non-significant (but test has low power. . .),

- ϵ-statistics:

  * Box's $\epsilon = 1/(4-1) = 0.333$,
  * Greenhouse-Geisser $\hat{\epsilon} = 0.867$,
  * Huynh-Feldt $\tilde{\epsilon} = 1.016 \Rightarrow 1$,

- ϵ-corrected df and P-values:

Source		split-plot	Box corr.	HF-corr.	GG-corr.
Age	df	(3,75)	(1,25)	(2.6,65)	(3,75)
	P	<.0001	<.0001	<.0001	<.0001
Sex × Age	df	(3,75)	(1,25)	(2.6,65)	(3,75)
	P	.078	.137	.088	.078

- Conclusion: small violation (possibly none) and of little consequence.

Summary: Recommendations on Methods

4 main approaches involving normal distribution models of full data:

1) multivariate: MANOVA, profile and growth curve analysis,
2) hierarchical: mixed model with compound symmetry assumption,
3) repeated measures ANOVA: test of sphericity, ε-statistics,
4) linear mixed model (next topic to follow).

Recommendations (Davis):

- method 3) not recommended,
- method 1) still worthwhile (if applicable),
  - ∗ valid, based on fewer assumptions than 4),
  - ∗ may perform better in small samples than 4) (simulation studies).

Recommendations (Henrik):

- method 2) should always be checked by testing the correlation structure (often acceptable for short series),
- method 3) may be used as descriptive method (to see impact of violation of assumptions) but the final analysis should be of different type.

Model 4a: Homogeneous Variances

- $y_{hij} = \alpha_h + \beta_h t_j + \epsilon_{hij}$,
- homogeneous variances: $\text{Var}(y_{hij})$ = constant, but unstructured correlations:

$$\text{Cov}(y) = \begin{pmatrix} \sigma^2 & & & \\ \rho_{12}\sigma^2 & \sigma^2 & & \\ \rho_{13}\sigma^2 & \rho_{23}\sigma^2 & \sigma^2 & \\ \rho_{14}\sigma^2 & \rho_{24}\sigma^2 & \rho_{34}\sigma^2 & \sigma^2 \end{pmatrix},$$

$$\text{Corr}(y) = \begin{pmatrix} 1 & & & \\ \rho_{12} & 1 & & \\ \rho_{13} & \rho_{23} & 1 & \\ \rho_{14} & \rho_{24} & \rho_{34} & 1 \end{pmatrix},$$

- no easy specification in `SAS,proc mixed`,
- LR test comparing Model 4a to Model 2 is

$$421.23 - 419.48 = 1.75, \quad \text{df} = 14 - 11 = 3, \quad p = .62,$$

- no evidence of inhomogeneous variances across ages.

Model 4b: ARMA(1,1) Correlation Structure

- $y_{hij} = \alpha_h + \beta_h t_j + \epsilon_{hij}$,
- homogeneous variances and ARMA(1,1) correlation structure:

$$\text{Cov}(y) = \begin{pmatrix} \sigma^2 & & & \\ \gamma\sigma^2 & \sigma^2 & & \\ \gamma\rho\sigma^2 & \gamma\sigma^2 & \sigma^2 & \\ \gamma\rho^2\sigma^2 & \gamma\rho\sigma^2 & \gamma\sigma^2 & \sigma^2 \end{pmatrix}, \text{Corr}(y) = \begin{pmatrix} 1 & & & \\ \gamma & 1 & & \\ \gamma\rho & \gamma & 1 & \\ \gamma\rho^2 & \gamma\rho & \gamma & 1 \end{pmatrix},$$

- <u>SAS</u> code for model:

```
proc mixed method=ml;
class id sex;
model distance=sex age*sex / noint s;
repeated / type=arma(1,1) subject=id r;
```

- LR test comparing Model 4b to Model 4 is

$$428.64 - 424.64 = 3.82, \quad \text{df} = 11 - 10 = 1, \quad p = .051,$$

- ARMA(1,1) structure does not fit well compared to Toeplitz structure (some indication of non-decreasing correlations over time).

Mixed Models Summary for Dental Study

All models analyzed by maximum likelihood (ML) estimation, to allow comparison between them using likelihood-ratio test statistics (G^2).

				test against larger model			
No.	Model	$-2\log L$	#param.	No.	G^2	df	P
1	unstructured	416.51	18	–	–	–	–
2	linear age effect	419.48	14	1	2.97	4	.56
3	parallel lines	426.15	13	2	6.68	1	.010
4a	homog. variances	421.23	11	2	1.75	3	.62
4	banded/Toeplitz	424.64	8	2	5.17	6	.40
				4a	3.41	3	0.33
4b	ARMA(1,1)	428.46	7	4a	3.82	1	.051
5	AR(1)	440.68	6	4	16.0	2	.0003
6	random slopes	427.81	8	2	8.33	6	.14
7	random interc./ compound symm.	428.64	6	6	0.83	2	.66
				4	4.00	2	.14
				9	12.0	1	.0005
				10	19.3	1	<.0001
8	independence	478.24	5	7	49.6	1	<.0001
9	compound symm. + sex var. het.	416.65	7	–	–	–	–
10	random interc. + sex var. het.	409.35	7	11	3.31	2	.19
				12	0.54	1	.46
11	random slopes + sex var. het.	406.04	9	–	–	–	–
12	random interc. + sex covar. het.	408.81	8	–	–	–	–