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Practical Information

Today's lecture:
continuation of random effects models (from Lecture 9):

- model building & checking + software (9L−13/14/15),
- last example: nested design (pig breeding data, 9L−10),
- split-plot or hierarchical design:
  - a special type of design which is modelled/analysed by random effects models,
  - arguably the most important application of random effects models.

Textbook reading:

- GO Chapter 12 (excl. Sections 6,7,9) and Chapter 16 (Sections 1-5); skip discussions involving Hasse diagrams[1] and restricted random effects,
- supplementary notes on linear mixed models, including split-plot designs; part of course curriculum.

Other news / practical information:

- 2nd home assignment due today; 3rd home assignment posted in the weekend; project outline due Monday,
- course exam set for April 21.

[1] Hasse diagrams is a general graphical tool to compute degrees of freedom and assess the structure of the ANOVA table for random effects models; it's not really needed for simple models but very useful for complex models.

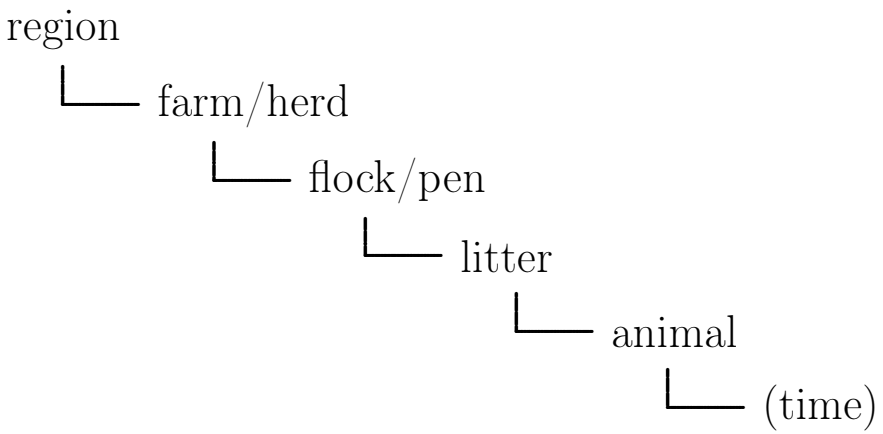
Hierarchical Data Structure

A hierarchical data structure:

- observations grouped at different levels,
- treatments applied at different levels.

may induce clustering in the data, that is, some observations are more alike than others, or put in another way: the observations are no longer independent.

Typical example from veterinary epidemiology:



Note: "time" as a bottom level $\sim$ longitudinal data / repeated measures on the same animal (next lecture), and raises some additional modelling issues.

Random effects models for hierarchical data:

- insert random effect(s) for each hierarchical level (above the bottom level).

Split-Plot Designs

Consider a two-factor design with blocks or replications:

- treatments (factors) A at a levels, and B at b levels,
- ab experimental units in each of c blocks, or replicated c times (assuming a balanced design).

Randomized (block) design:

- $N = abc$ units allocated randomly to treatments (A×B),
- all treatments estimated with same precision.

Split-plot design:

- A varies between (is applied to) larger units than B (for convenience or of necessity),
- conceptual two-step design construction:
  - i) A is allocated randomly to large units ("whole plots"),
  - ii) units for A are split into sub-units ("split plots"[2]), onto which B is allocated randomly,
- A = "whole-plot factor" and B = "split-plot factor",
- implication: A estimated with less precision than B and the interaction A∗B (not intuitively obvious!).

Analysis of split-plot design:

- include random effects for A-units (whole plots) in model!

[2] GO uses the term "split plots", other authors use sub plots.

Split-Plot Example: Memory Trials

Anxiety, tension, and memory data (GO Example 16.5):

- memory errors recorded in each of 4 memory trials taken (in random order $\sim$ cross-over design) by 12 subjects allocated to one of four groups defined by different levels of anxiety (low/high) and muscular tension (low/high),

Subject	1	2	3	4	5	6	7	8	9	10	11	12
Anxiety	1	1	1	1	1	1	2	2	2	2	2	2
Tension	1	1	1	2	2	2	1	1	1	2	2	2
Type 1	18	19	14	16	12	18	16	18	16	19	16	16
Type 2	14	12	10	12	8	10	10	8	12	16	14	12
Type 3	12	8	6	10	6	5	8	4	6	10	10	8
Type 4	6	4	2	4	2	1	4	1	2	8	9	8

  notation: $y_{ijkl} = \#$ memory errors for trial of type k for subject l in anxiety group i and tension group j,

  * whole plots = subjects (within anxiety$\times$tension group),
  * whole-plot factors: (A) = anxiety, (B) = (tension),
  * split plots = trials (for each subject$\times$type),
  * split-plot factor (C) = trial type,

- split-plot model with replication (instead of blocks):

$$y_{ijk} = \mu + \alpha_i + \beta_j + (\alpha\beta)_{ij} + \gamma_k + (\alpha\gamma)_{ik} + (\beta\gamma)_{jk} + (\alpha\beta\gamma)_{ijk} + D_{ijl} + \varepsilon_{ijkl},$$

  * $\text{Var}(\varepsilon_{ijkl}) = \sigma^2$ (variation between split plots),
  * $\text{Var}(D_{ijl}) = \sigma_D^2$ (extra variation btw. whole plots),
  * $D_{ijl} \sim$ whole-plot random effect for subject (i, j, l).

Memory Example Results

ANOVA table:

Source	DF	SS	MS	EMS	F	P
Anxiety	1	10.08	10.1	$\sigma^2+4\sigma^2_D+\sigma^2_\alpha$	$\text{MS}_A/\text{MS}_D=0.98$	0.35
Tension	1	8.33	8.3	$\sigma^2+4\sigma^2_D+\sigma^2_\beta$	$\text{MS}_B/\text{MS}_D=0.81$	0.40
A $*$ Tn	1	80.08	80.1	$\sigma^2+4\sigma^2_D+\sigma^2_{\alpha\beta}$	$\text{MS}_{AB}/\text{MS}_D=7.77$	0.024
Type	3	991.50	330.5	$\sigma^2+\sigma^2_\gamma$	$\text{MS}_C/\text{MS}_E=152$	$<.001$
A $*$ Tp	3	8.42	2.8	$\sigma^2+\sigma^2_{\alpha\gamma}$	$\text{MS}_{AC}/\text{MS}_E=1.29$	0.30
Tn $*$ Tp	3	12.17	4.1	$\sigma^2+\sigma^2_{\alpha\gamma}$	$\text{MS}_{BC}/\text{MS}_E=1.87$	0.16
A$*$Tn$*$Tp	3	12.75	4.3	$\sigma^2+\sigma^2_{\alpha\beta\gamma}$	$\text{MS}_{ABC}/\text{MS}_E=1.96$	0.15
Whole plot	8	82.50	10.3	$\sigma^2+4\sigma^2_D$	$\text{MS}_D/\text{MS}_E=4.74$	$<.001$
Split plot	24	52.17	2.2	σ^2		
Total	47	1258.0				

- clearly significant effect of type (and no interactions),
- weakly significant interaction between anxiety and tension $\Rightarrow$ interpretation in interaction plot,
- variance components:

$$\hat{\sigma}^2=\text{MS}_E=2.174,\quad \hat{\sigma}^2_D=(\text{MS}_D-\text{MS}_E)/4=2.035,$$

Standard errors of means, and pairwise comparisons:

- whole-plot factors (+ interaction): usual formulae, using MS_D instead of MS_E ($\sim$ analysis of whole-plot means),
- split-plot factor (type): pairwise comparisons using MS_E,
- interactions with split-plot factor: within whole-plot factor pairwise comparisons by usual formulae using MS_E,

– otherwise by approximation method (details in notes).

Correlations in Random Effects Models

Fact: random effects introduce (positive) *correlations* between the observations,

- observations are no longer independent, or
  − (same meaning) observations are clustered,
- observations *at the same level of a random factor* are correlated, whereas observations at different levels of all random factors are still independent,
- rule to compute *intra-class correlations* (ICCs):
  - compute the total variance, $\mathrm{Var}(y)$, of an (any) observation − as the sum of all variance components,
  - for the two observations, y_1 and y_2, in question, compute the covariance between them, $\mathrm{Cov}(y_1, y_2)$ − as the sum of all variance components for which y_1 and y_2 are *at the same level*,
  - the correlation (ρ) between y_1 and y_2, $\mathrm{Corr}(y_1, y_2)$, is the ratio of these:

$$\rho \text{ (or ICC)} = \mathrm{Corr}(y_1, y_2) = \mathrm{Cov}(y_1, y_2)/\mathrm{Var}(y).$$

Example: split-plot model (with σ^2_{AC} and σ^2 as whole-plot and split-plot variances, respectively),

$$\mathrm{Corr}(y_1, y_2) = \begin{cases} \sigma^2_{AC}/(\sigma^2_{AC}+\sigma^2), & \text{(same whole plot)}, \\ 0, & \text{(different whole plots)}, \end{cases}$$

More about Nesting and Subsampling

Recall crossed vs. nested factors A and B:

- A and B are *crossed*, if every level of A and B have the same meaning across the entire experiment,
- A is *nested* within B, if levels of A are specific to levels of B and don't generalize across levels of B.

Subsampling:

- multiple measures taken on the same experimental unit,
- often "identical" subsamples, e.g. duplicates,
- split-plot designs: split (sub) plots $\sim$ subsampling of whole plots and allocation of split-factor treatments,
- rarely realistic to assume independence between subsamples; two possible approaches/solutions:
  - average observations to level of experimental units,
  - include random effects $\sim$ units subsampled.[3]

Steps to build an ANOVA model (GO Section 12.3):

1. Determine the sources of variation,
2. Decide which factors cross and which nest,
3. Decide which factors are fixed and which are random,
4. Decide which interactions should be in the model.

[3] Keeping the original observations but adding suitable random effects is the equivalent approach to split-plot modelling.

Split-Plot Example: Wetland Weeds

Weed biomass in wetlands (GO Example 16.7, p. 432):

- percent of nonweed biomass after 8 weeks of growth of seeds in clipping-treated halves of weed-treated wetlands placed in 8 trays, onto which nitrogen treatments were applied, positioned on 2 separate tables (in greenhouse),

Table	N	Weed = 1		Weed = 2		Weed = 3	
		C = 1	C = 2	C = 1	C = 2	C = 1	C = 2
1	1	87.2	88.8	70.4	75.7	75.0	80.6
	2	80.5	83.8	59.2	61.5	59.5	62.5
	3	76.8	80.8	47.8	49.5	48.4	52.9
	4	77.7	81.5	35.7	37.3	38.3	42.4
2	1	78.2	80.5	65.1	68.3	65.3	66.6
	2	79.8	85.2	57.6	61.4	58.5	61.6
	3	82.4	83.1	50.5	54.0	51.6	54.7
	4	75.7	78.7	39.0	43.9	41.9	45.1

C=clipping tx

- a split-split-plot design with blocks:
  - whole plots = trays (8),
  - whole-plot factor = N levels (4),
  - split plots = wetlands (24, three in each tray),
  - split-plot factor = weed treatment (3),
  - split-split plots = wetland halves (48),
  - split-split-plot factor = clipping treatment (2),
  - blocks = tables (2),
- notation: y_{ijkl} = biomass percentage at clipping tx k, weed tx j and nitrogen tx i in block l.

Wetland Example Results

Model:

$$y_{ijkl} = \mu + \alpha_i + \beta_j + \gamma_k + (\alpha\beta)_{ij} + (\alpha\gamma)_{ik} + (\beta\gamma)_{jk} + (\alpha\beta\gamma)_{ijk} + \delta_l + (AD)_{il} + (ABD)_{ijl} + \varepsilon_{ijkl},$$

with the whole-plot errors $AD_{il} \sim \mathrm{N}(0, \sigma^2_{AD})$, the split-plot errors $ABD_{ijl} \sim \mathrm{N}(0, \sigma^2_{ABD})$, and the split-split-plot errors $\varepsilon_{ijkl} \sim \mathrm{N}(0, \sigma^2)$, and all variables independent.

Analysis:

- exact model specification in Minitab not possible, but possible with a table×weed interaction split from the wetland variation,[4]
- variance components (from REML-estimation in Stata): $\hat{\sigma}^2_{AD} = 11.17, \quad \hat{\sigma}^2_{ABD} = 2.62, \quad \hat{\sigma}^2 = 1.07,$
- residuals: split-split-plot level ok, split-plot and whole-plot levels from analysis of respective means also ok,
- interaction `n*weed` clearly significant ⇒ interaction plot: less biomass (i.e., more weeds) with increasing N, especially when weeds have been seeded,[5]
- strong main effect of clipping: slight increase of biomass,
- presentation of results: separate for `n*weed` interaction and clipping main effect (because additive), by graphs or (least squares) means with standard errors.

[4] Minitab model specification (incl. `table*weed` interaction) with random `table` effect: `biomass = n|table n|weed|clip table*weed n*table*weed`.

[5] The interaction may be explored in the split-plot model for wetland means.

Final Remarks on Split-Plot Designs

Split-plot vs. hierarchical data structure:
much the same thing. . . :

- split plots constitute a level below the whole plots:

  whole plot
  └ split plot similarly to herd
  └ animal

- in a hierarchical structure, upper level units $\sim$ whole plots and lower level units $\sim$ split plots,
- explanatory variables may vary at upper or lower levels (possibly not randomised as in a split-plot design).

Two types of split-plot designs:

- with blocks (wetland weeds example),
- with replicates instead of blocks (memory example).

How to identify a "split-plot" structure?:

- *measurement* units are smaller than *experimental* units (for some treatment factors),
- expl. variables vary between "units" of different size,
- GO: follow the randomization!,
- think about whether subsampling was done,
- ask yourself: how many exper. units for this factor?
- draw a sketch of the experimental layout!

Stata Do-file (selection)

```
* Example 16.5
import delimited ch16ta1.csv, clear
anova errors anxiety##tension / subject|anxiety#tension
      anxiety##tension##type
predict pred, xb
predict stdres, rstandard
scatter stdres pred
qnorm stdres
swilk stdres
* random effect checks
preserve /* run next 7 lines together with this one */
collapse (mean) errors, by(anxiety tension subject)
anova errors anxiety##tension
predict pred2, xb
predict stdres2, rstandard
scatter stdres2 pred2
qnorm stdres2
swilk stdres2
* likelihood-based analysis
egen id=group(anxiety tension subject)
mixed errors anxiety##tension##type || id:, reml
predict pred2, fitted
predict stdres2, rstandard
scatter stdres2 pred2
qnorm stdres2
predict pred_ref, reffects
bysort id: gen within_n=_n
qnorm pred_ref if within_n==1
swilk pred_ref if within_n==1

* Example 16.7
import delimited ch16ta2.csv, clear
anova biomass n table / n#table n##weed / n#table#weed n##weed##clip
mixed biomass table n##weed##clip || tray: || wetland:, reml
```