Introduction to Linear Mixed-Effects Models

Niels Hagenbuch

ETH Zürich, 2010-03-01

1 Introduction

In the context of analysis of variance (ANOVA), a response variable y is modelled by one or more discrete or categorical covariates (also called factors). In the classical ANOVA, these covariates are considered as **fixed factors**, i.e. their levels pose a theoretically meaningful set of comparisons. We cannot change the levels of these factors without fundamentally changing the research question itself. Often, all potential level of such a covariate are implemented in the experimental design. **Examples:** different varieties of crops in a field experiment, dosages of drugs in a comparative study, production methods in a quality control study, gender in experiments where sex differences are an issue.

Often, though, the levels of a covariate do not carry themselves much meaning, being but a sample of possible values. These covariates are called **random effects** and are brought into the analysis (1) to assess variability, (2) to reduce threats to validity related to concrete implementations of abstract treatments, (3) to increase generalizability. **Examples** are subjects in psychological or medical tests, experimental units like batches or samples, different plots in a field study.

When should a factor be considered random? (1) When its specific levels could be replaced by other equally acceptable levels without changing the research question or the conclusion drawn from the study (the chosen levels are arbitrary or substitutable). (2) When the conclusion of the experiment is to be generalized to examined and unexamined levels. (3) When conclusions drawn for each separate level are uninteresting, arbitrary particulars.

What happens if random factors are misclassified as fixed? In general a loss of control over Type I error in testing hypotheses of interest occurs. The inflation of the Type I error rate can be considered as a result of an unintended shift in which null hypothesis is being tested, leading to test results that are irrelevant as evidence for the conclusions drawn.

2 Examples of different models/datasets

Terms used:

nested design A factor is nested under (or within) another factor if any given level of the nested factor appears at only one level of the nesting factor. Another way of putting it is to say that a factor is nested if its levels are divided among the levels of another factor. A nested design is also called *hierarchical*.

crossed design Two factors are *crossed* if all levels of the first factor appear in combination with all levels of the other factor; the levels of the factors are "multiplied" to produce all possible combinations of the levels of the first factor and the levels of the second factor. A crossed design is also called *factorial*.

interaction If the effect of one covariate changes considerably as the value of another covariate changes. The resulting effect is no longer additive and, therefore, has to be modelled separately. *Example:* Both smoking and inhaling asbestos fibres increase the risk for lung carcinoma, but in smokers exposition to abestos increases the cancer risk much more than it does in non-smokers.

$\boldsymbol{\mu}$ Popoulation mean, intercept (fixed effect)

$\boldsymbol{\varepsilon}$ Error, variation in the data at the "lowest level" (usually the unit of observation, e.g. subjects, samples), denoted as variance (σ^2). If possible, the error is identified with a *within*-variability.

One factor or one-way classification

1. **Repeated measures (dataset: `Rail`, package: `nlme`)**

   Experiment: Six rails chosen at random, three measurements of travel time of a ultrasonic wave through each rail.

   Interest: Expected travel time, variation in travel time among rails (between-rail variability), variation in travel time for a single rail (within-rail variability or error-term).

   Model: $y_{ij} = \mu + b_i + \varepsilon_{ij}, \quad i = 1, \ldots, 6, \quad j = 1, 2, 3$
   b_i deviation from β for the i^{th} rail (random)

   Assumptions: $b_i \sim \mathcal{N}\langle 0, \sigma_b^2 \rangle, \quad \varepsilon_{ij} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_i \perp \varepsilon_{ij}$

   R:
   ```
   lme(fixed = travel ~ 1, random = ~ 1 | rail, data = Rail)
   lmer(travel ~ Type + (1|Subject), data = Rail)
   ```

Two factor or (randomized) blocked designs

2. **One fixed / one random factor, no replications (dataset: `ergoStool`, package: `nlme`)**

   Experiment: Nine testers had to sit in four different ergonomic stools and their effort to raise was measured once.

   Interest: Expected effort to raise for each of the four stools, variation among stools (between-stool variability), variation within testers (error).

   Model: $y_{ij} = \mu + \beta_j + b_i + \varepsilon_{ij}, \quad i = 1, \ldots, 9, \quad j = 1, \ldots, 4$

   β_j : effect of stool type (fix), $\quad b_i$ effect of testing subject (random)

   Assumptions: $b_i \sim \mathcal{N}\langle 0, \sigma_b^2 \rangle, \quad \varepsilon_{ij} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_i \perp \varepsilon_{ij}$

   R:
   ```
   lme(fixed = effort ~ Type, random = ~ 1 | Subject, data = ergoStool)
   lmer(effort ~ Type + (1|Subject), data = ergoStool)
   ```

3. **One fixed / one random factor, with replications, no interaction (dataset: `Machines`, package: `nlme`)**

   Experiment: Six workers in a plant had to operate three different machines three times while their productivity scores were taken.

   Interest: Expected productivity score of the three different machines, variation among workers (between variability), variation within a worker (error).

   Model: $y_{ijk} = \mu + \beta_j + b_i + \varepsilon_{ijk}, \quad i = 1, \ldots, 6, \quad j = 1, 2, 3, \quad k = 1, 2, 3$ (replications)

   β_j : effect of machine (fix), $\quad b_i$ effect of worker (random)

   Assumptions: $b_i \sim \mathcal{N}\langle 0, \sigma_b^2 \rangle, \quad \varepsilon_{ijk} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_i \perp \varepsilon_{ijk}$

   R:
   ```
   lme(fixed = score ~ Machine, random = ~ 1 | Worker, data = Machines)
   lmer(score ~ Machine + (1|Worker), data = Machines)
   ```

4. **One fixed / one random factor, with replications, with interaction (dataset: `Machines`, package: `nlme`)**

   Experiment: See above.

   Interest: See above, interdependence of worker and machine.

   Model: $y_{ijk} = \mu + \beta_j + b_i + b_{ij} + \varepsilon_{ijk}, \quad i = 1, \ldots, 6, \quad j = 1, 2, 3, \quad k = 1, 2, 3$ (replications)

   β_j : effect of machine (fix), $\quad b_i$ effect of worker (random), $\quad b_{ij}$ interaction term (random)

   Assumptions: $b_i \sim \mathcal{N}\langle 0, \sigma_{b1}^2 \rangle, \quad b_{ij} \sim \mathcal{N}\langle 0, \sigma_{b2}^2 \rangle, \quad \varepsilon_{ijk} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_i \perp b_{ij}, \quad b_i, b_{ij} \perp \varepsilon_{ijk}$

   R:
   ```
   lme(fixed = score ~ Machine, random = ~ 1 | Worker/Machine, data = Machines)
   lmer(score ~ Machine + (1|Worker) + (1|Worker:Machine), data = Machines)
   ```

5. **Two random factors, no replications, crossed design (dataset: `manager1`)**

   Experiment: Three trained raters evaluate once the style of leadership of twenty individual managers. Each rater evaluates all managers.

   Interest: How much variability is there from rater to rater (can the method be generalized?).

   Model: $y_{ij} = \mu + b_{i1} + b_{j2} + \varepsilon_{ij}, \quad i = 1, 2, 3, \quad j = 1, \ldots, 20$

   b_{i1} effect of rater (random), $\quad b_{j2}$ effect of manager (random)

   Assumptions: $b_{i1} \sim \mathcal{N}\langle 0, \sigma_{b1}^2 \rangle, \quad b_{j2} \sim \mathcal{N}\langle 0, \sigma_{b2}^2 \rangle, \quad \varepsilon_{ij} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_{i1} \perp b_{j2}, \quad b_{i1}, b_{j2} \perp \varepsilon_{ij}$

   R: `lme()` does not support crossed designs
   ```
   lmer(score ~ 1 + (1|Rater) + (1|Manager), data = manager1)
   ```

6. **Two random factors, no replications, nested design (dataset: `manager2`)**

   Experiment: Three trained raters evaluate once the style of leadership of twenty individual managers. Each rater is assigned an independent sample of managers to evaluate.

   Interest: How much variability is there from rater to rater (can the method be generalized?).

   Model: $y_{ij} = \mu + b_i + b_{j(i)} + \varepsilon_{ij}, \quad i = 1, 2, 3, \quad j = 1, \ldots, 20$

   b_i effect of rater (random), $\quad b_{j(i)}$ effect of manager nested within rater (random)

   Assumptions: $b_i \sim \mathcal{N}\langle 0, \sigma_{b1}^2 \rangle, \quad b_{j(i)} \sim \mathcal{N}\langle 0, \sigma_{b2}^2 \rangle, \quad \varepsilon_{ij} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_i \perp b_{j(i)}, \quad b_i, b_{j(i)} \perp \varepsilon_{ij}$

   R:
   ```
   lme(fixed = score ~ 1, random = ~ 1 | Rater/Manager, data = manager2)
   lmer(score ~ 1 + (1|Rater) + (1|Manager), data = manager2)
   ```

7. **Two random factors, with replications, crossed design, no interaction (no dataset examined)**

Model: $y_{ijk} = \mu + b_{i1} + b_{j2} + \varepsilon_{ijk}, \quad i = 1, \ldots, n_i, \quad j = 1, \ldots, n_j, \quad k = 1, \ldots, n_k$ (replications)
b_{i1} random effect 1, b_{j2} random effect 2

Assumptions: $b_{i1} \sim \mathcal{N}\langle 0, \sigma^2_{b1} \rangle, \quad b_{j2} \sim \mathcal{N}\langle 0, \sigma^2_{b2} \rangle, \quad \varepsilon_{ij} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_{i1} \perp b_{j2}, \quad b_{i1}, b_{j2} \perp \varepsilon_{ijk}$

R: `lme()` does not support crossed designs

```
lmer(score ~ 1 + (1|b1) + (1|b2), data = ...)
```

8. **Two random factors, with replications, crossed design, with interaction (no dataset examined)**

Model: $y_{ijk} = \mu + b_{1i} + b_{2j} + b_{ij3} + \varepsilon_{ijk}, \quad i = 1, \ldots, n_i, \quad j = 1, \ldots, n_j, \quad k = 1, \ldots, n_k$ (replications)
b_{i1} random effect 1, b_{j2} random effect 2, b_{ij3} interaction term (random)

Assumptions: $b_{i1} \sim \mathcal{N}\langle 0, \sigma^2_{b1} \rangle, \quad b_{j2} \sim \mathcal{N}\langle 0, \sigma^2_{b2} \rangle, \quad b_{3ij} \sim \mathcal{N}\langle 0, \sigma^2_{b3} \rangle, \quad \varepsilon_{ijk} \sim \mathcal{N}\langle 0, \sigma^2 \rangle,$
$b_{i1} \perp b_{j2}, b_{ij3}, \quad b_{j2} \perp b_{ij3}, \quad b_{i1}, b_{j2}, b_{ij3} \perp \varepsilon_{ijk}$

R: `lme()` does not support crossed designs

```
lmer(score ~ 1 + (1|b1) + (1|b2) + (1|b1:b2), data = ...)
```

9. **Two random factors, with replications, nested design (dataset: `Pastes`, package: `lme4a`)**

Experiment: From ten independent batch deliveries of a chemical paste, three casks (samples) were taken in order to perform a quality check. From each sample two measurements were taken.

Interest: Expected strength of paste, variability between batches, variability between samples, variability within samples (error).

Model: $y_{ijk} = \mu + b_i + b_{j(i)} + \varepsilon_{ijk}, \quad i = 1, \ldots, 10, \quad j = 1, 2, 3, \quad k = 1, 2$ (replications)
b_i batch (random), $b_{j(i)}$ sample within batch

Assumptions: $b_i \sim \mathcal{N}\langle 0, \sigma^2_{b1} \rangle, \quad b_{j(i)} \sim \mathcal{N}\langle 0, \sigma^2_{b2} \rangle, \quad \varepsilon_{ijk} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_i \perp b_{j(i)}, \quad b_i, b_{j(i)} \perp \varepsilon_{ijk}$

R:

```
lmer(strength ~ 1 + (1|batch) + (1|sample), data = Pastes)
lme(fixed = strength ~ 1, random = ~ 1 | batch/sample, data = Pastes)
```

Three factor or split-plot designs

10. **Two fixed / one random factor, 3 × 4 full factorial design with interaction of the fixed factors, one fixed factor nested within the random factor, no replication (dataset: `Oats`, package: `lme`)**

Experiment: Three different oat varieties were randomly assigned to three plots, which were further subdivided into four subplots for the application of four different concentrations of nitrogen fertilizer. There were six of these "blocks", and the yield of oat was measured at the end of the experiment.

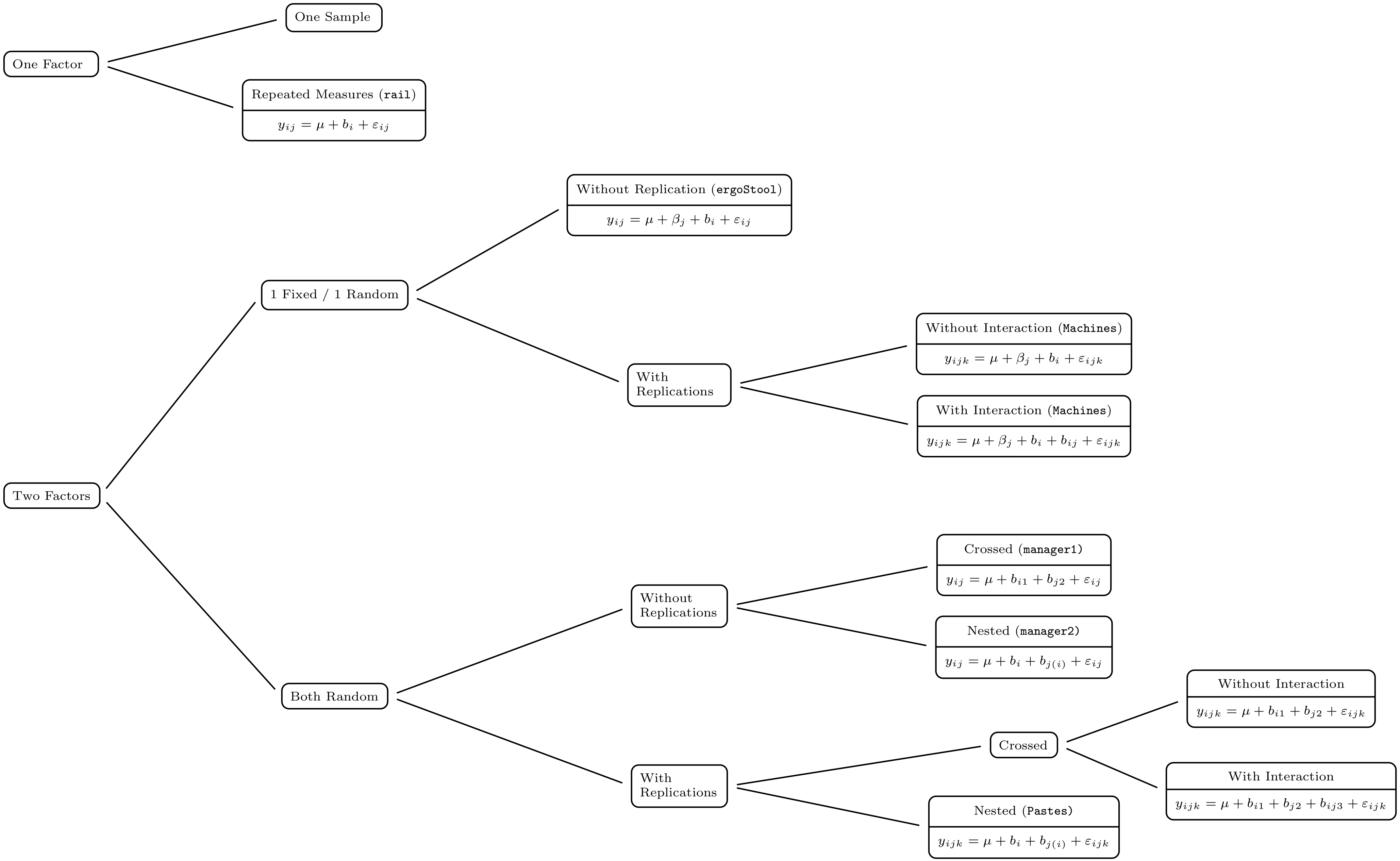
Interest: Expected yield of the different oat varieties depending on fertilizer-concentration, variability between blocks, variability between varieties, error.

Model: $y_{ijk} = \mu + \beta_{j1} + \beta_{k2} + \beta_{jk3} + b_i + b_{k(i)} + \varepsilon_{ijk}, \quad i = 1, \ldots, 6, \quad j = 1, \ldots, 4, \quad k = 1, 2, 3$
β_1 nitrogen-conc. (= subplot) (fix), β_2 crop variety (= plot) (fix),
β_3 interaction nitrogen × variety (fix), b_i block (random), $b_{k(i)}$ variety within block (random)

Assumptions: $b_i \sim \mathcal{N}\langle 0, \sigma^2_{b1} \rangle, \quad b_{k(i)} \sim \mathcal{N}\langle 0, \sigma^2_{b2} \rangle, \quad \varepsilon_{ijk} \sim \mathcal{N}\langle 0, \sigma^2 \rangle, \quad b_i \perp b_{k(i)}, \quad b_i, b_{k(i)} \perp \varepsilon_{ijk}$

R:

```
lme(fixed = yield ~ ordered(nitro) * Variety, random = ~ 1 | Block/Variety, data = Oats)
lmer(yield ~ ordered(nitro) * Variety + (1|Block) + (1|Block/Variety), data = Oats)
```


One Factor
One Sample
Repeated Measures (rail)
$y_{ij} = \mu + b_i + \varepsilon_{ij}$
Two Factors
1 Fixed / 1 Random
Without Replication (ergoStool)
$y_{ij} = \mu + \beta_j + b_i + \varepsilon_{ij}$
With Replications
Without Interaction (Machines)
$y_{ijk} = \mu + \beta_j + b_i + \varepsilon_{ijk}$
With Interaction (Machines)
$y_{ijk} = \mu + \beta_j + b_i + b_{ij} + \varepsilon_{ijk}$
Both Random
Without Replications
Crossed (manager1)
$y_{ij} = \mu + b_{i1} + b_{j2} + \varepsilon_{ij}$
Nested (manager2)
$y_{ij} = \mu + b_i + b_{j(i)} + \varepsilon_{ij}$
With Replications
Crossed
Without Interaction
$y_{ijk} = \mu + b_{i1} + b_{j2} + \varepsilon_{ijk}$
With Interaction
$y_{ijk} = \mu + b_{i1} + b_{j2} + b_{ij3} + \varepsilon_{ijk}$
Nested (Pastes)
$y_{ijk} = \mu + b_i + b_{j(i)} + \varepsilon_{ijk}$