Introduction to mixed models

Session 10

MATH 80667A: Experimental Design and Statistical Methods
HEC Montréal

Outline

Blocking

Mixed effects

Blocking

Terminology for *nuisance*

Block

Source of variation, but of no interest known and controllable

Example

timing
lab technician
machine

Noise factor

Under which setting is response least affected?

Example

temperature
processing

Why blocking?

Design experiment to reduce the effect of uncontrolled variations

In general, increases the power of the F test for treatment effects.

Group units in sets as alike as possible.

(Often) compare only treatments, so interactions are not included.

Assignment to treatment

Divide subjects within each block

Randomly allocate to treatment within block

(stratified sampling)

Block-treatment design

Without interaction,

$$\underset{\text{response}}{Y_{ij}} = \underset{\text{global mean}}{\mu} + \underset{\text{treatment}}{\alpha_i} + \underset{\text{blocking}}{\beta_j} + \underset{\text{error}}{\varepsilon_{ij}}$$

Compromise between

- reduced variability for residuals,
- loss of degrees of freedom due to estimation of β's.

Example: Resting metabolic rate

From Dean, Voss and Draguljić (2017), Example 10.4.1 (p. 311)

> experiment that was run to compare the effects of inpatient and outpatient protocols on the in-laboratory measurement of resting metabolic rate (RMR) in humans. A previous study had indicated measurements of RMR on elderly individuals to be 8% higher using an outpatient protocol than with an inpatient protocol. If the measurements depend on the protocol, then comparison of the results of studies conducted by different laboratories using different protocols would be difficult. The experimenters hoped to conclude that the effect on RMR of different protocols was negligible.

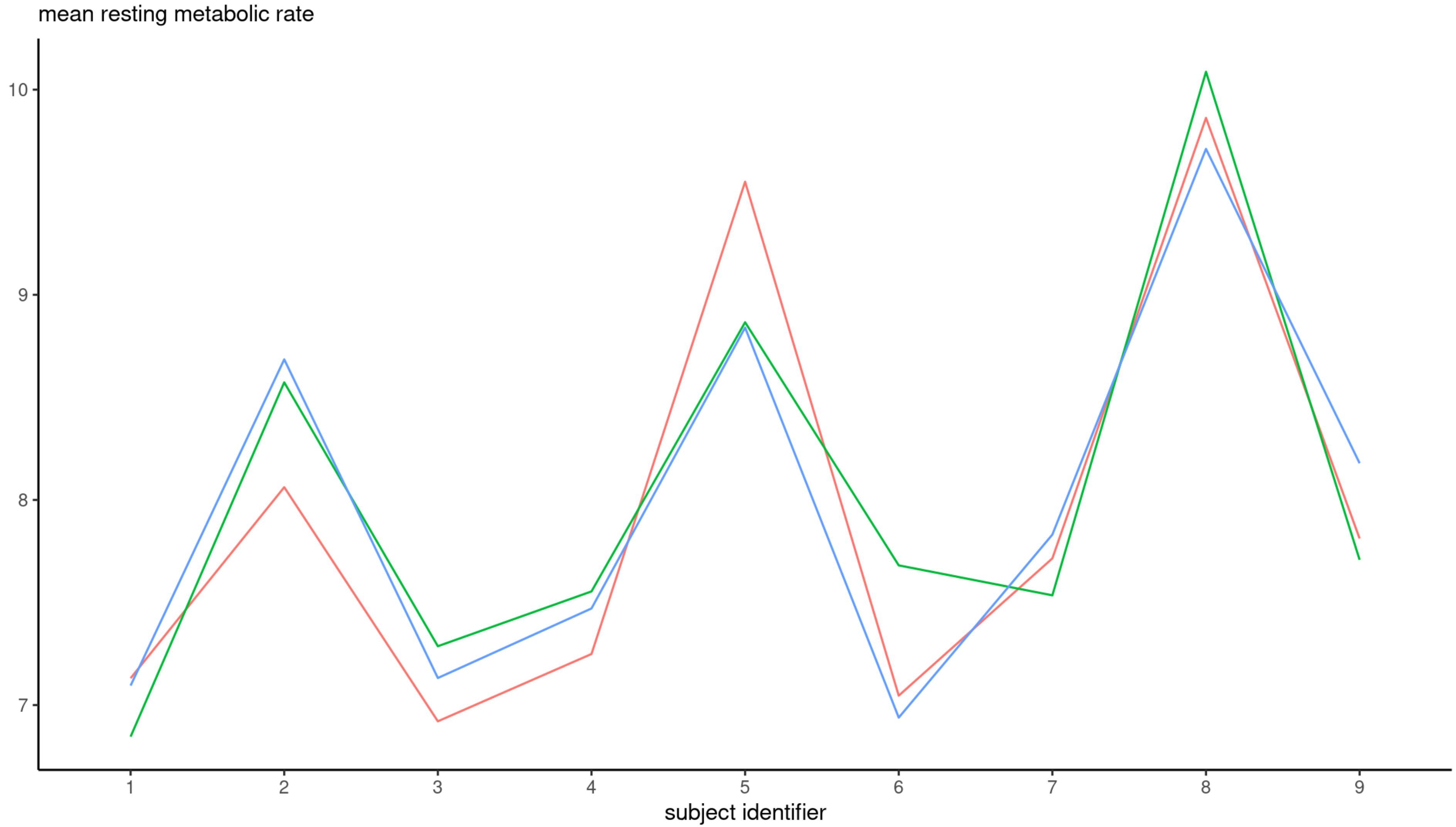
Fitting the complete block design

Load | Fit | Plot

```r
url <- "https://edsm.rbind.io/files/data/resting_metabolic_rate.txt"
# transform integers to factors (categorical)
resting <- read.table(url, header = TRUE) |>
  dplyr::mutate(
    subject = factor(subject), #blocking factor
    protocol = factor(protocol), #experimental factor
    rate = rate/1000)
```

This is *de facto* a repeated measure design.

Interaction plot



Impact of blocking

ANOVA table (with blocking) | ANOVA table (without blocking)

Analysis of variance table - with blocking

	Degrees of freedom	Sum of squares	Mean square	F statistic	p-value
subject	8	23.12	2.89	37.42	0.000
protocol	2	0.04	0.02	0.23	0.795
Residuals	16	1.24	0.08		

Random effects and mixed models

Fixed effects

All experiments so far treated factors as **fixed** effects.

- We estimate a mean parameter for each factor (including blocking factors in repeated measures).

Change of scenery

Change of scenery

Assume that the levels of a factor form a random sample from a large population.

We are interested in making inference about the **variability** of the factor.

- measures of performance of employees
- results from different labs in an experiment
- **subjects in repeated measures**

We treat these factors as **random** effects.

Fixed vs random effects

There is no consensual definition, but Gelman (2005) lists a handful, of which:

> When a sample exhausts the population, the corresponding variable is fixed; when the sample is a small (i.e., negligible) part of the population the corresponding variable is random [Green and Tukey (1960)].
>
> Effects are fixed if they are interesting in themselves or random if there is interest in the underlying population (e.g., Searle, Casella and McCulloch [(1992), Section 1.4])

Random effect model

Consider a one-way model

$$\underbrace{Y_{ij}}_{\text{response}} = \underbrace{\mu}_{\text{global mean}} + \underbrace{\alpha_j}_{\text{random effect}} + \underbrace{\varepsilon_{ij}}_{\text{error term}}.$$

where

- $\alpha_j \sim \mathsf{Normal}(0, \sigma_\alpha^2)$ is normal with mean zero and variance σ_α^2.
- ε_{ij} are independent $\mathsf{Normal}(0, \sigma_\varepsilon^2)$

Fictional example

Consider the weekly number of hours spent by staff members at HEC since September.

We collect a random sample of 40 employees and ask them to measure the number of hours they work from school (as opposed to remotely) for eight consecutive weeks.

Fitting mixed models in **R**

We use the `lme4` package in **R** to fit mixed models.

The `lmerTest` package provides additional functionalities for testing.

- `lmer` function fits linear mixed effect regression

Random effects are specified using the notation `(1 | factor)`.

Model fit

```r
library(lmerTest) # also loads lme4
rmod <- lmer(time ~ (1 | id), data = hecedsm::workhours)
summary_rmod <- summary(rmod)
```

```
Random effects:
 Groups   Name        Variance Std.Dev.
 id       (Intercept) 38.63    6.215
 Residual              5.68    2.383
Number of obs: 320, groups:  id, 40

Fixed effects:
            Estimate Std. Error      df t value Pr(>|t|)
(Intercept)  23.3016     0.9917 39.0000    23.5   <2e-16 ***
```

Note that std. dev is square root of variance

Intra-class correlation

We are interested in the variance of the **random effect**, σ_α^2.

Measurements from the same individuals are correlated. The intra-class correlation between measurements Y_{ij} and Y_{ik} from subject i at times $j \neq k$ is

$$\rho = \frac{\sigma_\alpha^2}{\sigma_\alpha^2 + \sigma_\varepsilon^2}.$$

In the example, $\widehat{\sigma}_\alpha^2 = 38.63$, $\widehat{\sigma}_\varepsilon^2 = 5.68$ and $\hat{\rho} = 0.87$.

The mean number of working hours on the premises is $\widehat{\mu} = 23.3$ hours.

Confidence intervals

We can use confidence intervals for the parameters.

Those are based on profile likelihood methods (asymmetric).

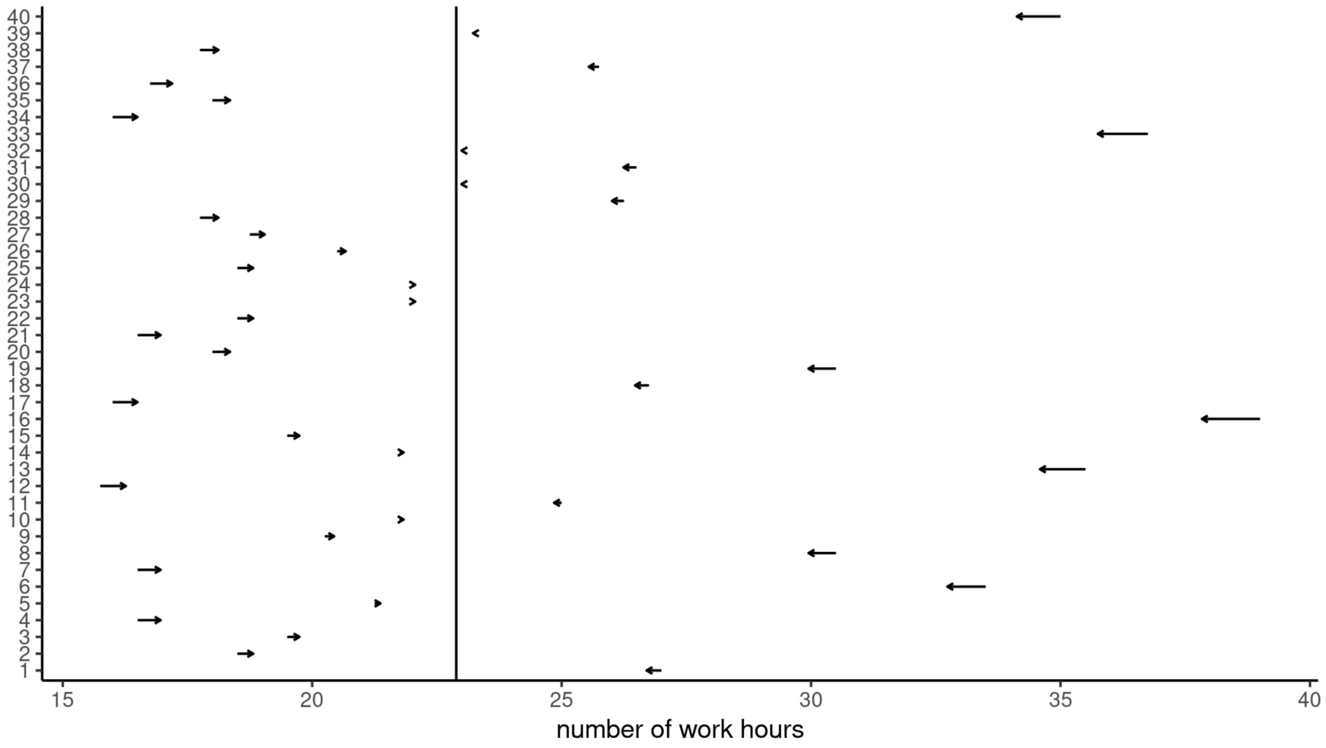
```
(conf <- confint(rmod, oldNames = FALSE))
```

```
##                         2.5 %    97.5 %
## sd_(Intercept)|id  4.978127  7.799018
## sigma              2.198813  2.595272
## (Intercept)       21.335343 25.267782
```

The variability of the measurements and the week-to-week correlation of employee measures are different from zero.

Shrinkage

Fixed versus random effects



Predictions of random effects are shrunk towards global mean, more so for larger values and when there are fewer measurements.

Mixed models

Mixed models include both fixed effects and random effects.

- Fixed effects for experimental manipulations
- Random effects for subject, lab factors

Mixed models make it easier to

- handle correlations between measurements and
- account for more complex designs.

Repeated measures ANOVA using mixed model

Data need to be in long format, i.e., one response per line with an id column.

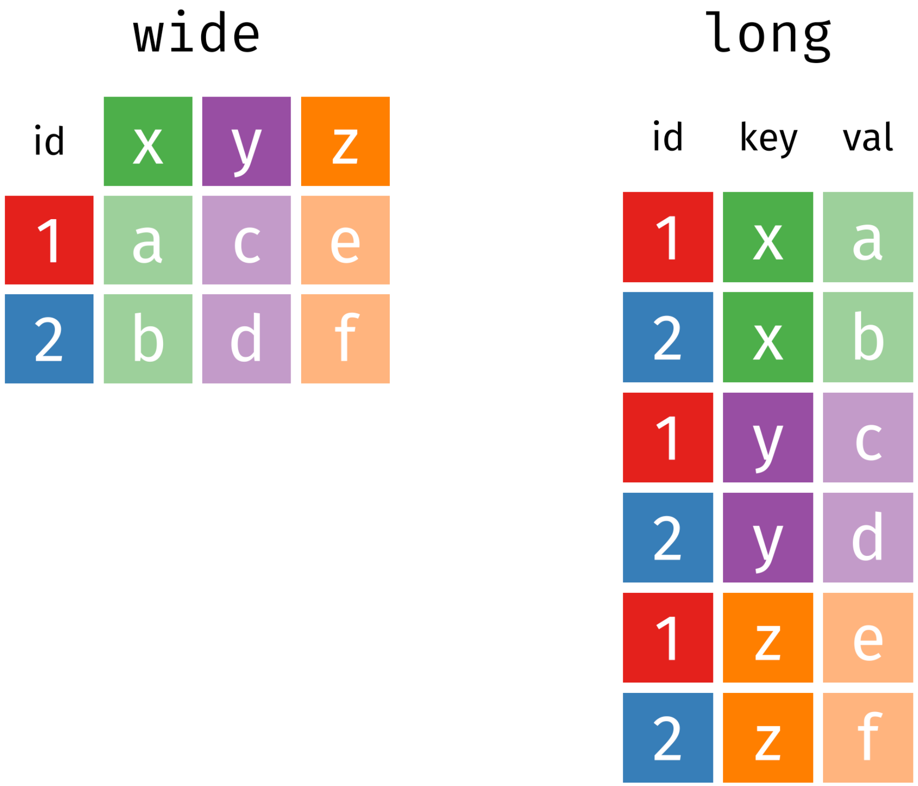


Illustration by Garrick Adden-Buie

Example: two-way ANOVA

We consider a repeated measure ANOVA (2 by 2 design, within-between) from Hatano et al. (2022).

```
data(HOSM22_E3, package = "hecedsm")
fmod <- afex::aov_ez(
  id = "id",
  dv = "imscore",
  between = "waiting",
  within = "ratingtype",
  data = HOSM22_E3)
anova(fmod)
```

```
## Anova Table (Type 3 tests)
##
## Response: imscore
##                     num Df den Df     MSE       F      ges    Pr(>F)
## waiting                  1     61 2.48926 11.2551 0.126246   0.00137 **
## ratingtype               1     61 0.68953 38.4330 0.120236 5.388e-08 ***
## waiting:ratingtype       1     61 0.68953  0.0819 0.000291   0.77575
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Repeated measures with linear mixed models

Results are the same as for repeated measures ANOVA if the correlation estimate between observations of the same id are nonnegative.

```
mixmod <- lmerTest::lmer(
  imscore ~ waiting*ratingtype +
    (1 | id), # random intercept per id
  data = HOSM22_E3)
anova(mixmod, type = 3)
```

```
## Type III Analysis of Variance Table with Satterthwaite's method
##                     Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)
## waiting             7.7608  7.7608     1    61 11.2551   0.00137 **
## ratingtype         26.5009 26.5009     1    61 38.4330 5.388e-08 ***
## waiting:ratingtype  0.0565  0.0565     1    61  0.0819   0.77575
## ---
```

Theory

Full coverage of linear mixed models and general designs is beyond the scope of the course, but note

- Estimation is performed via restricted maximum likelihood (REML)
- Testing results may differ from repeated measure ANOVA
- Different approximations for F degrees of freedom, either
  - Kenward–Roger (costly) or
  - Satterthwaite's approximation

Structure of the design

It is important to understand how data were gathered.

Oelhert (2010) guidelines

1. Identify sources of variation
2. Identify whether factors are crossed or nested
3. Determine whether factors should be fixed or random
4. Figure out which interactions can exist and whether they can be fitted.

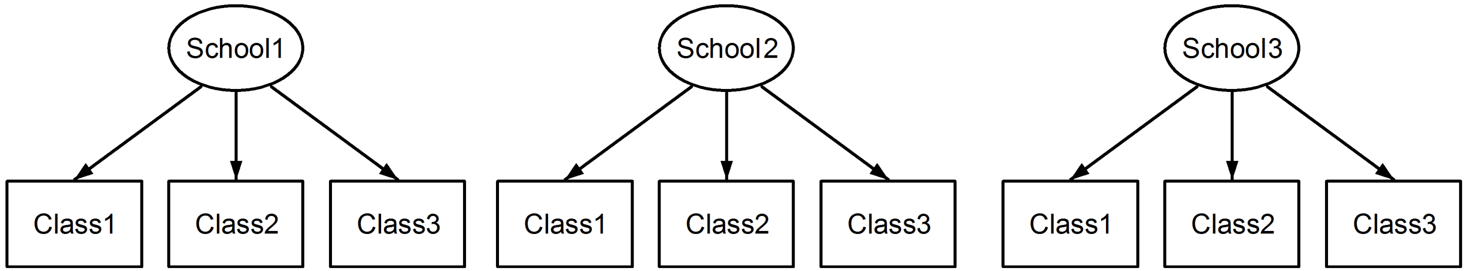
Crossed vs nested effects

Nested effects if a factor appears only within a particular level of another factor.

Crossed is for everything else (typically combinations of factors are possible).

Example of nested random effects: class nested within schools

- class 1 is not the same in school 1 than in school 2



Formulae in **R**

R uses the following notation

- `group1/group2` means `group2` is nested within `group1`.

The formula expands to `group1 + group1:group2`.

- `group1*group2` means `group` and `group2` are **crossed**

The formula is a shorthand for `group1 + group2 + group1:group2`.

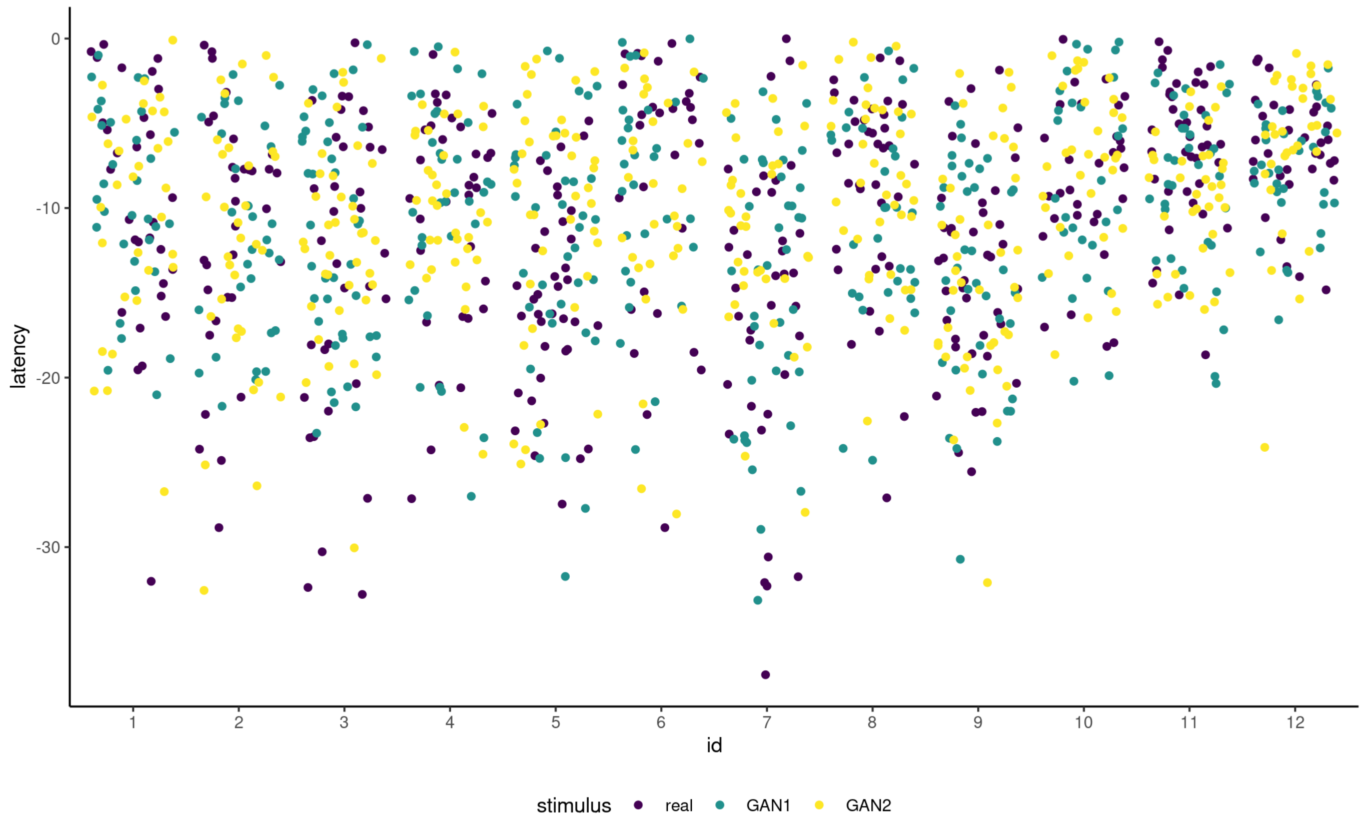
To fit the model, identifiers of subjects must be declared as factors (categorical variables).

Specifying interactions

Consider factors A, B and C.

- If factor A is treated as random, interactions with A must be random too.
- There must be repeated measurements to estimate variability of those interactions.
- Testing relies on the variance components.

Example: happy fakes



Jittered scatterplot of measurements per participant and stimulus type.

Interaction with random and fixed effect

Add student `id` as random effect, `stimulus` as fixed effect and their interaction as random effect (since one parent is random)

```
data(AA21, package = "hecedsm")
anova(ddf = "Kenward-Roger", # other option is "Satterthwaite"
  lmerTest::lmer(
    data = AA21 |> dplyr::filter(latency > -40),
    latency ~ stimulus + (1|id) + (1|id:stimulus)))
```

```
## Type III Analysis of Variance Table with Kenward-Roger's method
##          Sum Sq Mean Sq NumDF  DenDF F value Pr(>F)
## stimulus 65.573  32.786     2 21.878  0.8465 0.4425
```

```
# Approximately 22 degrees of freedom (as for repeated measures)
```

Data structure

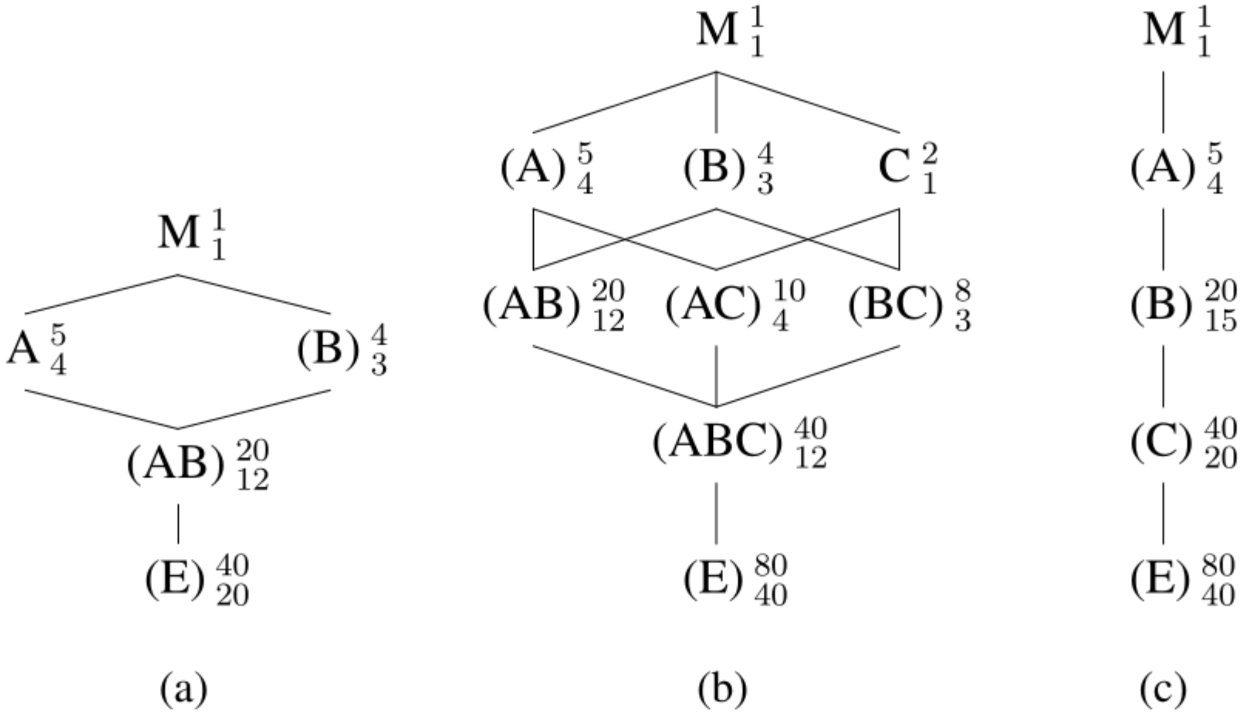


Figure 12.1: Hasse diagrams: (a) two-way factorial with A fixed and B random, A and B crossed; (b) three-way factorial with A and B random, C fixed, all factors crossed; (c) fully nested, with B fixed, A and C random. In all cases, A has 5 levels, B has 4 levels, and C has 2 levels.

Example: Curley et al. (2022)

> Two variables were manipulated within participants: (a) evidence anchor (strong-first versus weak-first); (b) verdict system (two- versus three-verdict systems). Total pre-trial bias score was used as a covariate in the analysis (this score is based on the PJAQ and is explained further in the Materials section). Participants were also given two vignettes (Vignette 1 and Vignette 2); thus, the vignette variable was included in the data analysis [...]
>
> The dependent variable was the final belief of guilt score, which was measured on an accumulated scale from 0–14, with 0 representing no belief of guilt and 14 representing a total belief that the person is guilty

Example: chocolate rating

Example from L. Meier, adapted from Oehlert (2010)

> A group of 10 rural and 10 urban raters rated 4 different chocolate types. Every rater got to eat two samples from the same chocolate type in random order.