Analysis of within-cases normal data[1]

STA312 Fall 2022

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Overview

Independent Observations

- Most statistical models assume independent observations.
- Sometimes the assumption of independence is unreasonable.
- For example, times series and within cases designs.

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- A study can have both within cases and between cases factors.

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- **Longitudinal**: The same variables are measured repeatedly over time. Usually lots of variables, including categorical ones, and large samples. If there's an experimental treatment, its usually once at the beginning, like a surgery. Basically its *tracking* what happens over time.

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- **Longitudinal**: The same variables are measured repeatedly over time. Usually lots of variables, including categorical ones, and large samples. If there's an experimental treatment, its usually once at the beginning, like a surgery. Basically its *tracking* what happens over time.
- **Repeated measures**: Usually, same subjects experience two or more experimental treatments. Usually categorical explanatory variables and small samples.

General Mixed Linear Model

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{b} + \boldsymbol{\epsilon}$$

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- $\mathbf{X}$ is an $n \times p$ matrix of known constants.
- $\boldsymbol{\beta}$ is a $p \times 1$ vector of unknown constants.
- $\mathbf{Z}$ is an $n \times q$ matrix of known constants.
- $\mathbf{b} \sim N_q(\mathbf{0}, \boldsymbol{\Sigma}_b)$ with $\boldsymbol{\Sigma}_b$ unknown but often diagonal.
- $\boldsymbol{\epsilon} \sim N(\mathbf{0}, \sigma^2\mathbf{I}_n)$, where $\sigma^2 > 0$ is an unknown constant.

Random vs. fixed effects

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{b} + \boldsymbol{\epsilon}$$

- Elements of $\boldsymbol{\beta}$ are called fixed effects.
- Elements of $\mathbf{b}$ are called random effects.
- Models with both are called *mixed*.

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- Randomly select 15 homeopathic medicines for arthritis (there are quite a few), and then randomly assign arthritis patients to try them. Drug is a random effects factor.

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- Randomly select 15 homeopathic medicines for arthritis (there are quite a few), and then randomly assign arthritis patients to try them. Drug is a random effects factor.
- Randomly select 15 lakes. In each lake, measure how clear the water is at 20 randomly chosen points. Lake is a random effects factor.

One random factor

A nice simple example

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- Randomly select 10 cows from each farm, milk them, and record the amount of milk from each one.
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- Randomly select 10 cows from each farm, milk them, and record the amount of milk from each one.
- The one random factor is Farm.
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The idea is that “Farm” is a kind of random shock that pushes all the amounts of milk in a particular farm up or down by the same amount.

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$i = 1, \ldots q$ and $j = 1, \ldots, k$

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There are $q = 5$ farms and $k = 10$ cows from each farm.

General Mixed Linear Model Notation

$$
\begin{aligned}
Y_{ij} &= \mu + \tau_i + \epsilon_{ij} \\
\mathbf{Y} &= \mathbf{X}\boldsymbol{\beta} \; + \; \mathbf{Zb} \; + \; \boldsymbol{\epsilon}
\end{aligned}
$$

$$
\begin{pmatrix} Y_{1,1} \\ Y_{1,2} \\ Y_{1,3} \\ \vdots \\ Y_{5,9} \\ Y_{5,10} \end{pmatrix} = \begin{pmatrix} 1 \\ 1 \\ 1 \\ \vdots \\ 1 \\ 1 \end{pmatrix} (\mu) + \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} \tau_1 \\ \tau_2 \\ \tau_3 \\ \tau_4 \\ \tau_5 \end{pmatrix} + \begin{pmatrix} \epsilon_{1,1} \\ \epsilon_{1,2} \\ \epsilon_{1,3} \\ \vdots \\ \epsilon_{5,9} \\ \epsilon_{5,10} \end{pmatrix}
$$

Distribution of $Y_{ij} = \mu + \tau_i + \epsilon_{ij}$

$i = 1, \ldots 10$ cows and $j = 1, \ldots, 5$ farms

- $Y_{ij} \sim N(\mu, \sigma_\tau^2 + \sigma^2)$
- $Cov(Y_{ij}, Y_{i,j'}) = \sigma_\tau^2$ for $j \neq j'$
- $Cov(Y_{ij}, Y_{i',j'}) = 0$ for $i \neq i'$

Classical approach: Skipping lots of details

- Distribution theory.
- Components of variance.
- Testing $H_0 : \sigma_\tau^2 = 0$.
- Extension to mixed models.
- Nested effects.
- Choice of F statistics based on expected mean squares.

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- One can view "subject" as just another random effects factor, because subjects supposedly were randomly sampled.
- Subject would be nested within sex, but might cross stimulus intensity.
- This is the classical (old fashioned) way to analyze repeated measures.

Problems with the classical approach

- Normality matters in a serious way for the tests of random effects.
- Sometimes (especially for complicated mixed models) a valid F-test for an effect of interest just doesn't exist.
- When sample sizes are unbalanced, everything falls apart.
- Hard to incorporate covariates.

A modern approach using the general mixed linear model

$$\mathbf{y} \;=\; \mathbf{X}\boldsymbol{\beta} \;+\; \mathbf{Z}\mathbf{b} \;+\; \boldsymbol{\epsilon}$$

- $\mathbf{y} \sim N_n(\mathbf{X}\boldsymbol{\beta}, \mathbf{Z}\boldsymbol{\Sigma}_b\mathbf{Z}' + \sigma^2 I_n)$
- Estimate $\boldsymbol{\beta}$ as usual with $(\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\mathbf{Y}$.
- Estimate $\boldsymbol{\Sigma}_b$ and σ^2 by maximum likelihood

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- Estimate $\boldsymbol{\Sigma}_b$ and σ^2 by maximum likelihood, or by "restricted" maximum likelihood.

Restricted maximum likelihood

For the record

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{b} + \boldsymbol{\epsilon}$$

- Transform $\mathbf{y}$ by the $q \times n$ matrix $\mathbf{K}$.
- The rows of $\mathbf{K}$ are orthoganal to the columns of $\mathbf{X}$, meaning $\mathbf{KX} = \mathbf{0}$.
- Then

$$\begin{aligned}
\mathbf{Ky} &= \mathbf{KX}\boldsymbol{\beta} + \mathbf{KZb} + \mathbf{K}\boldsymbol{\epsilon} \\
&= \mathbf{KZb} + \mathbf{K}\boldsymbol{\epsilon} \\
&\sim N(\mathbf{0}, \mathbf{KZ}\boldsymbol{\Sigma}_b\mathbf{Z}'\mathbf{K}' + \sigma^2\mathbf{KK}')
\end{aligned}$$

- Estimate $\boldsymbol{\Sigma}_b$ and σ^2 by maximum likelihood.
- A big theorem says the resulting "restricted" MLE does not depend on the choice of $\mathbf{K}$.

Nice results from restricted maximum likelihood

- F statistics that correspond to the classical ones for balanced designs.
- For unbalanced designs, "F statistics" that are actually excellent F approximations — not quite F, but very close.
- R's `nlme4` package and SAS `proc mixed`.

Random Intercept Models for Within-cases

- Drop the complicated classical mixed model machinery.
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- Each subject (person, case) contributes an individual shock that pushes all the data values from that person up or down by the same amount.
- Because cases are randomly sampled (pretend), it's a random shock.
- This is still a mixed model, but it's much simpler.

Example: The Noise study

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- Model:

For $i = 1, \ldots, n$ and $j = 1, \ldots, 3$,

$$Y_{i,j} = \beta_0 + \beta_1 s_i + \beta_2 d_{i,j,1} + \beta_3 d_{i,j,2} + \beta_4 s_i d_{i,j,1} + \beta_5 s_i d_{i,j,2} + b_i + \epsilon_{i,j}$$

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You could say that the intercept is $N(\beta_0, \sigma_b^2)$. It's a *random intercept*.

In matrix form: $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{b} + \boldsymbol{\epsilon}$

For 2 females and 2 males

$$Y_{i,j} = \beta_0 + \beta_1 s_i + \beta_2 d_{i,j,1} + \beta_3 d_{i,j,2} + \beta_4 s_i d_{i,j,1} + \beta_5 s_i d_{i,j,2} + b_i + \epsilon_{i,j}$$

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Continuing $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{b} + \boldsymbol{\epsilon}$

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where $cov(\mathbf{b}) = \sigma_b^2 \mathbf{I}_4$.

lme4

Linear Mixed Effects Models

`lme4`

Linear Mixed Effects Models

- Download and install the package.
- The `lmer` function acts like an extended version of `lm`.
- We will use just a fraction of its capabilities.

Syntax

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noise1 = lmer(discrim ~ sex*noise + (1 | ident))
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  - It creates the $\mathbf{Z}$ matrix in $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{b} + \boldsymbol{\epsilon}$.
  - With a new independent copy for every value of B.

Another example

Compare `noise1 = lmer(discrim ~ sex*noise + (1 | ident))`

- Reaction time tested every day for days 0-9 of sleep deprivation.
- Ten observations on each of 18 subjects.
- Roughly linear, and each subject has her own slope and intercept.

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Random slope and intercept.

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