Kurs Bio144:

Datenanalyse in der Biologie

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Lecture 12 (~~part 2~~): Measurement error in regression models

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Overview

- ME in covariates (x) and in the response (y) of regression models.
- Effects of ME on regression parameters.
- When do I have to worry?
- Simple methods to correct for ME.

Course material covered today

The lecture material of today is partially based on the following literature:

- Chapter 6.1 in “Lineare regression” (BC reading)

Sources of measurement uncertainty / measurement error (ME)

- **Measurement imprecision** in the field or in the lab (length, weight, blood pressure, etc.).
- Errors due to **incomplete** or **biased observations** (e.g., self-reported dietary aspects, health history).
- Biased observations due to **preferential sampling or repeated observations**.
- Rounding error, digit preference.
- **Misclassification error** (e.g., exposure or disease classification).
- ...

"Error" is often used synonymous to "uncertainty".

The fundamental assumptions of regression analyses

A fundamental assumption always is that some **distributional assumptions are fulfilled**, for example:

- **Linear regression (including ANOVA):**

$$\epsilon_i \sim \mathsf{N}(0, \sigma^2) \ .$$

- **Generalized linear model:** Implicit assumptions that can be checked by model diagnostic plots.

Another fundamental assumption (often neglected!)

- It is a fundamental assumption that explanatory variables are measured or estimated without error, for instance for
  - the calculation of correlations.
  - linear regression and ANOVA.
  - Generalized linear and non-linear regressions (e.g. logistic and Poisson).
- Violation of this assumption may lead to biased parameter estimates, altered standard errors and p-values, incorrect covariate importances, and to misleading conclusions.
- Even standard statistics textbooks do often not mention these problems.

$\rightarrow$ Measurement error in the covariates ($\mathbf{x}$) violates an assumption of standard regression analyses!!

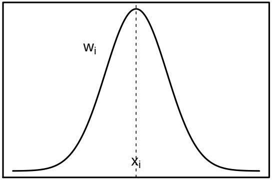
Classical measurement error

A very common error type:

Let x_i be the **correct but unobserved** variable and w_i the observed proxy with error u_i. Then

$$
\begin{aligned}
w_i &= x_i + u_i \\
u_i &\sim \mathrm{N}(0, \sigma_u^2) \quad ,
\end{aligned}
$$

is the **classical ME model**.



Examples: Imprecise measurements of a concentration, a mass, a length etc.

$\rightarrow$The observed value w_i varies around the true value x_i.

Illustration of the problem

Find regression parameters β_0 and β_x for the model with covariate $\mathbf{x}$:

$$y_i = 1 \cdot x_i + \epsilon_i , \quad \epsilon_i \sim \mathrm{N}(0, \sigma^2) \ .$$

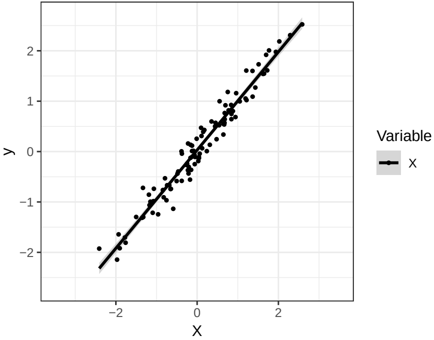
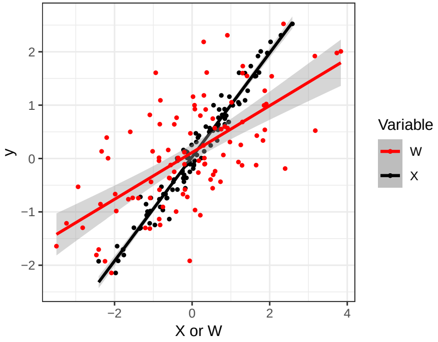


Illustration of the problem II

However, assume that only an erroneous proxy **w** is observed with classical ME

$$w_i = x_i + u_i \ , \qquad u_i \sim \mathrm{N}(0, \sigma_u^2) \quad \text{with} \quad \sigma_u^2 = \sigma_x^2 \ .$$



Simulations and apps

Illustration with shiny apps for two error types in linear, logistic and Poisson regression:

- Classical error
- Berkson error

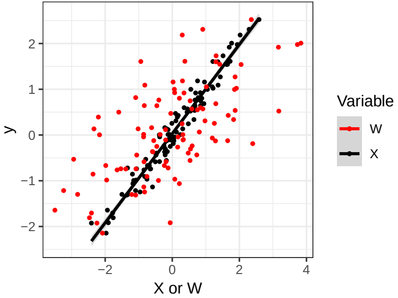
The “Triple Whammy of Measurement Error”

(Carroll et al., 2006)

1. Bias: The inclusion of erroneous variables in downstream analyses may lead to biased parameter estimates.

2. ME leads to a loss of power for detecting signals.

3. ME masks imporant features of the data, making graphical model inspection difficult.



How to correct for error?

- Generally, to correct for the error we need an **error model** and knowledge of the **error model parameters**.

  Example: If classical error $w_i = x_i + u_i$ with $u_i \sim \mathrm{N}(0, \sigma_u^2)$ is present, knowledge of the **error variance** σ_u^2 is needed.

  Strategy: Take repeated measurements to estimate the error variance!

- In simple cases, formulas for the bias exist.
- In most cases, such simple relations don't exist. Specific error modeling methods are then needed!

Attenuation in simple linear regression

Given the simple linear regression equation $y_i = \beta_0 + \beta_x x_i + \epsilon_i$ with $w_i = x_i + u_i$. Assume that w_i instead of x_i is used in the regression:

$$y_i = \beta_0^\star + \beta_x^\star w_i + \epsilon_i \ .$$

The **naive slope parameter** $\beta_x^\star$ is then underestimated with respect to the true slope β_x, with **attenuation factor** λ:

$$\beta_x^\star = \underbrace{\left(\frac{\sigma_x^2}{\sigma_x^2 + \sigma_u^2} \right)}_{=\lambda} \beta_x \ .$$

$\rightarrow$ knowing σ_u^2 and σ_x^2, the correct slope can be retrieved!

Example: $\sigma_x^2 = 5$, $\sigma_u^2 = 1 \rightarrow \lambda = \frac{5}{6} = 0.83$.

Error modeling

The **two most popular approaches**:

- **SIMEX**: SIMulation EXtrapolation, a heuristic and intuitive idea.
- **Bayesian methods**: Prior information about the error enters a model. Then use
$$\text{Likelihood} \times \text{prior} = \text{posterior}$$
to calculate the parameter distribution after error correction.

In any case, assessing the biasing effect of the error, as well as error modeling, can be done only if the error structure (model) and the respective model parameters (e.g., error variances) are known!

Therefore: Information about the error mechanism is essential, and potential errors must be identified already in the planning phase.

SIMEX: A very intuitive idea

Suggested by Cook and Stefanski (1994).

Idea:

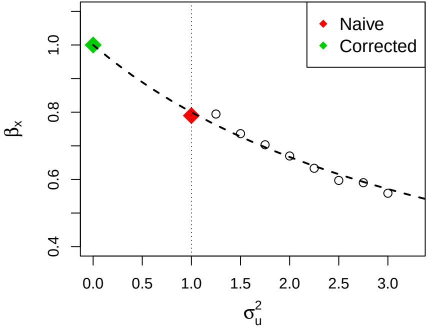
- **Simulation phase:** The error in the data is progressively aggravated in order to determine how the quantity of interest is affected by the error.
- **Extrapolation phase:** The observed trend is then extrapolated back to a hypothetical error-free value.

Illustration of the SIMEX idea

Parameter of interest: β_x (*e.g.* a regression slope).

Problem: The respective covariate x was estimated with error:

$$w = x + u \; , \quad u \sim \mathrm{N}(0, \sigma_u^2) \; .$$



Example of SIMEX use

Let's consider a linear regression model

$$y_i = \beta_0 + \beta_x x_i + \beta_z z_i + \epsilon_i \ , \quad \epsilon_i = \mathrm{N}(0, \sigma^2)$$

with

- $\mathbf{y} = (y_1, \ldots, y_{100})^\top$: variable with % Bodyfat of 100 individuals.
- $\mathbf{x} = (x_1, \ldots, x_{100})^\top$ the BMI of the individuals.
  Problem: The BMI was self-reported and thus suffers from measurement error! Not x_i are observed, but rather

  $$w_i = x_i + u_i \ , \quad u_i \sim \mathrm{N}(0, 4) \ .$$

- $\mathbf{z} = (z_1, \ldots, z_{100})^\top$ a binary covariate that indicates if the i-th person was a male ($z_i = 1$) or female ($z_i = 0$).

$\rightarrow$ Apply the SIMEX procedure!

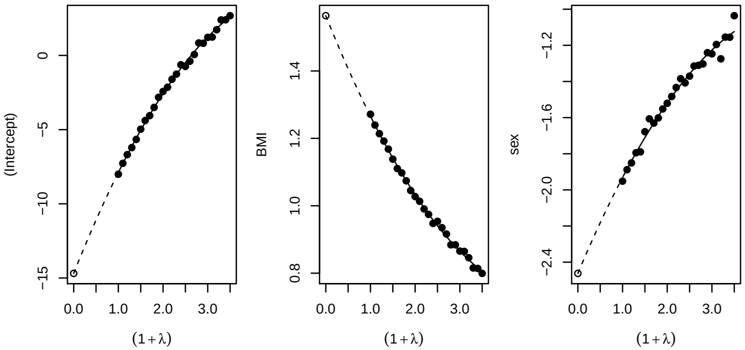
Use the error-prone BMI variable to fit a "naive" regression:

```
r.lm <- lm(bodyfat ~ BMI + sex,data,x=TRUE)
summary(r.lm)$coef

##              Estimate Std. Error   t value     Pr(>|t|)
## (Intercept) -8.003714 2.07060335 -3.865402 2.005407e-04
## BMI          1.271558 0.08821382 14.414504 7.478782e-26
## sex         -1.951735 0.73625960 -2.650879 9.376840e-03
```

Then run the simex procedure using the `simex()` function from the respective package:

```
library(simex)
r.simex <- simex(r.lm,SIMEXvariable="BMI",measurement.error=sqrt(4),
                 lambda=seq(0.1,2.5,0.1),B=100,fitting.method="quadratic")
summary(r.simex)$coef$asymptotic

##               Estimate Std. Error   t value     Pr(>|t|)
## (Intercept) -14.689940  2.6954519 -5.449899 3.825138e-07
## BMI           1.564059  0.1159075 13.494022 5.467540e-24
## sex          -2.462127  0.7906688 -3.113980 2.426632e-03
```

Graphical results with quadratic extrapolation function:



Note: The `sex` variable has *not* been mismeasured, nevertheless it is affected by the error in BMI!

Reason: `sex` and BMI are correlated.

Practical advice

- Think about error problems **before** you start collecting your data!
- Ideally, take **repeated measurements**, maybe of a subset of data points.
- Figure out if error is a problem and what the bias in your parameters might be. You might need simulations to find out.
- If needed, model the error. **Seek help from a statistician!**

References:

Carroll, R. J., D. Ruppert, L. A. Stefanski, and C. M. Crainiceanu (2006). *Measurement Error in Nonlinear Models: A Modern Perspective* (2 ed.). Boca Raton: Chapman & Hall.

Cook, J. R. and L. A. Stefanski (1994). Simulation-extrapolation estimation in parametric measurement error models. *Journal of the American Statistical Association 89*, 1314–1328.