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LME4CENS: Linear Mixed Models with Censored Observations

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Background

An observation Y is censored if it is only known to have occurred within a certain interval. In regression analysis this phenomenon is well-known in time-to-event regression, but it also occurs when there is a detection limit in the device that measures Y, e.g. if a concentration is not known exactly but only that it is below a lower limit.

Linear mixed model regression allows to model hierarchical data, using a parametric approach. Simple linear mixed models with censored observations can be fitted in the statistical software R via add-on packages (e.g. censReg[1]) but not via lme4, R's main package for mixed model package.

Methods

A linear mixed model is described by the n-dim. random vector $Y \in \mathbb{R}^n$ of responses and the q-dim. vector $B \in \mathbb{R}^q$ of random effects. B is not observed but is supposed to follow a central normal distribution,

$$\mathbf{B \sim \mathcal{N}(0, \Sigma_\theta)}$$

The conditional distribution of Y given B = b is modelled as multivariate normal with mean described by the contribution of fixed effects ($X\beta$) and random effects (Zb):

$$\mathbf{Y_{|B=b} \sim \mathcal{N}(X\beta + Zb, \sigma^2 \mathcal{I}_n)}$$

In the framework of maximum likelihood (ML) the parameters of the linear mixed model — the fixed effects coefficients β and the variance parameters σ^2 and θ — are estimated by maximising the likelihood function

$$\mathbf{L(\theta, \beta, \sigma^2 \mid y) = f_Y(y) = \int f_{Y,B}(y,b)\, db = \int f_{Y|B}(y \mid b) \cdot f_B(b)\, db}$$

Censored observations make that the multivariate conditional density $f_{Y|B}$ involves the cumulative normal distribution function Φ. The integral complicates the optimisation of the likelihood function but numeric integration via Gauß-Hermite rule is an efficient solution.

Results

We have implemented simple linear mixed models with censored observations in our new R-package lme4cens[2]. The rationale for the development of lme4cens was to achieve a tight integration with R's standard packages. In lme4cens, censored observations are encoded via Surv-objects from R's survival-package so that censoring levels are specified per observation and left-, right- and interval-censoring is supported.

lme4cens leverages the well-known model specification formalism from lme4. A linear random-intercept model fit in lme4cens for panel data with response variable distance, between-subject variable sex and within-subject variable age would read:

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lmercens(Surv(distance, status) ~ sex + age + (1|SubjectID),
                      data = dataf)
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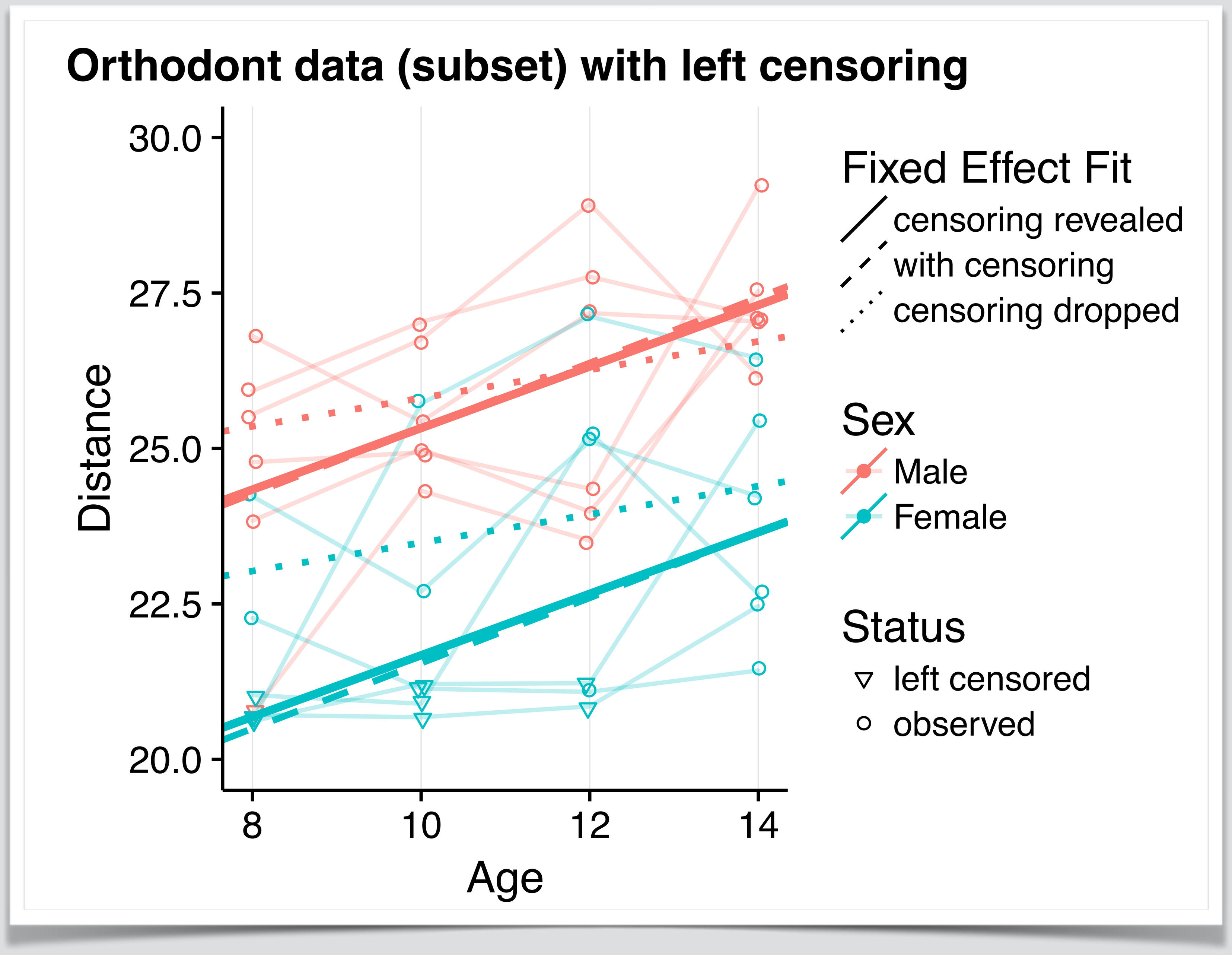
As an example, we show a subset of the well-known Orthodont panel dataset and applied random left censoring for the lower range of the response variable. The fit with censoring (dashed line) recovers the best fit when full data is available (solid line). When the censored observations are dropped the resulting fit (dotted line) shows a biased intercept and an attenuated slope.



Discussion

We introduce the new R-package lme4cens[2] for fitting simple linear mixed models where the response contains censored observations. It inherits notational features from the standard R-packages survival and lme4. We aim to further integrate lme4cens into lme4's modular structure, i.e. make use of lme4's optimisation and output module.[3]

Currently, lme4cens only supports simple random-intercept models. We plan next to implement linear mixed-models for censored observations with more complex random-effect structures. The ultimate goal is to support also non-linear mixed models with censored observations as this was our initial motivation to get started.

1. Arne Henningsen (2017). censReg: Censored Regression (Tobit) Models. R package version 0.5-26. https://CRAN.R-project.org/package=censReg
2. Available at https://github.com/lenz99-/lme4cens
3. Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. Journal of Statistical Software, 67(1), 1 - 48. doi:http://dx.doi.org/10.18637/jss.v067.i01

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