This exercise sheet concentrates on the concrete estimation of the fixed effects in linear and marginal mixed models under different assumptions for the correlation structure, as well as on appropriate test procedures for the fixed effects. The exercises refer to the content of the fourth and fifth lecture slides.

Exercise 1: (Remainder of sheet 2)

Consider now the following model:

$$\texttt{RESPONSE}_{ij} = \beta_0 + \beta_1 \texttt{logT}_{ij} + \beta_2 \texttt{GROUP1}_i + \beta_3 \texttt{GROUP2}_i + \beta_4 \texttt{GROUP1}_i \cdot \texttt{logT}_{ij} + \beta_5 \texttt{GROUP2}_i \cdot \texttt{logT}_{ij} + b_{0i} + \varepsilon_{ij}.$$

Is it reasonable to assume that the random effects assumption is fulfilled here? Give reasons for your answer.

Exercise 2:

In this exercise, we are working with the orthodontic growth data from the data set `Orthodont` included in the package `nlme`, which is already in `groupedData` format. The data set contains measurements of jaw sizes of 27 boys and girls aged 8 to 14 years.

a) Familiarize yourself with the data and their grouping structure at first. For this purpose use `?Orthodont`, `str(Orthodont)` and `getGroups(Orthodont)`.

b) For the following analysis transform the ages of the children as follows

$$\texttt{newage}_{ij} = (\texttt{age}_{ij} - 11),\ i = 1, \ldots, N,\ j = 1, \ldots, n_i.$$

What could be the reason for this transformation of age?

c) Now estimate the random intercept model `m_RI`

$$Y_{ij} = \beta_0 + \beta_1 \texttt{newage}_{ij} + \beta_2 \texttt{Sex}_i + b_{0i} + \varepsilon_{ij}.$$

d) The function `lme()` uses REML estimation by default.

- **i)** Now estimate the model `m_RI` again with the ML method (`method='ML'`) and name the new model `m_RI_ml`.
- **ii)** Compare the resulting covariance matrix of the random effects with the one resulting from the REML estimation.
- **(iii)** Compare also the estimated fixed effects of the two options.

What do you notice?

e) Based on content-related considerations the interaction of sex and age of the children will now be included in the model. Extend and fit the model `m_RI` and name it `m_RI_int`.

i) Regarding the content, does it seem appropriate to include this interaction? How would you interpret such an effect?

ii) To test the utility of this extension, the following test is performed: `anova(m_RI,m_RI_int)`. Why is this test inadmissible? What about the test, which is performed in `R` by default? Name possible alternatives.

f) Now marginal models with different assumptions for the correlation structure shall be compared. Such marginal models can be estimated in `R` with the function `gls()` (**G**eneralized **L**east **S**quares) (cp. sheet 1).

(i) Estimate a model with the same fixed effects as before (incl. interaction). Assume that measurements between subjects are independent and specify an unstructured correlation structure for measurements within a subject.

Compare the estimated correlation matrix with the correlation matrix, which results from the marginal approach of the model `m_RI_int`. Interpret the result.

(ii) Now estimate a model with simplified correlation structure which corresponds to the marginal correlation structure of the model `m_RI_int`.

(iii) Is the model suggested in (ii) equivalent to `m_RI_int`? Give reasons for your answer.