TU Dortmund University
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Statistics in toxicology – Exercise sheet 3

Exercise 4: 4pLL model (7 points)

Consider the 4pLL model as defined in Chapter 3.2, slide 5 of the lecture:

$$y = \theta_1 + \frac{\theta_4 - \theta_1}{1 + \exp\left((x - \theta_2)\theta_3\right)}$$

(a) Calculate the slope of the 4pLL model at the concentration θ_2.

(b) Show that for $\theta_3 > 0$, it holds $\lim_{x \to \infty} \theta_1 + \frac{\theta_4 - \theta_1}{1+\exp((x-\theta_2)\theta_3)} = \theta_1$ and that for $\theta_3 < 0$, it holds $\lim_{x \to \infty} \theta_1 + \frac{\theta_4 - \theta_1}{1+\exp((x-\theta_2)\theta_3)} = \theta_4$.

(c) Show the equivalence of the (sigmoidal) Emax model as defined in Chapter 3.2, slide 25 to the 4pLL model. Define the parameters of the (sigmoidal) Emax model in terms of the parameters $\theta_1, \theta_2, \theta_3, \theta_4$.
Hint: Use the second parameterization of the 4pLL model as defined in Chapter 3.2, slide 21.

Exercise 5: 3pLL model with treatment effects (8 points)

The R-dataset `SimulatedTreatmentEffect-3pLL.RData` contains simulated concentration-response data for three treatments. The column `conc` contains the log-transformed concentration values (where a very small constant was added to concentration 0 in order to log-transform it). The response values are stored in the column `resp`, and the column `treat` contains information about the treatment. Note that for the third treatment, only measurements for the control are available.
Use the function `gnls` from the R-package `nlme` to fit the following models to the dataset:

(a) Fit a 3pLL-model, where the lower asymptote, i.e. parameter θ_1, is fixed to take a value of 0, to the entire dataset. Do not differentiate between treatments. Use code analogously to Chapter 3.2, slide 12 of the lecture. For the argument `start`, use the vector $(1, 2, 100)$, and for the argument `control` use the same settings as in the lecture. Interpret the resulting parameter estimates.

(b) Fit a 3pLL-model ($\theta_1 = 0$) to the dataset. Here, a differentiation between the treatments should be made: For this, create three dummy variables as explained in Chapter 3.2, slide 15 of the lecture. Similar to the situation from the lecture, the third treatment is used for the estimation of the upper asymptote (i.e. parameter θ_4) only. In contrast to the example from the lecture, no parameter is shared across treatments. Use the same starting values and control arguments as before. Interpret the resulting parameter estimates.

(c) Fit a 3pLL-model ($\theta_1 = 0$) to the dataset. Now, parameter θ_4 is shared across all three treatments and θ_2 and θ_3 are estimated separately for the first and the second treatment (i.e. the `params` argument is of the form (th21+th22+th31+th32+th4 $\sim$ 1)). Use the same starting values and control arguments as before. Interpret the resulting parameter estimates.

(d) Are the models from (a) and (b) equivalent? Perform a likelihood-ratio test analogously to Chapter 3.2, slide 18 of the lecture and interpret the result.

Upload the processed exercise sheets in the Moodle until Wednesday, 27 April 2022, 14:15. Please note the information listed in the Moodle on the submission formalities for this course.