

Statistics in toxicology – Exercise sheet 2

Exercise 2: PAVA I (7 points)

In a toxicological dose-response-study with a control x_1 and six increasing doses $x_2 < x_3 < x_4 < x_5 < x_6 < x_7$, the maximum-likelihood estimates of the responses are denoted by $\hat{\mu}(x_i)$ and the sample sizes by n_i , $i = 1, \dots, 7$. The values are given by

Concentration	x_1	x_2	x_3	x_4	x_5	x_6	x_7
$\hat{\mu}(x_i)$	0.5	2.5	1.5	4.5	2	1.5	5
n_i	3	3	7	8	6	4	2

- Perform the PAVA algorithm on the data by hand to obtain the isotonic regression.
- Using the data calculate the values for the CSD (cumulative sum diagram) by hand and plot the CSD and the GCM (greatest convex minorant). Explain, how the pooling performed by the PAVA algorithm is represented in this plot. State the number of final sets and explain, how this number can be retrieved from this plot.

Exercise 3: PAVA II (8 points)

The file `Simulated-Isotonic.RData` contains the concentration-gene expression data for three fictional, simulated genes for a control (concentration 0) and five increasing concentrations 1 to 5. The corresponding sample sizes are given by $(4, 3, 5, 6, 4, 5)$, such that for each gene, 27 measurements are available.

Using the R-package `Iso` and the function `pava`, perform the following three analyses for each gene separately:

- Perform an isotonic regression for the original data as introduced in the lecture.
- Perform an antitonic regression for the original data by setting the argument `decreasing = TRUE` in the `pava`-function.
- Now reverse the data by considering -concentration as predictor (see Chapter 2, slide 24 in the lecture). Perform an isotonic regression for the reversed data.

For each of the analyses, plot the unrestricted means together with the result from the iso-/antitonic regression. Interpret the results for each gene separately.

Upload the processed exercise sheets in the Moodle until Wednesday, 20 April 2022, 14:15. Please note the information listed in the Moodle on the submission formalities for this course.