Comparison of observation-based and model-based identification of alert concentrations

In many toxicological assays or when measuring gene expression data, a response variable is measured for increasing concentrations of a compound and a negative control. The general goal in these cases is to determine an 'alert concentration', where a critical level of the response variable is exceeded.

This can be done in a discrete ('observation-based') way by only considering the concentrations at which the effect was actually measured, or in a continuous ('model-based') way by first fitting a parametric dose-response-curve (DRC) to the data. When not only the concentration at which a threshold is exceeded is of interest, but the concentration at which a threshold is exceeded significantly, the t-test or the Dunnett-procedure that adjusts for multiplicity can be used for discrete testing of the concentrations.

We propose a normal-distribution based test that can be applied to a fitted DRC to assess whether the response at a specific concentration significantly exceeds a threshold compared to the response for the negative control. In a simulation study, we compare the classical t-test, the Dunnett-procedure and the newly proposed test in different situations of real concentration-response-relations.

The simulations are based on the assumption that the true relation between concentration and response is sigmoidal-shaped and can therefore be modelled by a four-parameter log-logistic function.