Internal Standard Calculations for Non-linear Detectors

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Internal Standard (ISTD) is a well-known chromatographic technique, where known amount of a component, called internal standard is added to both standard and unknown samples. The classic Internal Standard quantification method plots the response ratio (analyte to internal standard) versus amount ratio (again analyte to internal standard). Internal standard component itself does not have any calibration curve. Quantification procedure uses this plot to get concentration ratio from response ratio.

This approach may cause systematic errors in the case of non-linear (or linear, not going through origin) detector response to concentration of internal standard. In most softwares it is recommended to keep amount of internal standard in this case precisely constant.

Offered calculation scheme allows wide variations of standard and analyte concentrations. In the case of non-directly proportional dependencies it requires that External standard dependencies of both internal standard component and analyte are measured from time to time. Internal standard calculations are split into two parts:

1. Calculation of Relative concentration, i.e. concentration of analyte, provided concentration of Internal Standard is known.

2. Improvement of calibration curves of the analytes.

The calculation scheme can be further extended to the case of linear dependencies and can successfully replace the method with response ratio calculations.

The described calculation scheme is successfully implemented for Internal Standard calculations in commercial chromatographic software.