

Calibration overview

Instrument Calibration

- What do we want from the calibration?
 - Accurate translation of instrument response to analyte amount
 - Minimize the errors introduced by the calibration itself



What sort of error do we want to minimize?

	Relative error	Absolute error
100 ± 1	1%	1
1 ± 1	100%	1

Relative vs. Absolute Errors

- How does the system behave?
- Which kind of error are we measuring with our QC?
- Which is more important from the risk standpoint?

Characteristics of Variance

- Method 3520/8270, 8 replicates prepared and analyzed at 100ppb, 10ppb, 1ppb
Average of 84 analytes

	100ppb	10ppb	1ppb
Std. Dev.	4.163	0.610	0.042
SD relative to 1ppb SD	88	13	1

What do we care most about?

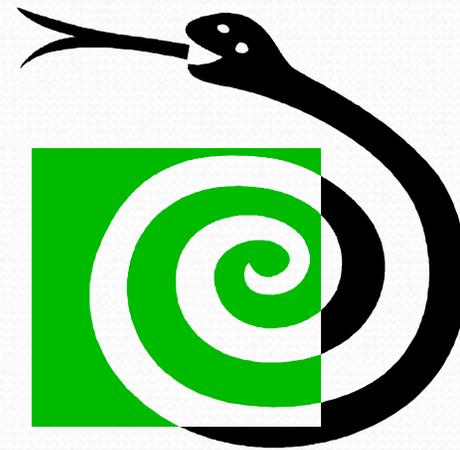
Calibration curve 1-100ppb

- Do we prefer and expect:
 - +/- 5ppb at all levels (Absolute error)
 - +/- 10% at all levels (Relative error)

True	1	10	25	50	100
+/- 5	(-4) - 6	5-15	20-30	45-55	95-105
+/-10%	0.9-1.1	9-10	22.5-27.5	45-55	90-110

Risk

The difference in risk level between a concentration of 100 and 110 is small, but the difference between 0 and 1 may be very large.



What do we need

- A calibration fit that minimizes relative error
- A way of measuring and assessing the relative error against a limit and comparing different curve fits

Current calibration options

- Average response factor
- Regression, Linear or Quadratic
- Weighting
 - Important if variance changes with concentration and we want to reduce relative error
 - Average RF = linear regression with $1/x^2$ weighting and forced through the origin
- Single point plus blank

Unweighted linear regression

- Unweighted regressions minimize the square of the absolute residuals
 - In a calibration from 1-100, an error (residual) of 5 at the 1.0 point has the same weight as an error of 5 at the 100 point.

Coleman and Vanatta

- 40 part series in American Laboratory
 - Proposes approaches that use a large quantity of data, typically several runs at each concentration, in order to fully characterize the response/concentration relationship
 - Cost/Benefit?

Evaluation of calibration curves

- Average Response Factor
 - % Relative Standard Deviation
- Linear or quadratic regression
 - Correlation coefficient (r) or Coefficient of Determination (r^2)

Correlation coefficient

- For most applications, and calibration curves in particular, the correlation coefficient must be regarded as a relic of the past
 - Meier and Zund, *Statistical Methods in Analytical Chemistry*, 2000

Correlation coefficient

- The correlation coefficient in the context of linearity testing is potentially misleading and should be avoided
 - Royal Society of Chemistry, Technical brief
- The author has seen cases where a correlation coefficient of 0.997 was believed to be a better fit than 0.996 of a 5 point calibration curve. One can even find requirements in quality assurance plans to recalibrate if the correlation coefficient is less than 0.995!
 - Taylor, Statistical Techniques for Data Analysis, 1990

IUPAC

- Guidelines for calibration in Analytical Chemistry, 1998
 - The correlation coefficient which is a measure of relationship of two random variables, has no meaning in calibration....because the values x are not random quantities in the calibration experiment

Correlation coefficient

- One practice that should be discouraged is the use of the correlation coefficient as a means of evaluating goodness of fit of linear models
 - Van Arendonk and Skogerboe, *Anal. Chem.* 53, 1981, 2349-2350

Premise

- The Correlation coefficient (and the coefficient of determination) are pretty much useless for evaluating the suitability of a calibration curve

Recent developments

- Relative Standard Error
 - Behaves in a similar way to RSD, but is applicable to all types of curves
- Evaluation of residuals

Calibration for Non-detects

- In Environmental analysis, most analytes are non-detects – some are always non-detects
- Currently, the same requirements as for detected analytes
- **Why?**

What we want a Procedure To Do

- Curve evaluation
 - Evaluate relative error
 - Encourage simpler calibration fits
 - Provide a way to compare different curve fits effectively
 - Straightforward calculations
 - Allow assessment against a limit
 - Easy application to existing methods