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