Linearity, linear range, sensitivity

Linearity

Methods ability to obtain signals which are **directly proportional** to the concentration of analyte in the sample.

Linear range

Range of concentrations where the signals are directly proportional to the concentration of the analyte in the sample.

Sensitivity

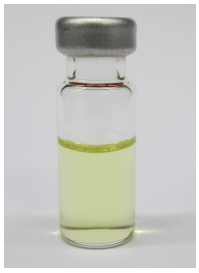
The change in instrument response which corresponds to a change in the measured quantity.

The **gradient** of the response curve.

Experiment planning for evaluation of linearity

- Type of calibration samples
- Concentration range
- Number of concentration levels
- Measurement protocol

Type of calibration samples



- Standard solutions
  - matrix-free
- Matrix-containing samples
  - Matrix-matched calibration
  - Blank matrix extract (preferably the same type as the sample)

Concentration range

- Appropriate for the method
  - Expected working range ± 10%…20%
  - 70%…130% of expected analyte concentration
  - Blank sample

Number of concentration levels

- Minimum 6 concentration levels are acceptable
  - Suggested 10
  - Evenly placed
  - Prepared from independent dilutions

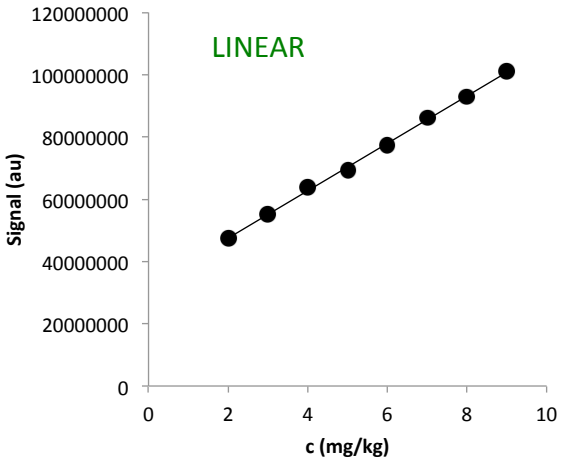
Measurement protocol

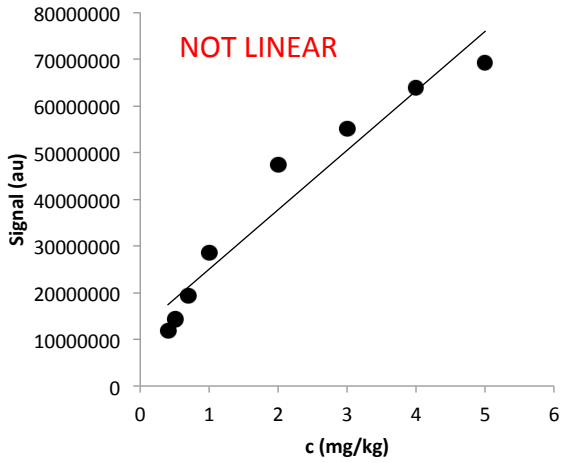
- As similar as possible to the real life situation
  - Random order
  - Between the samples
- Analysed at least twice

Evaluation of linearity

- Visual evaluation
- Residuals

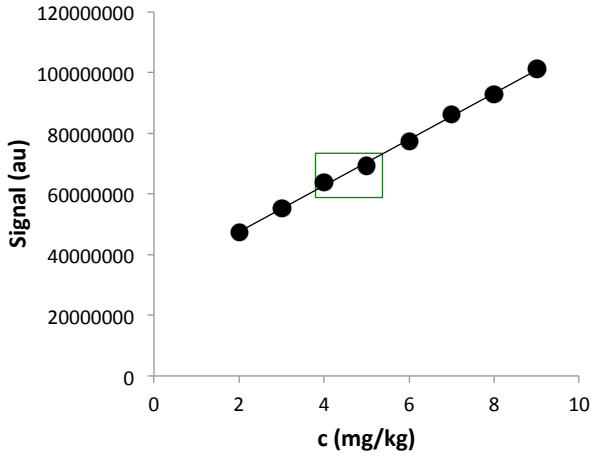
Visual evaluation

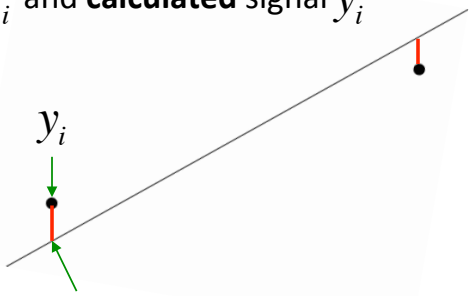




Residual

- Difference between **experimental** signal y_i and **calculated** signal $\hat{y}_i$

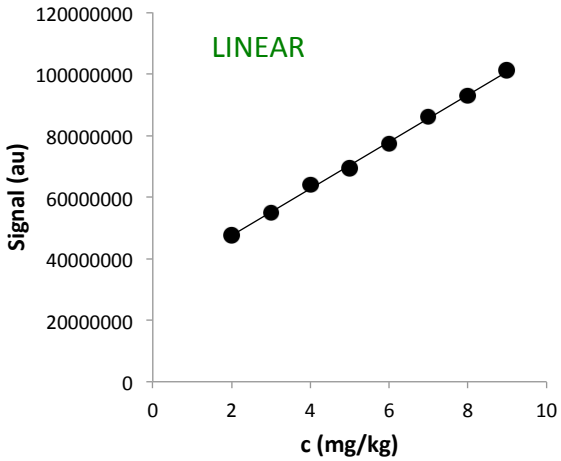


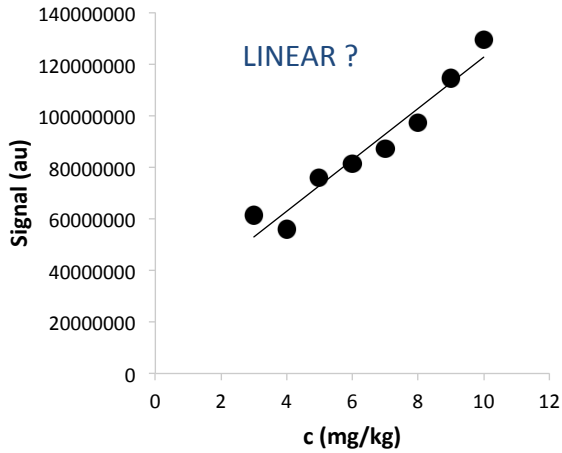


$$\hat{y}_i = slope \cdot x_i + intercept$$

$$\varepsilon_i = y_i - \hat{y}_i$$

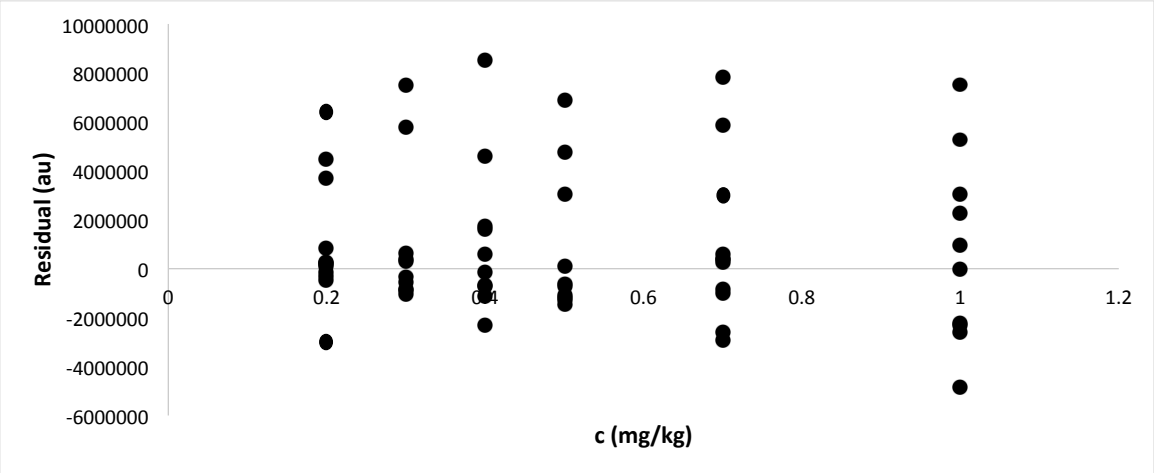
Visual evaluation



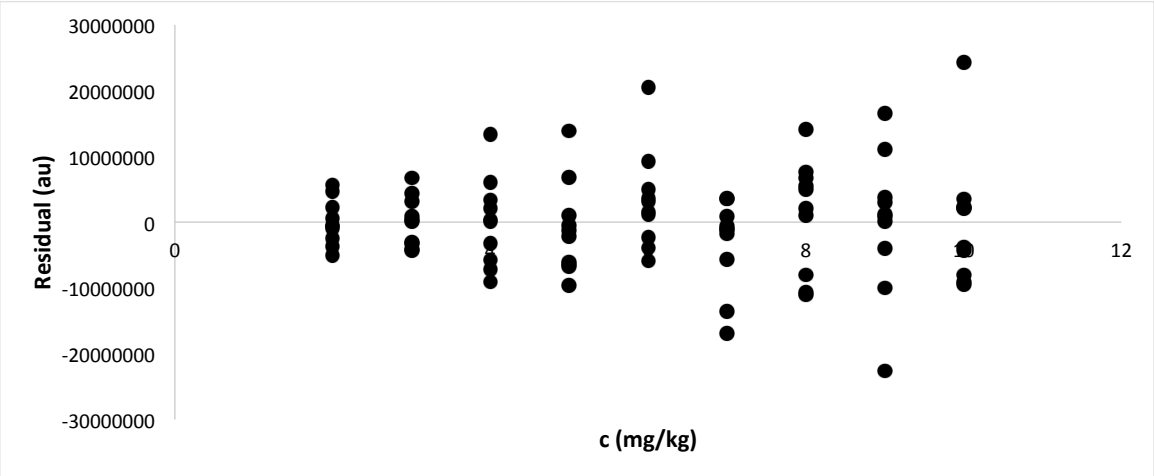


Plot of residuals

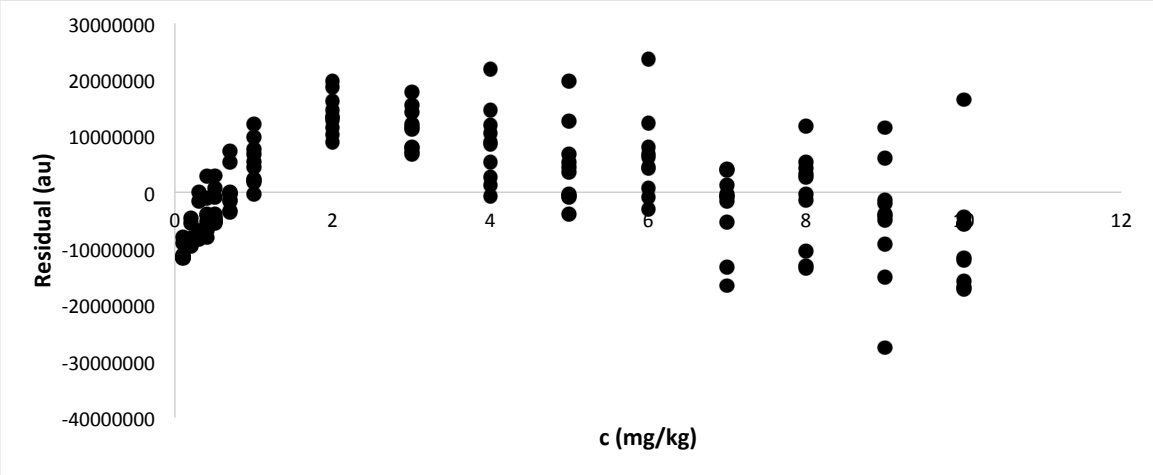
Linear, homoscedastic



Linear, heteroscedastic



Not linear, heteroscedastic



Relative residuals

- ±20% is acceptable

$$Y_i = \frac{y_i - \hat{y}_i}{\hat{y}_i}$$

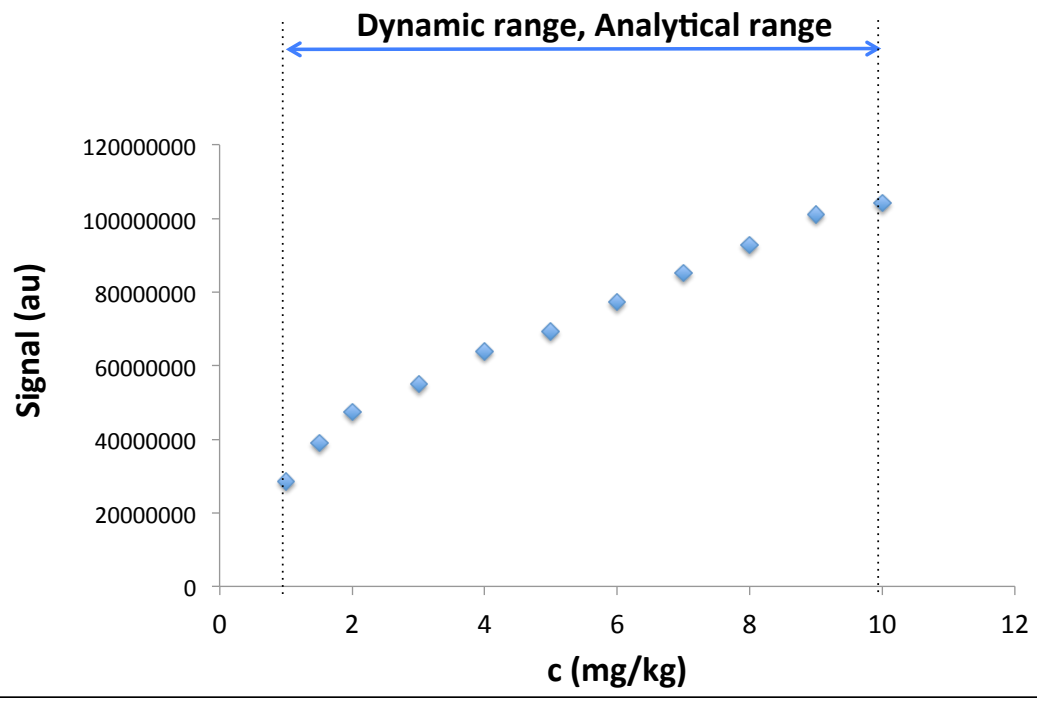
Correlation coefficient *r*
Coefficient of determination r^2

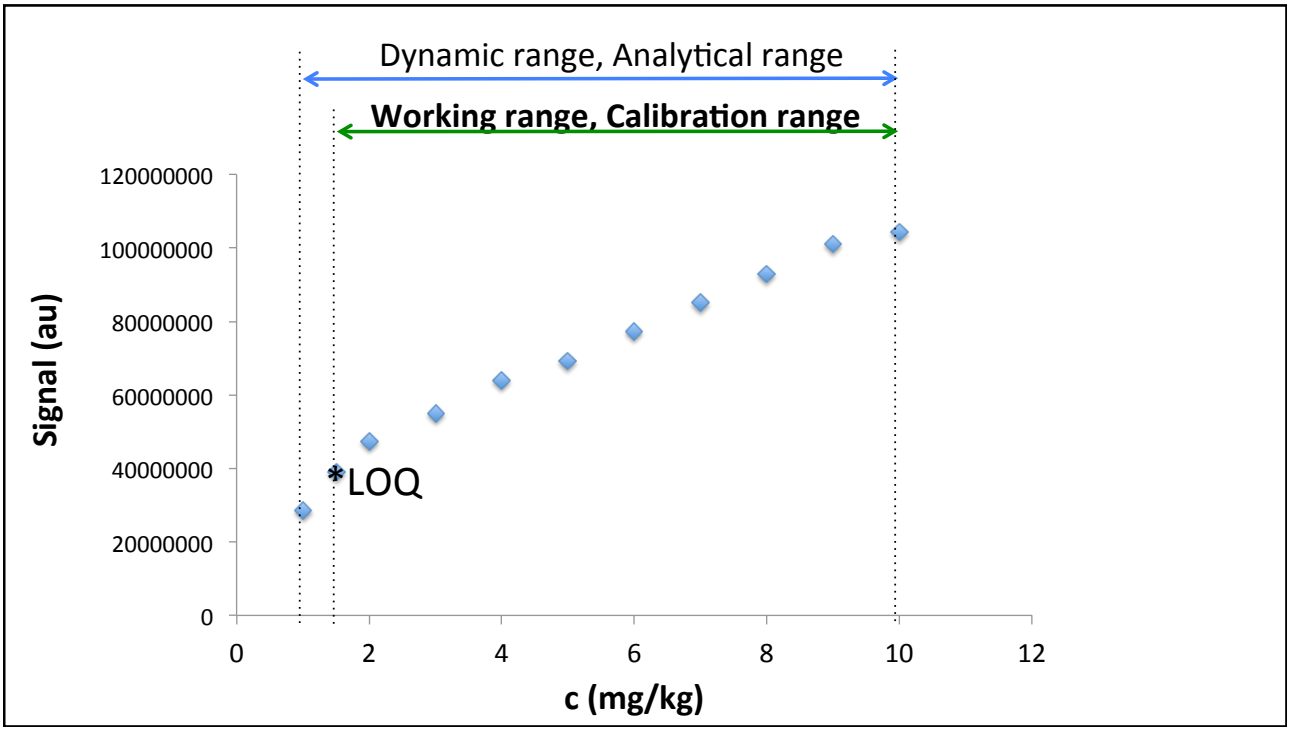
- Total variability in the response that is accounted for by the model

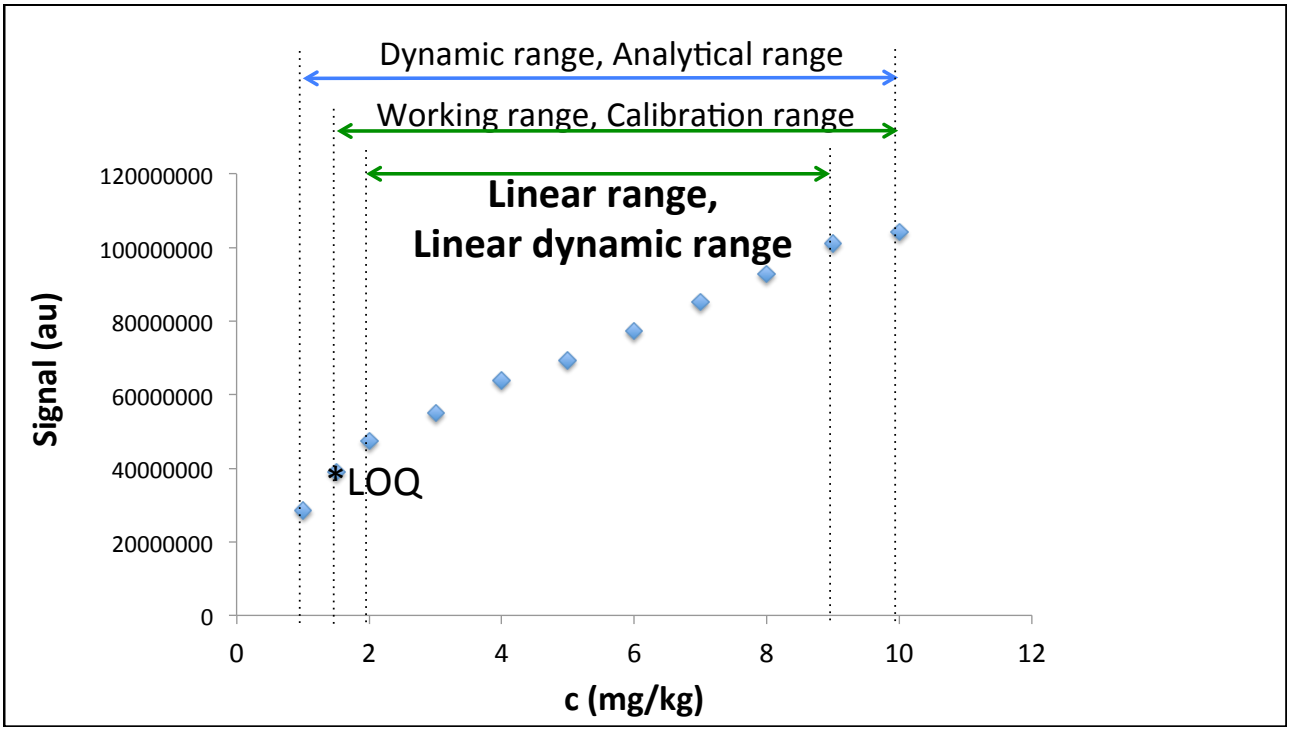
- **Not a measure of linearity!**

Linear range

“range”


Dynamic range, Analytical range
120000000
100000000
80000000
60000000
40000000
20000000
0
Signal (au)
0
2
4
6
8
10
12
c (mg/kg)

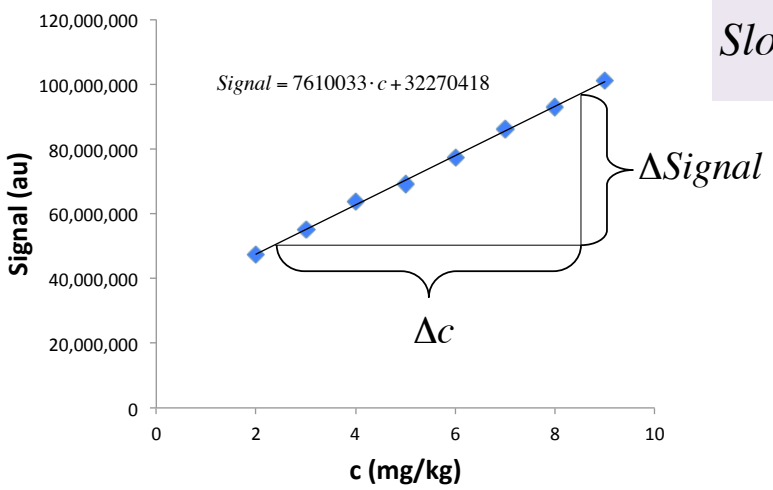

Dynamic range, Analytical range
Working range, Calibration range
*LOQ
Signal (au)
120000000
100000000
80000000
60000000
40000000
20000000
0
0
2
4
6
8
10
12
c (mg/kg)


Dynamic range, Analytical range
Working range, Calibration range
Linear range,
Linear dynamic range
*LOQ
Signal (au)
120000000
100000000
80000000
60000000
40000000
20000000
0
0
2
4
6
8
10
12
c (mg/kg)

Sensitivity

- gradient of the calibration graph

Sensitivity



$$Slope = \frac{\Delta Signal}{\Delta c}$$

Sensitivity

- Method optimization
- Quality assurance
- Routine monitoring of the instrument

Connected to other parameters

- Calculating matrix effect calibration graph method

$$\%ME = \frac{Slope_{matrix-matched}}{Slope_{solvent}} \cdot 100\%$$

- Calculating LoD and LoQ

$$LoD = 3.3 \times \frac{S_{y.x}}{Slope}$$

$$LoQ = 10 \times \frac{S_{y.x}}{Slope}$$