Different ways to evaluate robustness

Choosing the parameters

- LC parameters
  - pH
  - Concentration of additives in eluent
  - Organic solvent content in the eluent
  - Column temperature
  - Eluent flow rate
  - Column batch and age
- Sample and sample preparation parameters
  - Analyte extraction time
  - Injection solvent composition
  - Matrix effect
- Mass spectrometry parameters
  - Drying gas temp
  - Nebulizer gas pressure/flow rate
  - Ion source configuration and condition

Choosing the parameters

- How much a given method parameter can influence the critical characteristic

and

- how likely it is that this parameter will change uncontrollably

One Variable At a Time approach vs Experimental design

- One variable at the time approach
  - Simple
  - Time-consuming
  - Needs a knowledge of critical performance characteristics of the method
- Experimental design
  - Powerful tool
  - Needs a knowledge of critical performance characteristics of the method
  - Requires a knowledge and experience with mathematical statistics

One Variable At a Time approach

1) Change parameters one by one in both directions from the nominal (optimal) value. Changes in the parameters should be realistic in the context of normal use of the method

2) Do not stop there! Often parameters may be mutually unrelated (uncorrelated), but in some cases this does not hold

3) Effects from the change of parameters should be monitored (graphical or statistical analysis)

4) Regarding the robustness tests results, if necessary, measures to improve the performance of the method should be taken