Optimize Analyzer performance by estimating error source contributions

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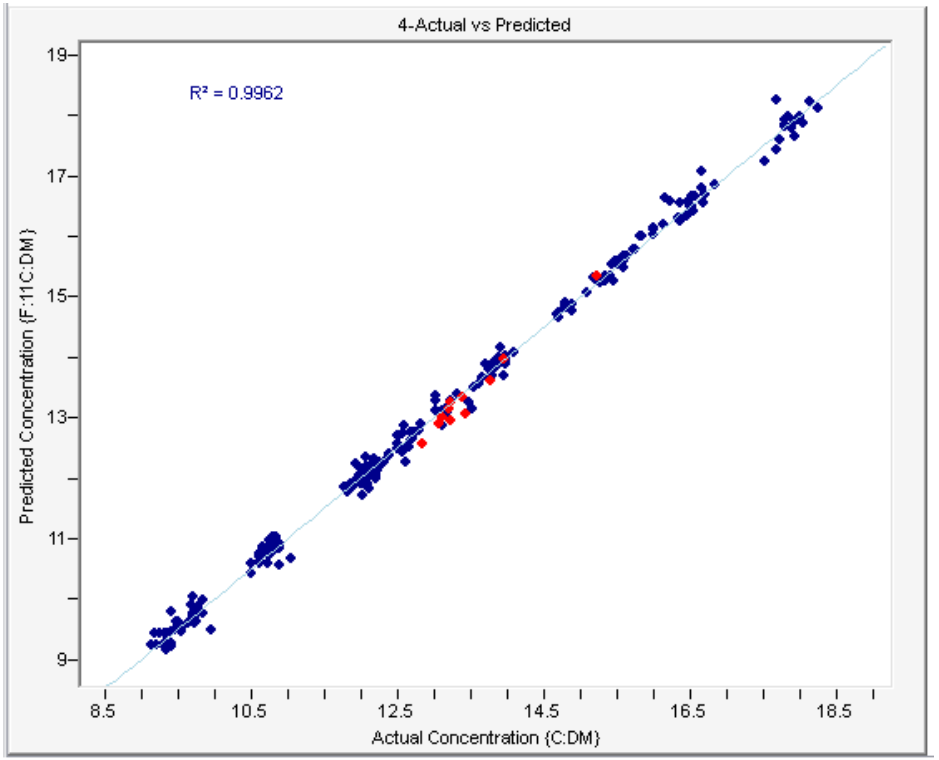
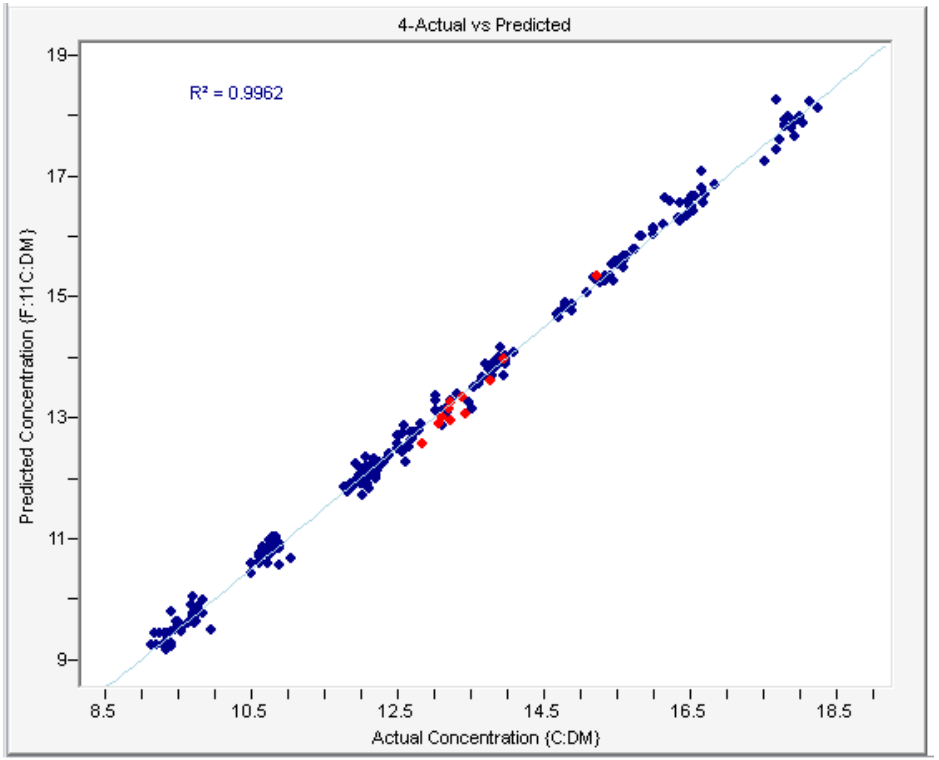
Is this familiar?

After 5 min, first try



8 hours later...



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How hard should we try?

- A fair question is: “what is good analyzer performance?”
  - When the model can fulfil it’s purpose and predict product and/or process quality with acceptable performance to support the business case
  - When the application is stable and will not easily be disturbed by external factors - error source contributions are known
  - When the optimal, best agreement has been obtained, with low SEP and Bias for multiple independent validation sets
- “superb” vs. “as good as it gets” vs .“good enough”

Budget

Error Budget

"An error budget is a way of estimating the potential performance of an analytical system"

Propagation of errors in sampling

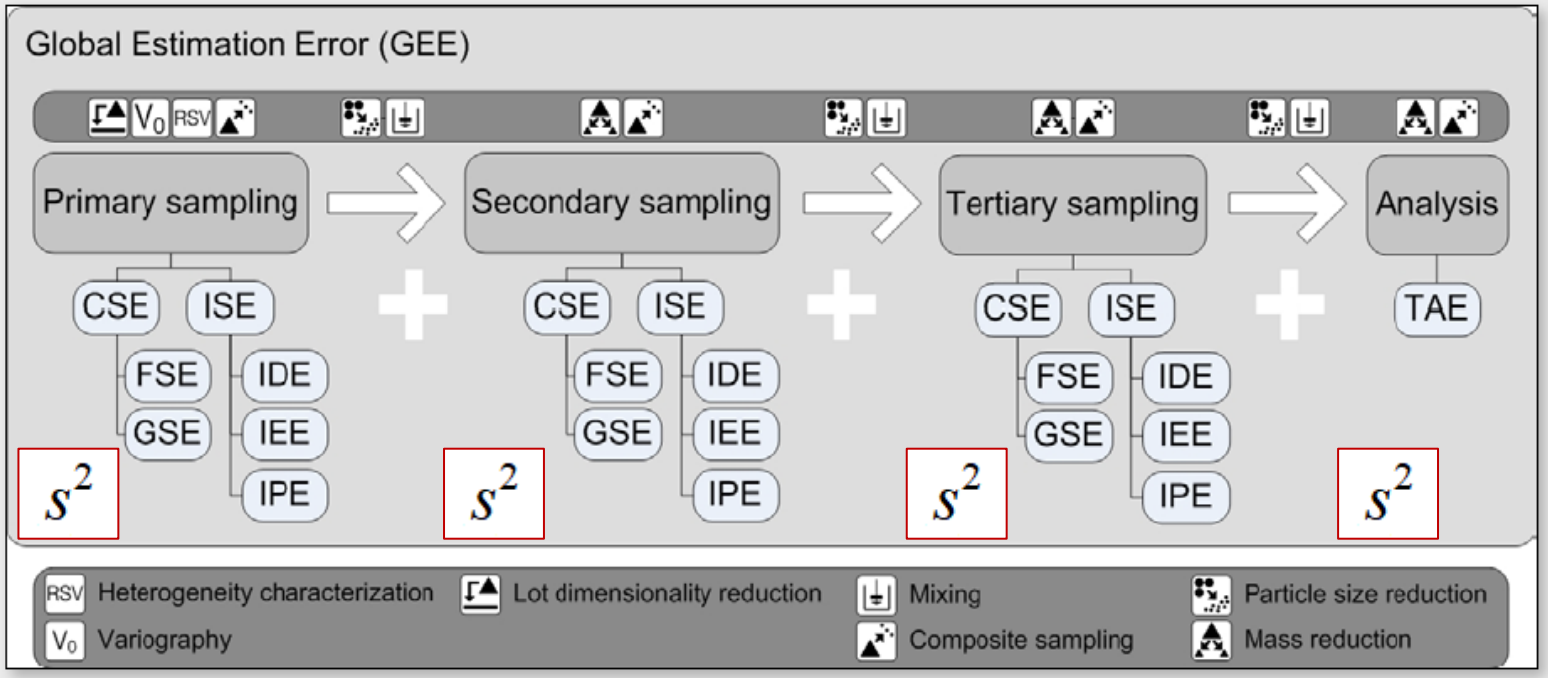

Figure 3. A minimum sampling competence encompasses FSP, TOS' paradigm of sampling correctness, five sampling errors (CSE/ISE) and four Sampling Unit Operations (SUO).

Ref.:

- DS 3077 Representative sampling – Horizontal standard
- Esbensen K. & Petersen, L. J. (2013), TOS Forum, Vol. 1, Iss. 1

$$s_x = \sqrt{\sum s_i^2}$$

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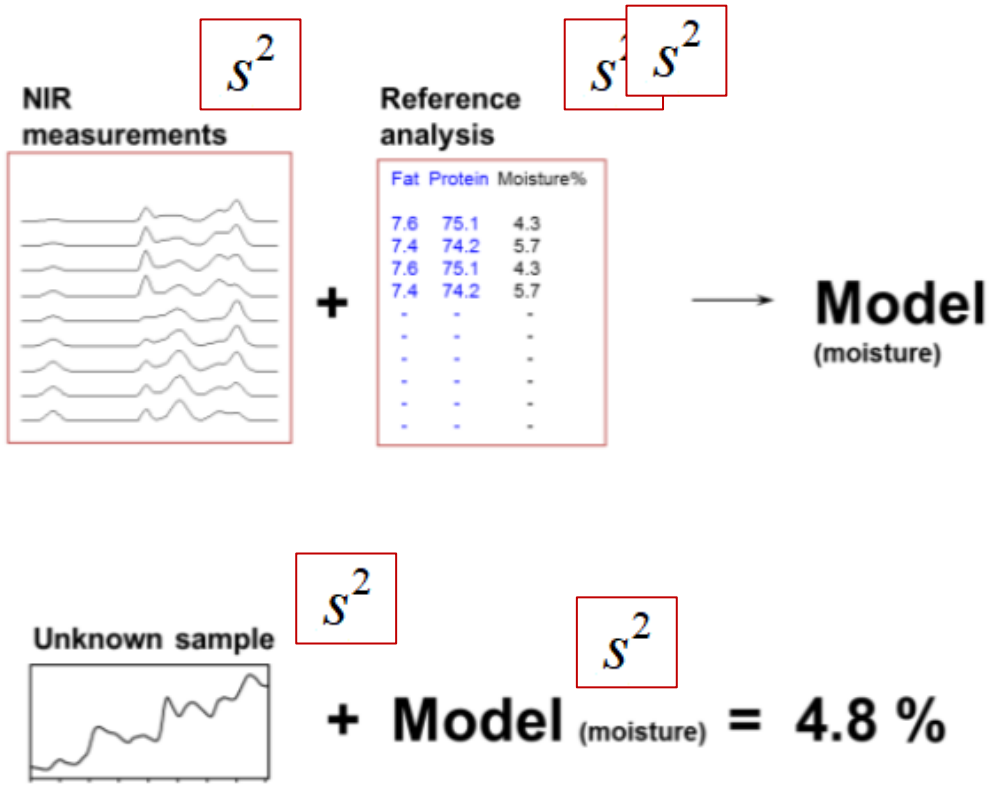
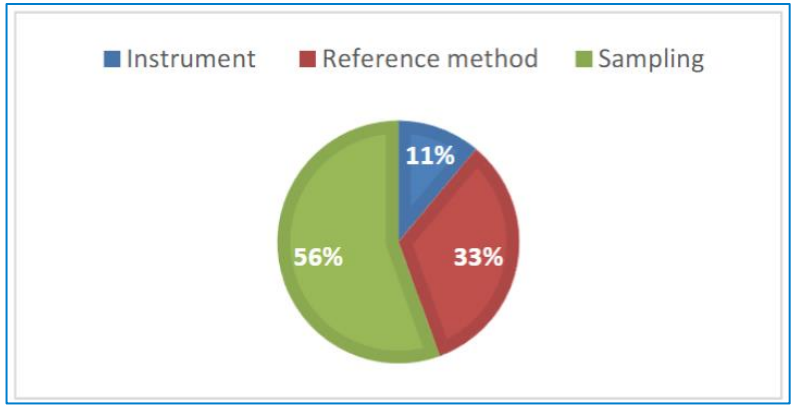
Propagation of errors in the ”error budget”



$$SEP \approx \sqrt{a^2 + b^2 + c^2}$$

a: Instrument measurement error
b: Reference method error
c: Combined effects of sampling errors



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Error budget example

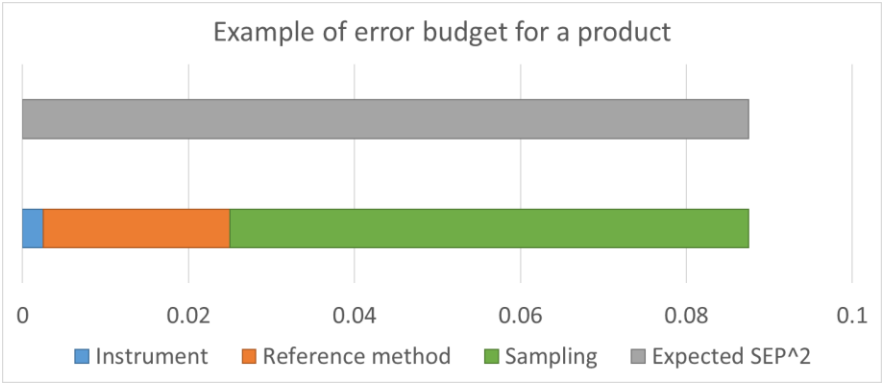
- For dry-matter in a powder.
  - Typical Instrument repeatability = 0.05%
  - Typical reference method repeatability (Drying oven) = 0.15%.
  - Expectations to application without sampling errors contribution:

$$SEP \approx \sqrt{0.05^2 + 0.152^2} = 0.160\ \%$$

- The sampling errors contribution constitutes the missing link between the sample extracted and the sample seen by the analyzer and reference method
  - Often in the range of 0.25% for moisture.
  - Expectations to the application with sampling errors:

$$SEP \approx \sqrt{0.05^2 + 0.152^2 + 0.25^2} = 0.30\%$$

  - Unfortunately much larger – but will be closer to reality
  - To get "best estimates" - perform a sampling replication study



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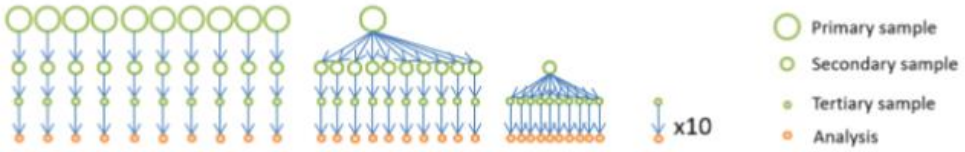
Error budget estimates

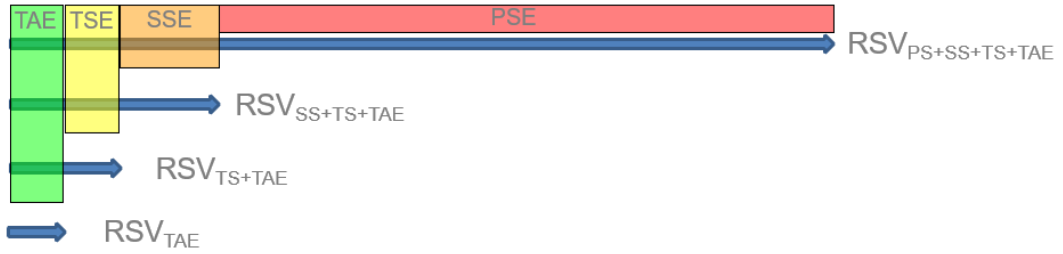
- Replication studies will reveal the contribution of individual error sources
  - "What can be done once, can also be repeated"



  - Relative Sampling Variability:

$$RSV = \frac{\text{Std.dev.}}{\text{Average}} \times 100$$

- SEP should be compared to the error budget calculations
  - If comparable, the application is in control
  - If not, SEP can be improved - address each of the contributions to the error budget - individually .



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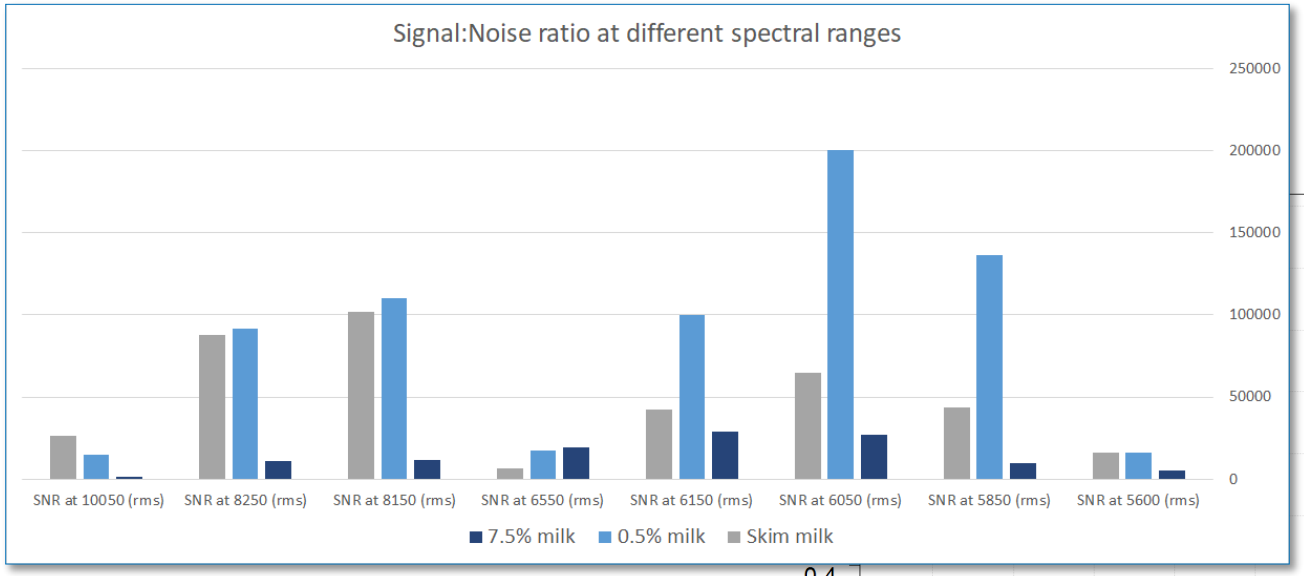
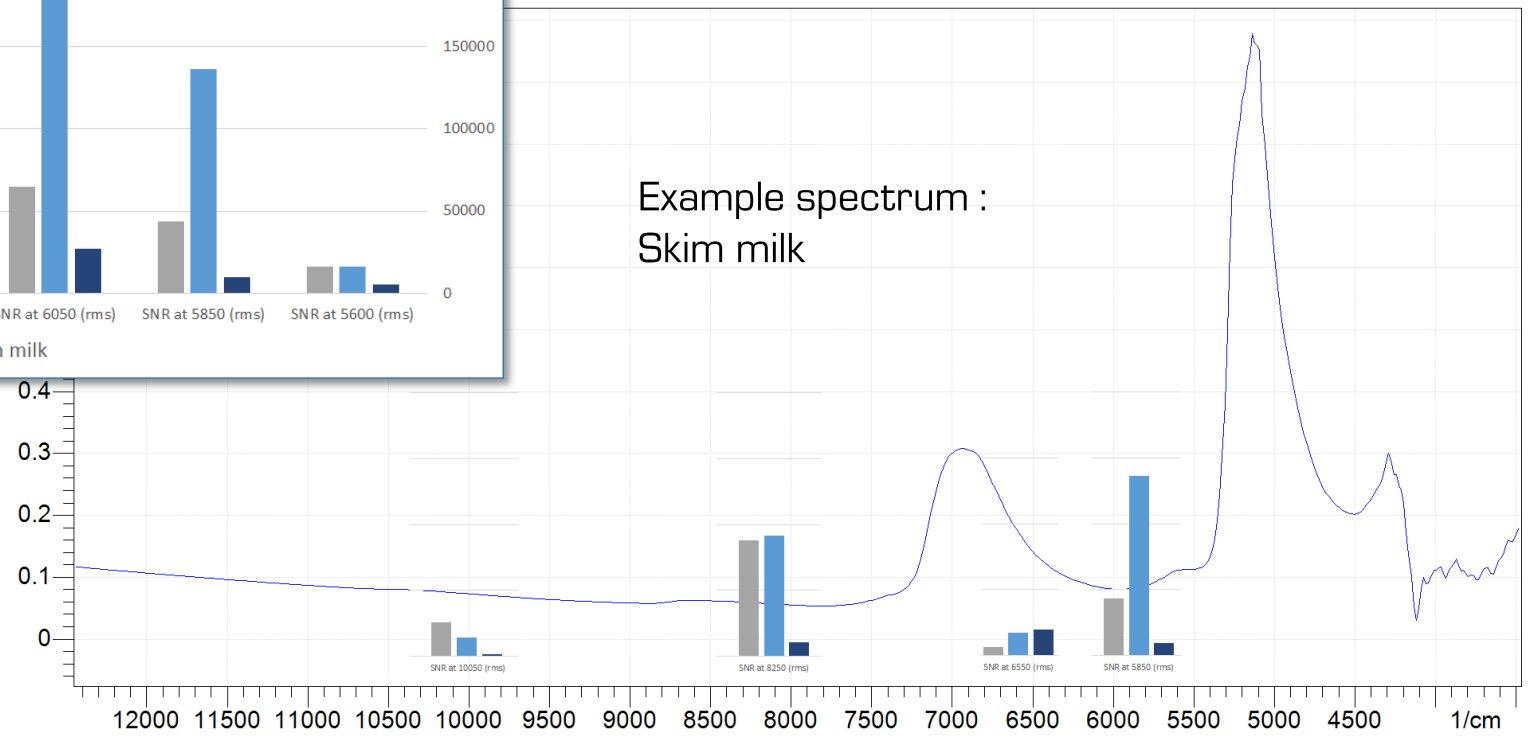
Instrument measurement errors



↑ Test conditions:

- 128 scans, resolution 16, 3 reps
- 3 instruments, InGaAs 2.1 detector
- One Pivette Sampler
- Skim milk and milk 0,5% and 7,5% fat



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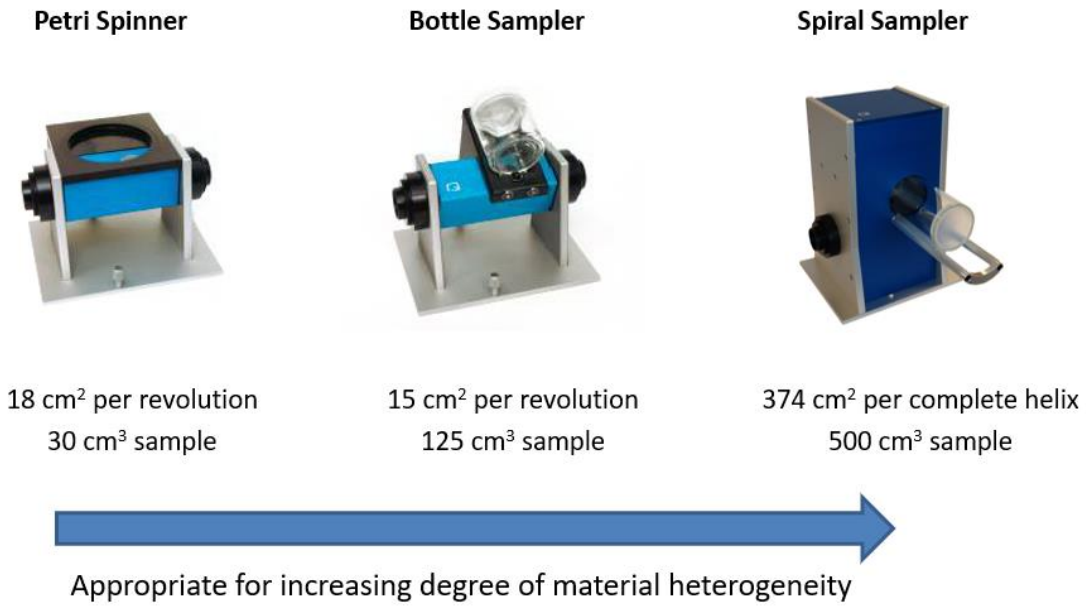
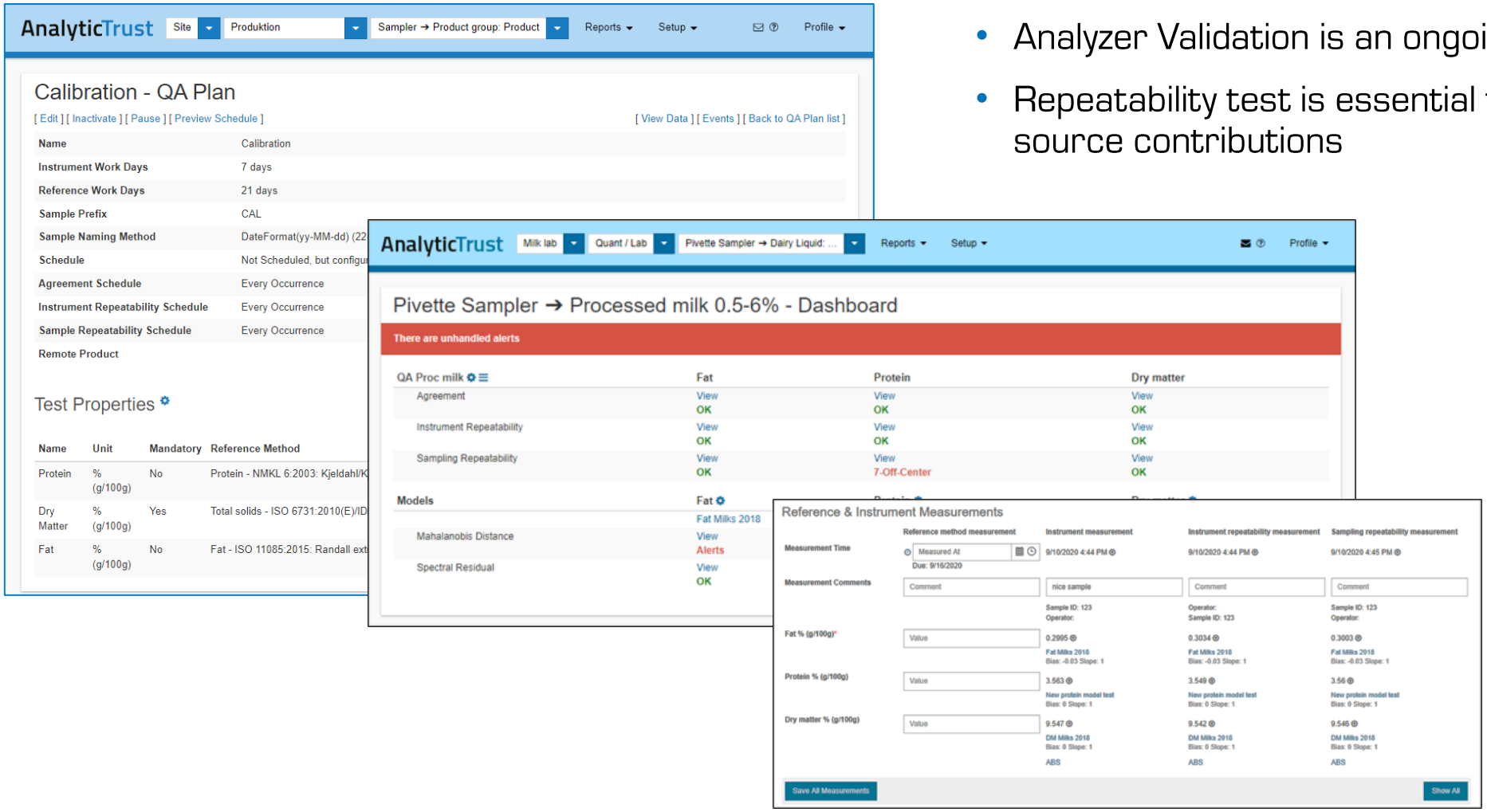
Sampling effects during spectrum acquisition



- The aim is to acquire a spectrum that represents the entire analytical sample well (surface/volume)
- The principles of TOS applies to spectral collection as well:
  - All particles in the sample must ideally have the same probability to influence the composite spectrum
  - Apply "composite sampling" – spinning methods enable acquisition of new sample surface during analysis
  - Spinning of bottle enables mixing of sample i.e. reduces grouping and segregation errors
  - Avoid sampling errors as segregation, sedimentation, drying, temperature-, particle size-, surface effects etc.

Application Performance Validation in AnalyticTrust



- Analyzer Validation is an ongoing process
- Repeatability test is essential to estimate error source contributions

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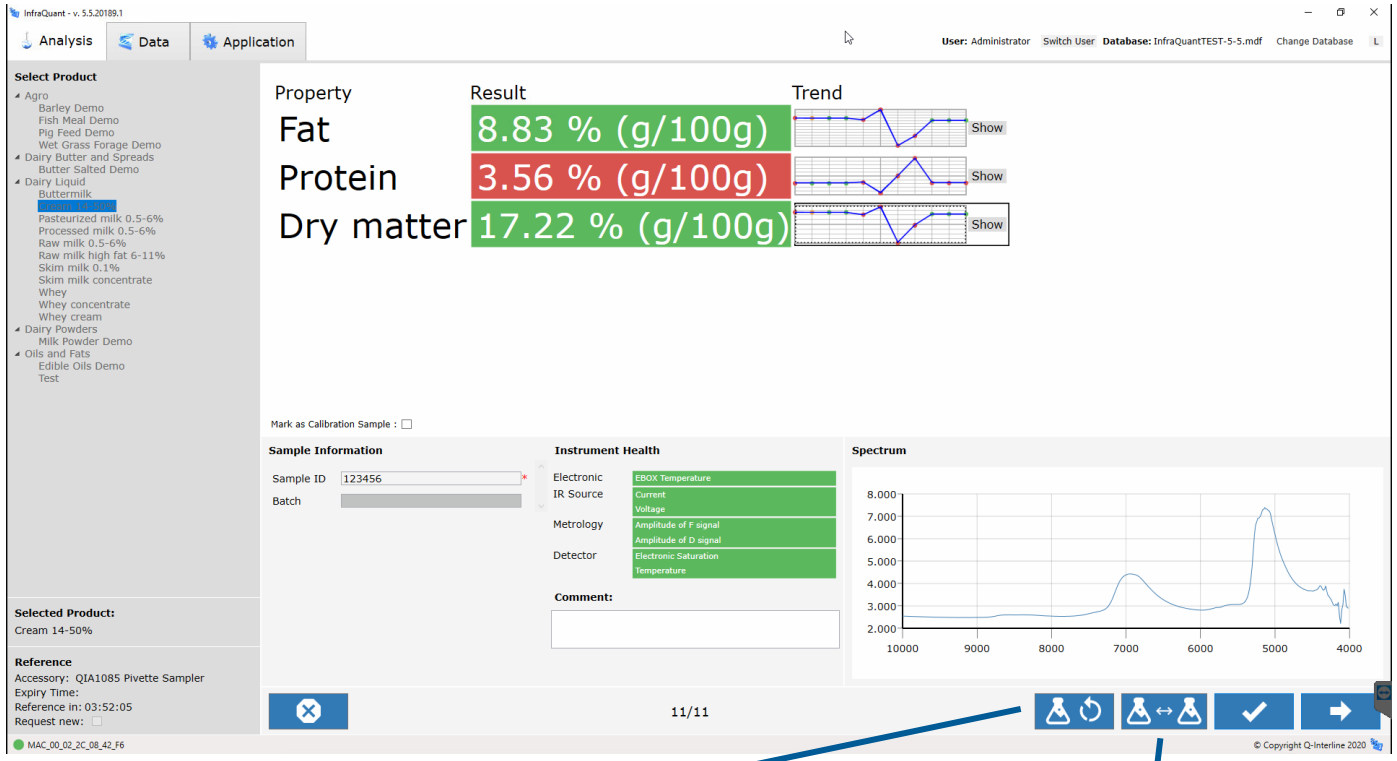
”Make it easy to do things right”

- The software support a workflow to acquire replicate measurements
  - “Repeat measurement of the sample” → Instrument repeatability test
  - “Repeat measurement of another subsample” → sampling repeatability test



Repeat measurement of the sample

Repeat measurement of another subsample

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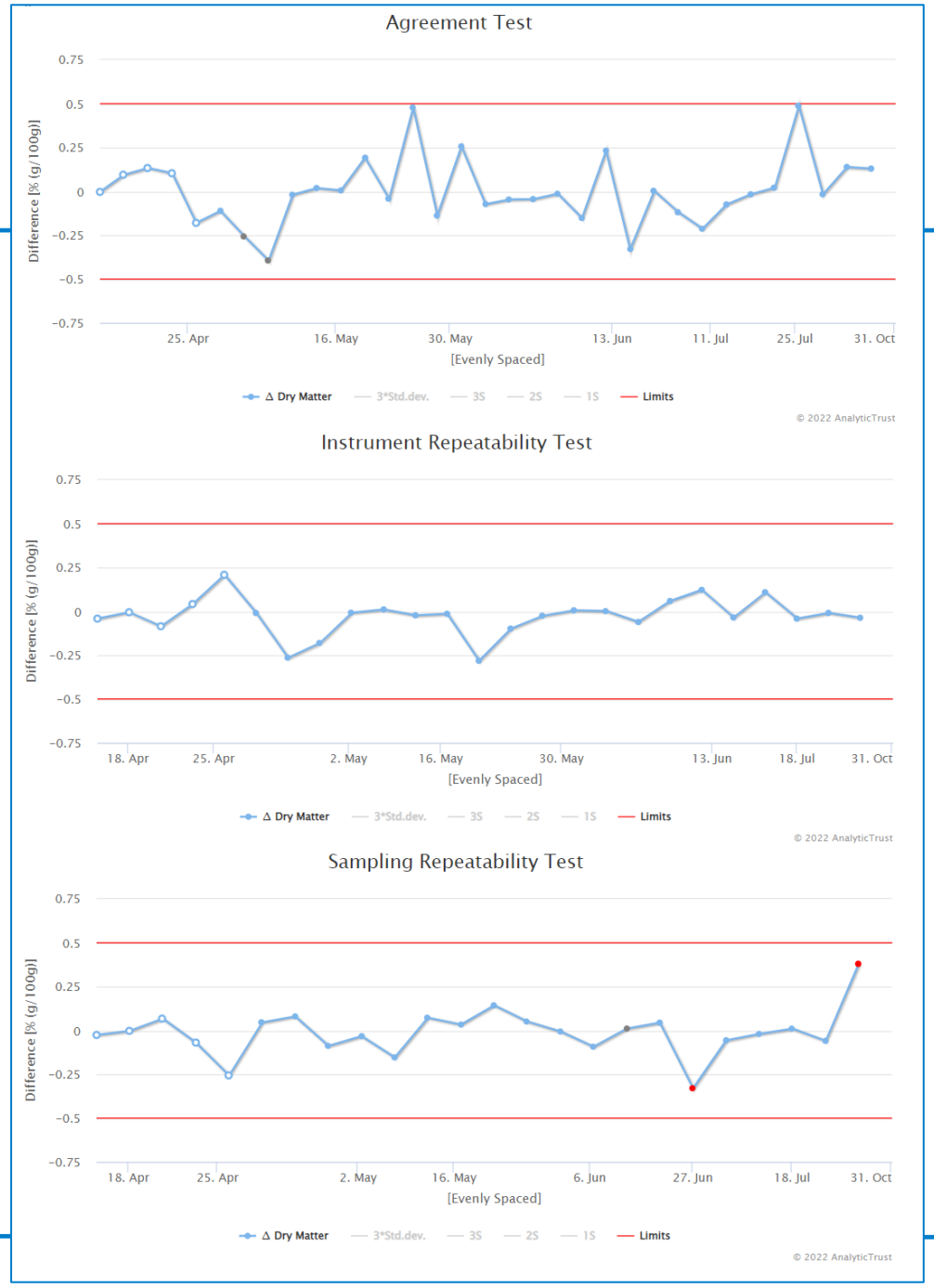
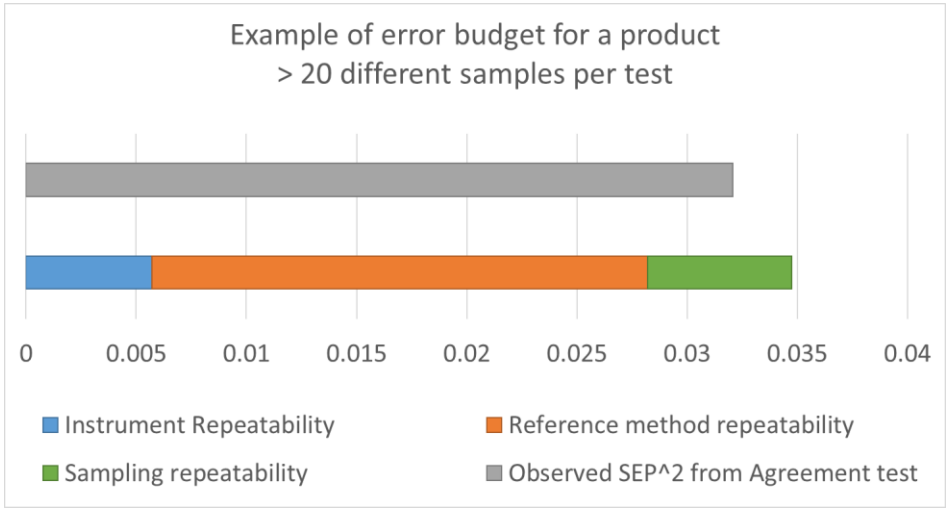


Example of data

- Dry-matter in a semi-liquid product
- Agreement and repeatability test as part of the QA plan Application Performance Validation
- > 20 samples in 6 months with instrument and sampling replicates



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Sampling effects in-line

- All processes shows heterogeneity
  - "Compositional Heterogeneity" - all parts are not evenly present at all spots in cross-section
  - "Distributed Heterogeneity" - the concentration of all parts are not the same at all times.
- We should avoid incorrect sampling errors – by being careful when placing probes - and sample extraction ports.
- Challenge: The probe will never see 100% the same sample as will emerge from the extraction point – a potential missing link between physical sample and the time/volume observed by the in-line NIR system
  - Create the extracted sample by composite sampling
  - One or few samples are not likely to give full insight in the process.
  - Do sampling when the process is relatively "stable"

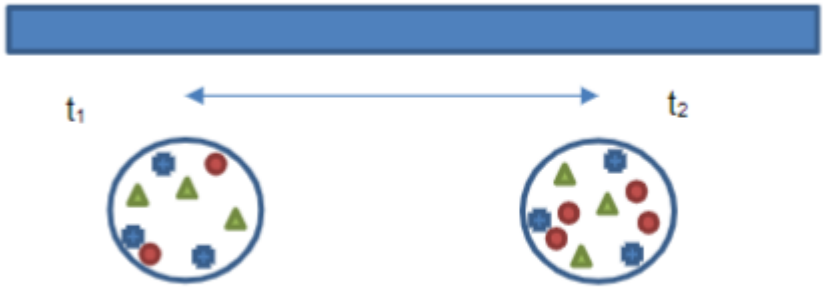

Figure 3 Simplified illustration of process variation and heterogeneity

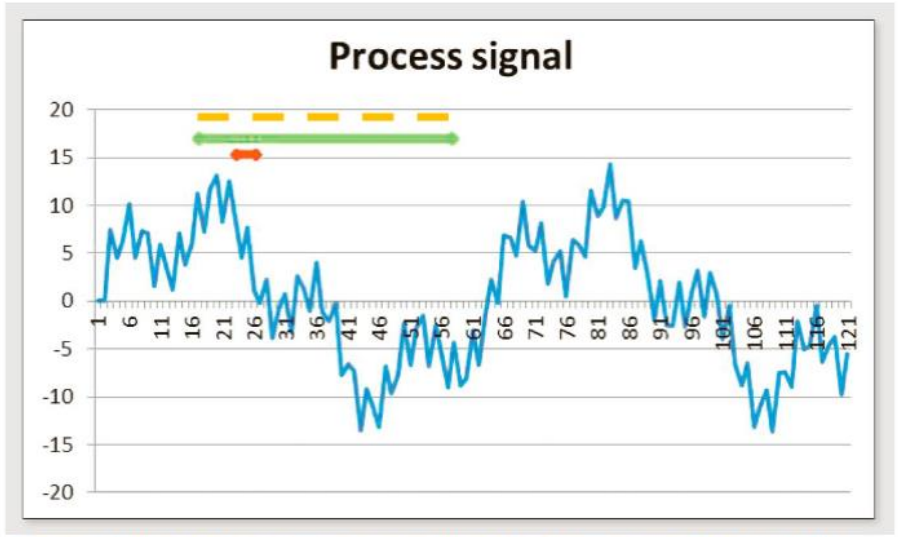

Figure 4 120 sec of a process with relative short term variation of +/- 15%

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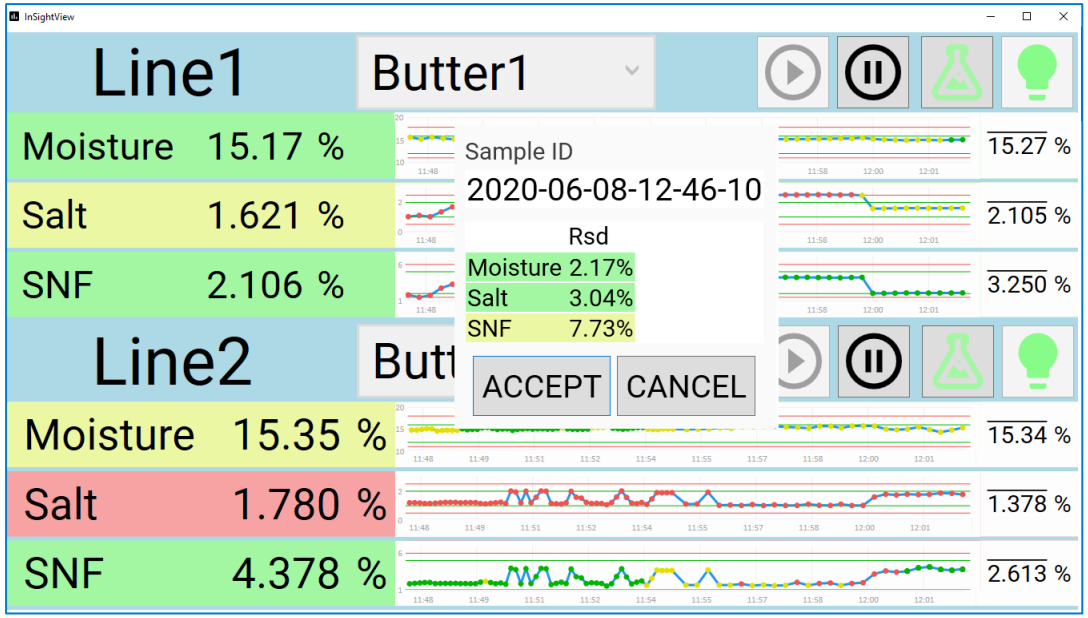
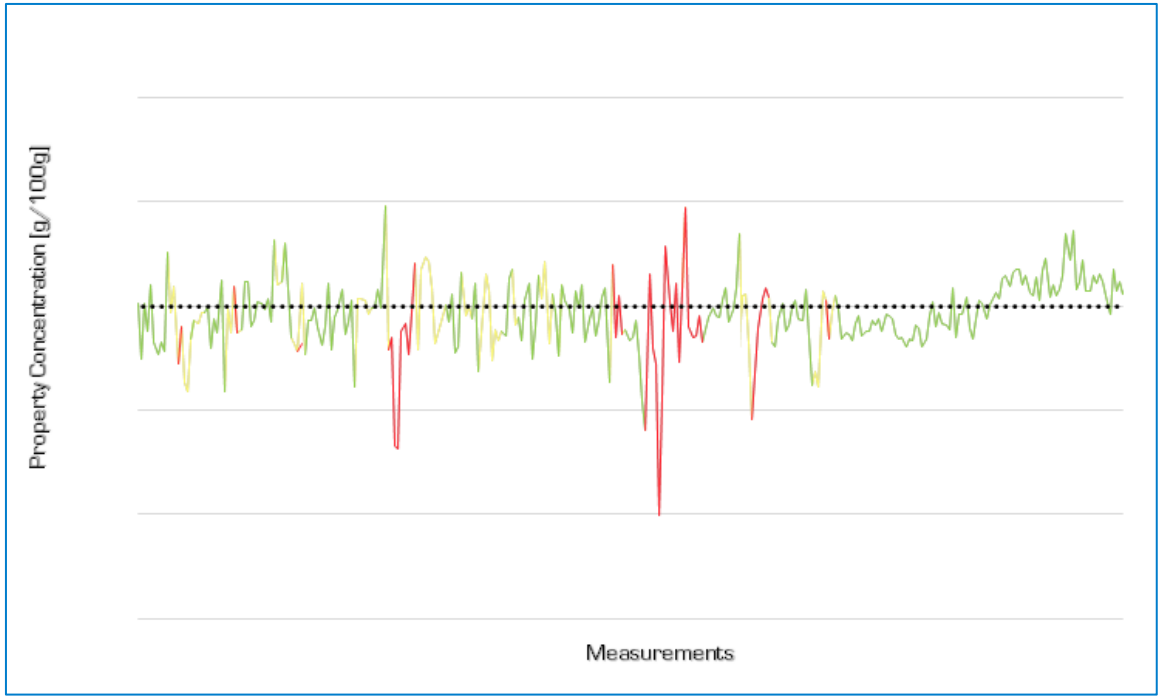
”Make it easy to do things right”

- Challenge the process variation: In-line software that guides the operator for sampling when the process is relatively “stable”
  - Relative Sampling Deviation (Rsd)





- Colour indication of process variation:
  - Green: Small variation
  - Yellow: Medium variation
  - Red: Large variation

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In summary...

”*Boys and girls: Remember the Error Budget* !”

Quote by Anders Larsen (1970 - 2022)
Innovator and founder of Q-Interline

Thank you

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