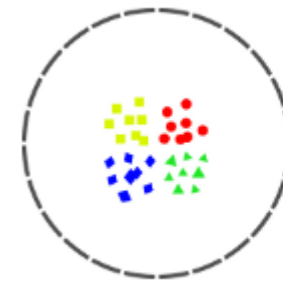


# Optimize Analyzer performance by estimating error source contributions

Marie Sørensen, M.Sc., Ph.D.  
Development Manager, Q-Interline.

Applied Chemometrics, dsk.2022

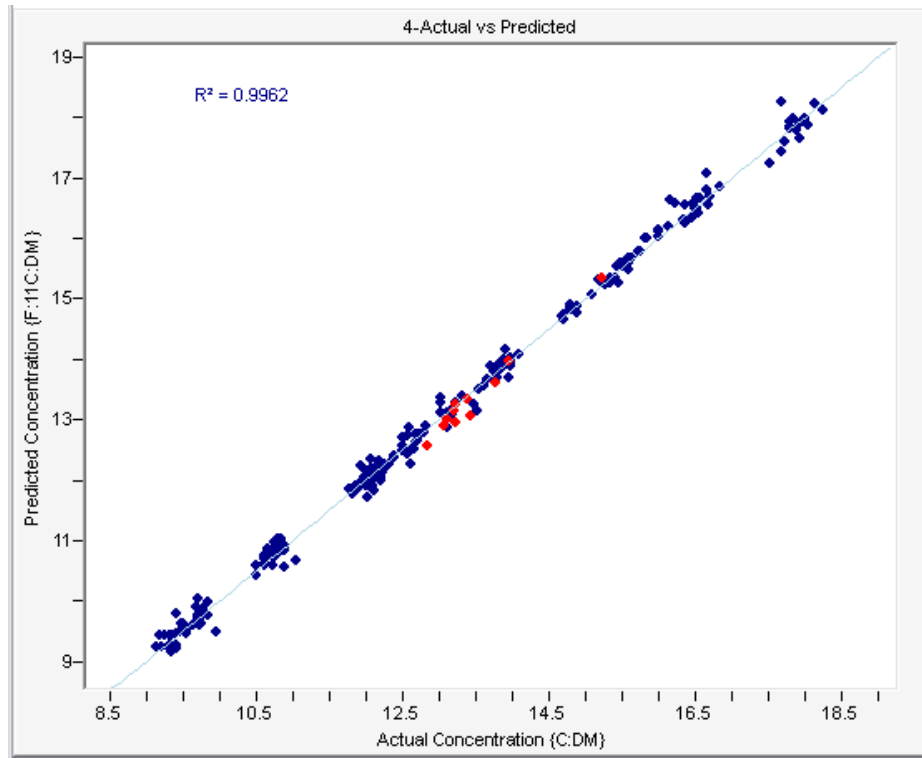


**dsk**

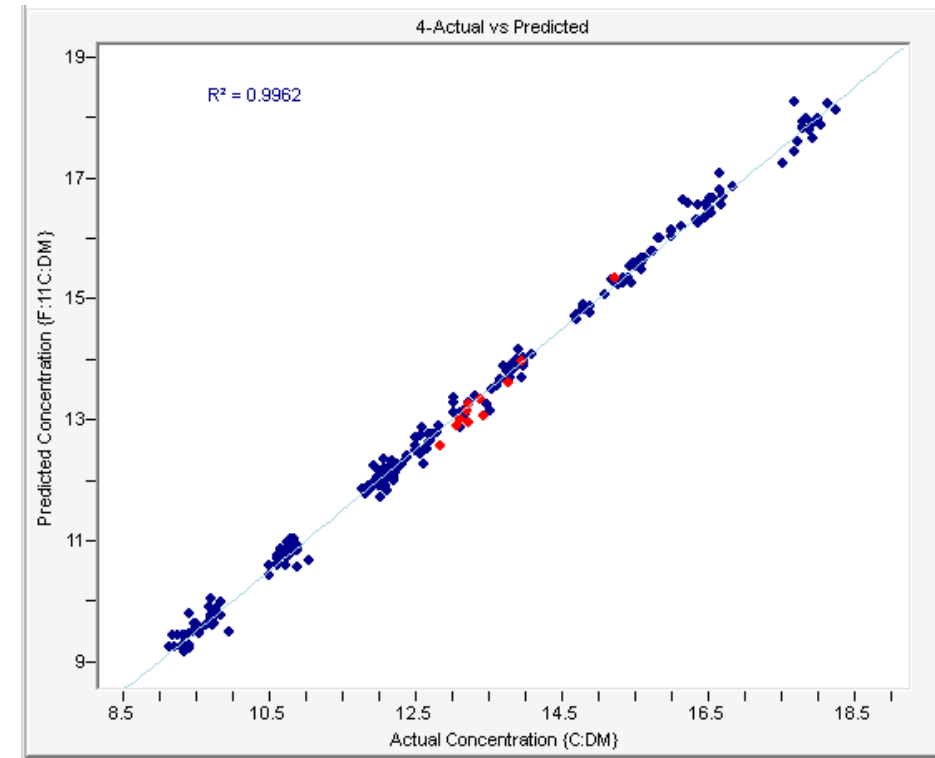
 interline

# Is this familiar?

After 5 min, first try



8 hours later...



# 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”

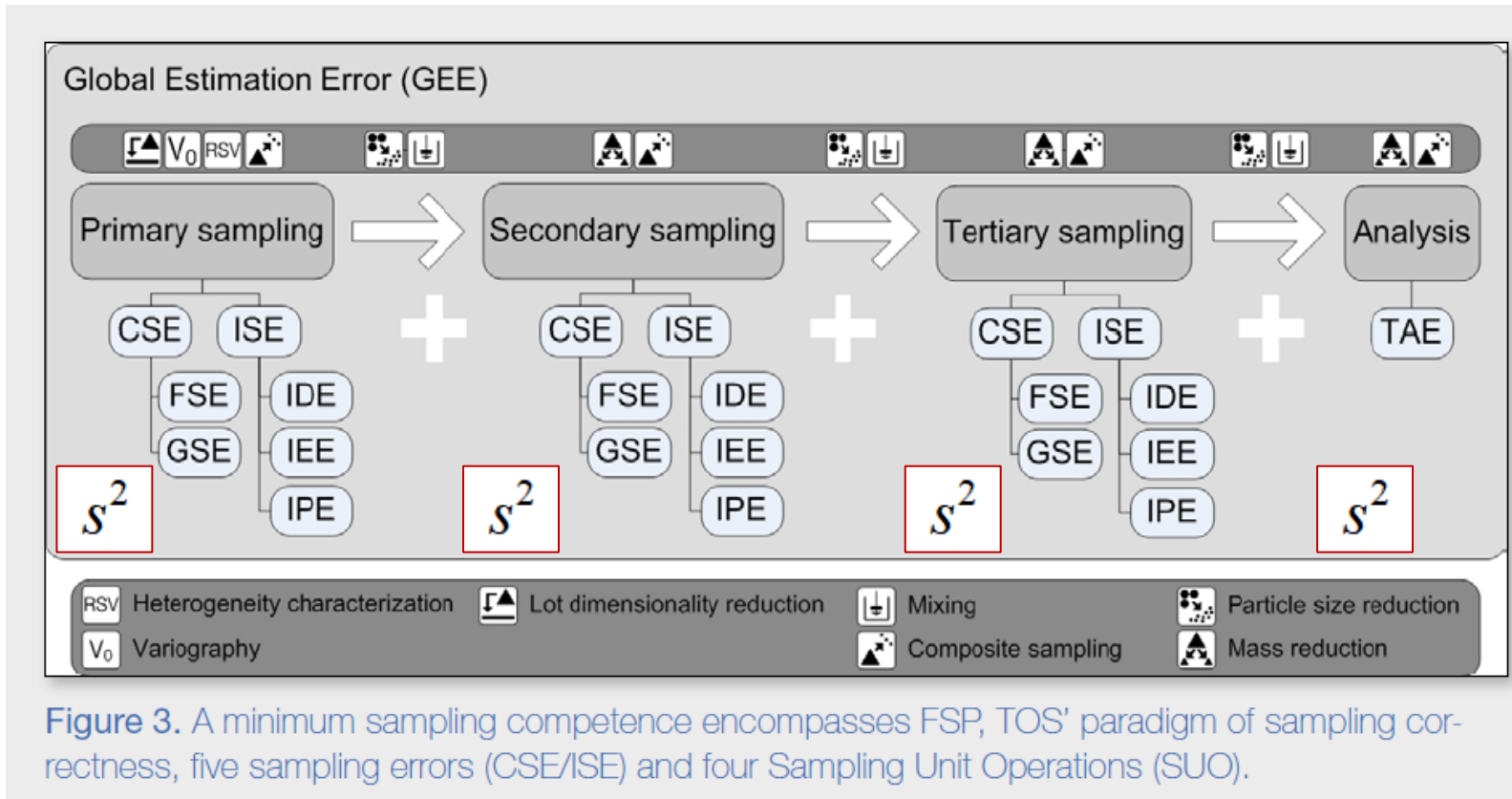
Budget

---

# Error Budget

*“An error budget is a way of estimating the potential performance of an analytical system”*

# Propagation of errors in sampling

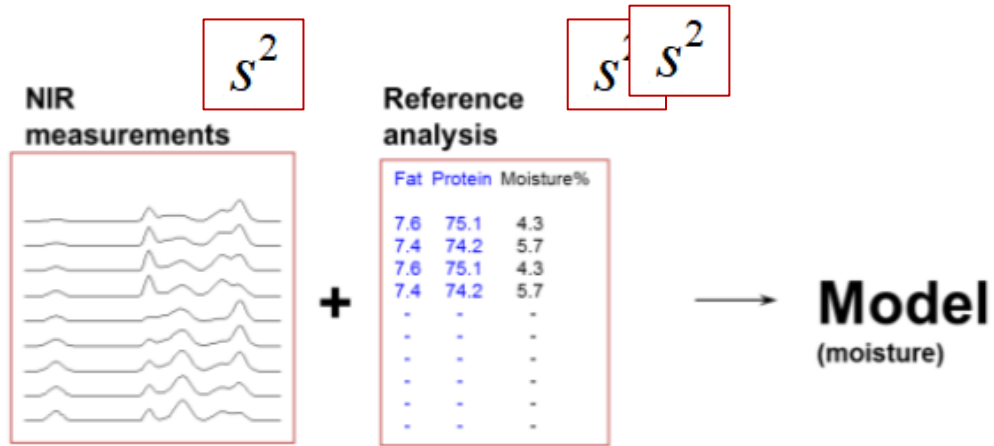


Ref.:

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

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

# Propagation of errors in the "error budget"

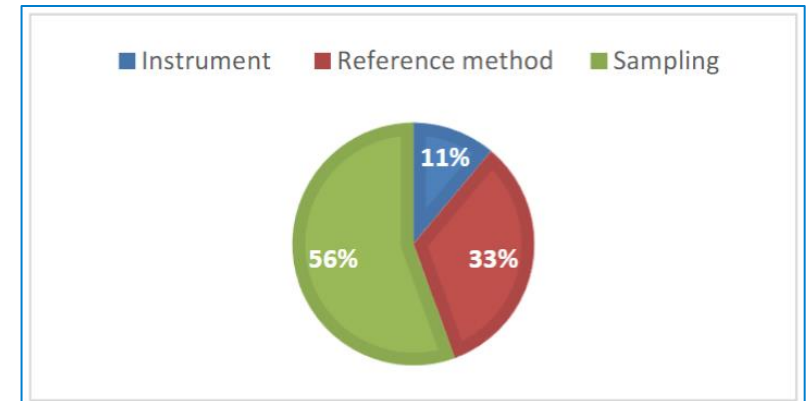


$$SEP \approx \sqrt{a^2 + b^2 + c^2}$$

*a*: Instrument measurement error

*b*: Reference method error

*c*: Combined effects of sampling errors



# Error budget example

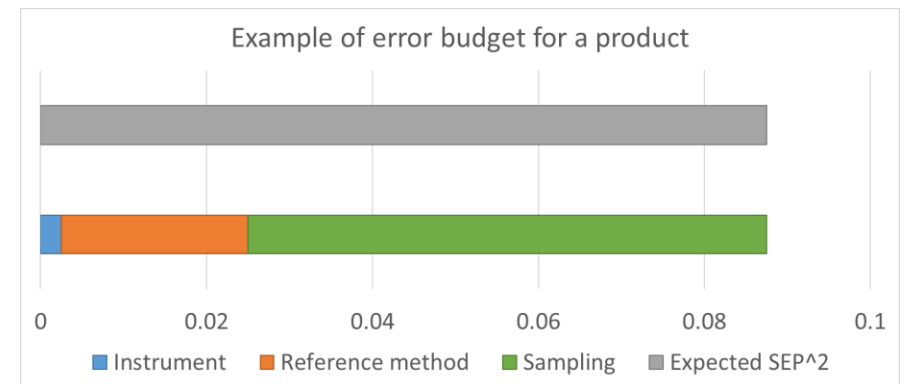
- For dry-matter in a powder.
  - Typical Instrument repeatability = 0.05%
  - Typical reference method repeatability (Drying oven ) = 0.15%.
  - Expectations to application without sampling errors contribution:

$$SEP \approx \sqrt{0.05^2 + 0.15^2} = 0.160 \%$$

- 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:

$$SEP \approx \sqrt{0.05^2 + 0.15^2 + 0.25^2} = 0.30\%$$

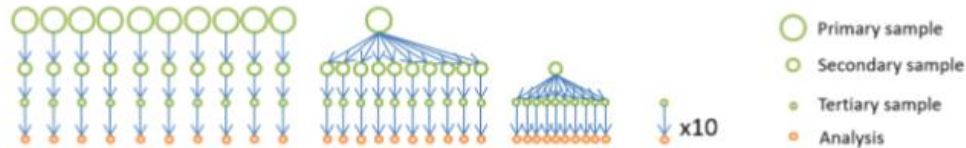
- Unfortunately much larger – but will be closer to reality
- To get “best estimates” - perform a sampling replication study





# Error budget estimates

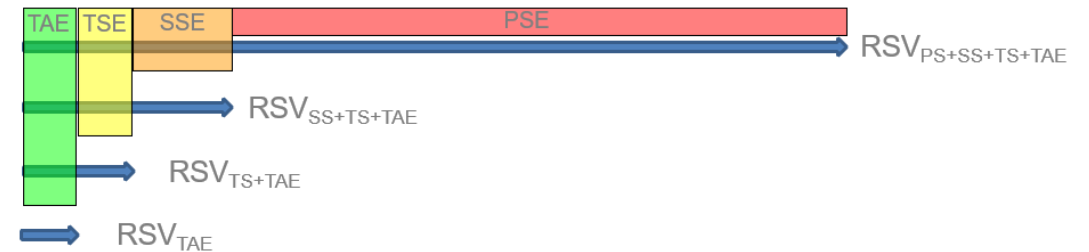
- Replication studies will reveal the contribution of individual error sources
  - “What can be done once, can also be repeated”



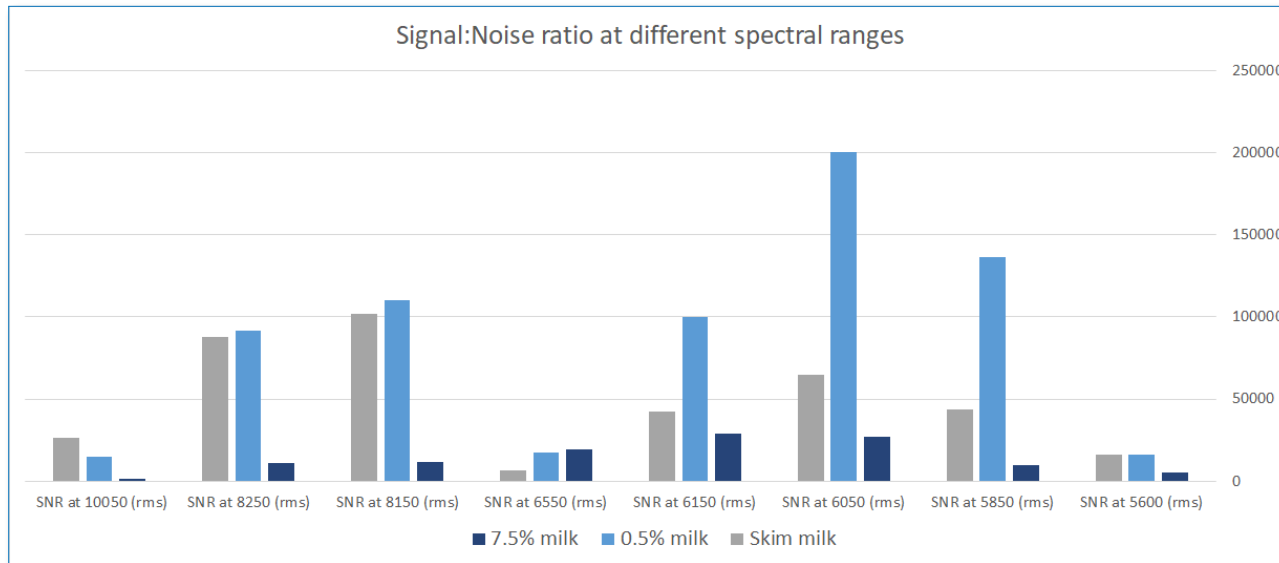
- Relative Sampling Variability:

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

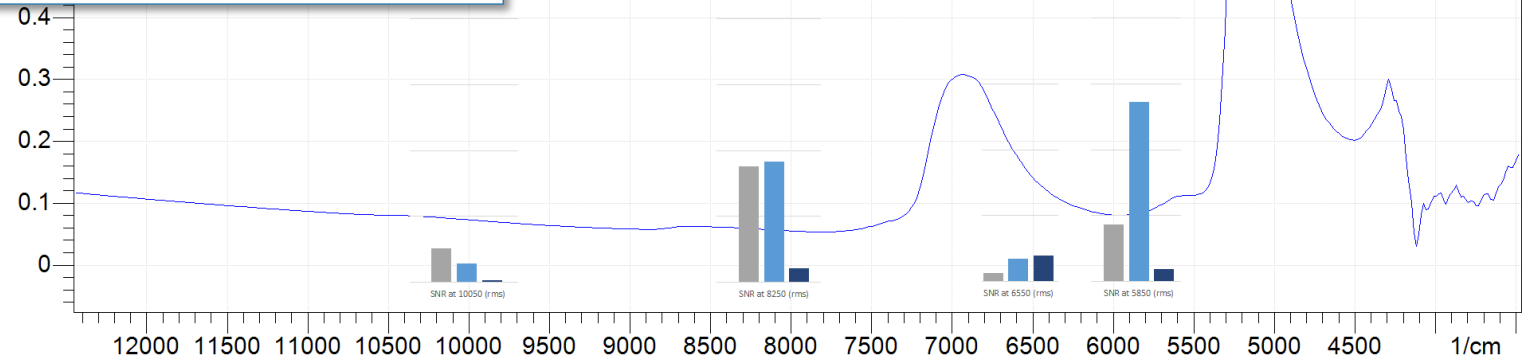
- SEP should be compared to the error budget calculations
  - If comparable, the application is in control
  - If not, SEP can be improved - address each of the contributions to the error budget - individually .



# Instrument measurement errors



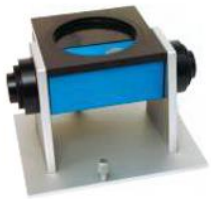
Example spectrum :  
Skim milk



- ↑ 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

# Sampling effects during spectrum acquisition

Petri Spinner



18 cm<sup>2</sup> per revolution  
30 cm<sup>3</sup> sample

Bottle Sampler




15 cm<sup>2</sup> per revolution  
125 cm<sup>3</sup> sample

Spiral Sampler



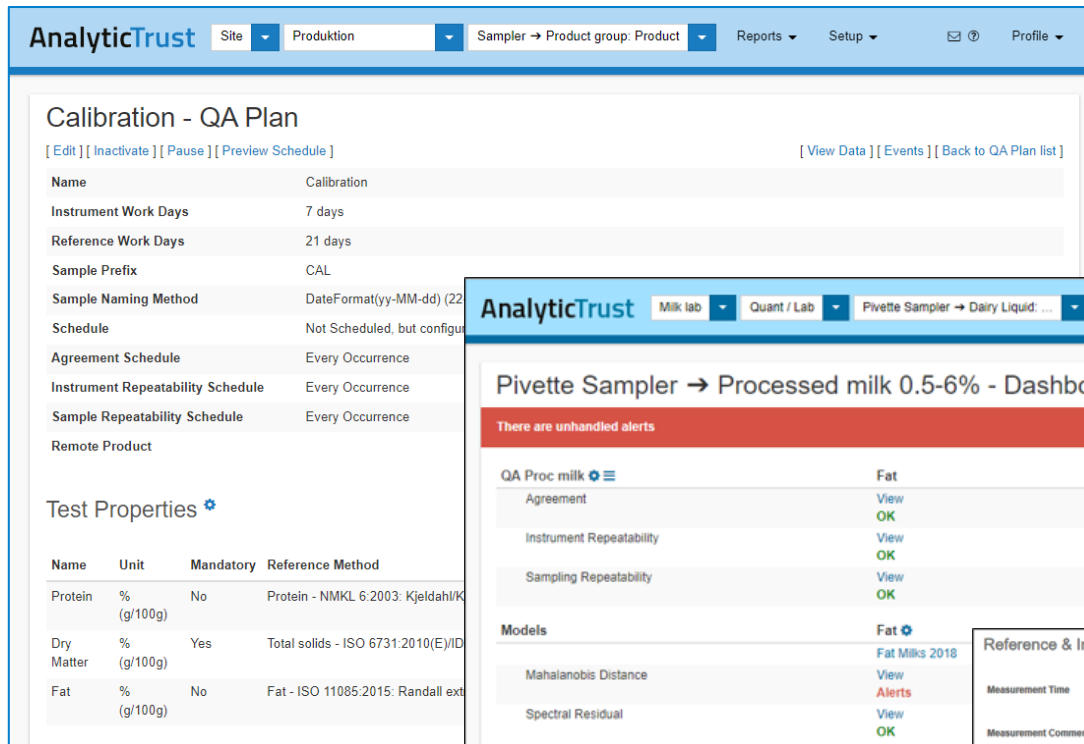
374 cm<sup>2</sup> per complete helix  
500 cm<sup>3</sup> sample

  
Appropriate for increasing degree of material heterogeneity

- 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

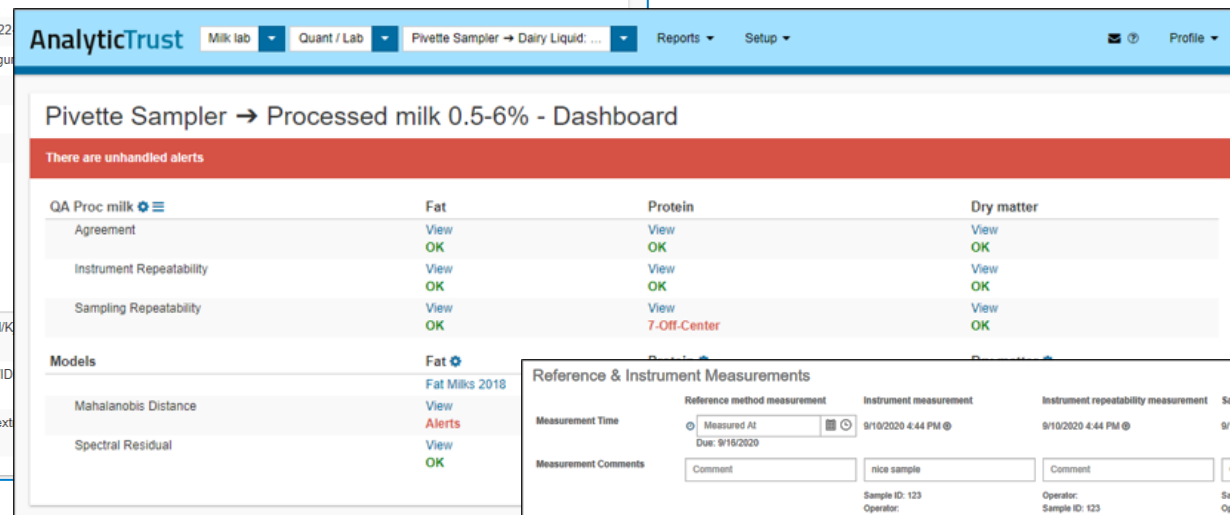


The screenshot shows the 'Calibration - QA Plan' page in AnalyticTrust. The top navigation bar includes 'AnalyticTrust', 'Site' (Produktion), 'Sampler → Product group: Product', 'Reports', 'Setup', and 'Profile'. The main content area displays calibration parameters:

Name	Calibration
Instrument Work Days	7 days
Reference Work Days	21 days
Sample Prefix	CAL
Sample Naming Method	DateFormat(yy-MM-dd) (22)
Schedule	Not Scheduled, but configured
Agreement Schedule	Every Occurrence
Instrument Repeatability Schedule	Every Occurrence
Sample Repeatability Schedule	Every Occurrence
Remote Product	

Below the parameters is a 'Test Properties' section with a table:

Name	Unit	Mandatory	Reference Method
Protein	% (g/100g)	No	Protein - NMKL 6:2003: Kjeldahl/K
Dry Matter	% (g/100g)	Yes	Total solids - ISO 6731:2010(E)/ID
Fat	% (g/100g)	No	Fat - ISO 11085:2015: Randall ext

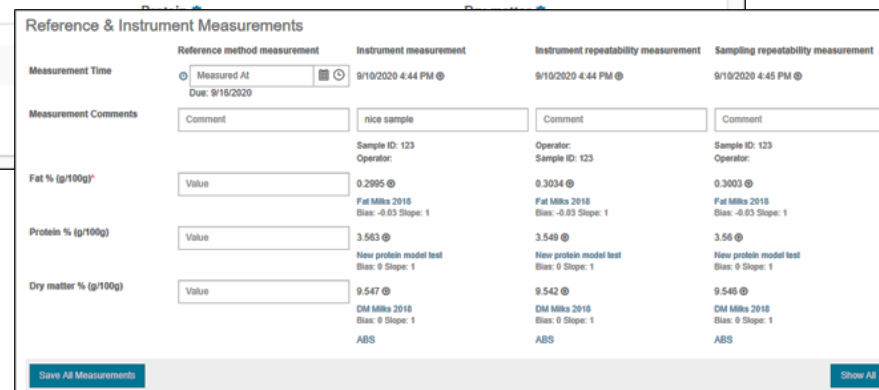


The screenshot shows the 'Pivette Sampler → Processed milk 0.5-6% - Dashboard' page. It features a red alert banner: 'There are unhandled alerts'. Below this is a table of test results:

QA Proc milk	Fat	Protein	Dry matter
Agreement	View OK	View OK	View OK
Instrument Repeatability	View OK	View OK	View OK
Sampling Repeatability	View OK	View 7-Off-Center	View OK

Below the table is a 'Models' section with a table:

Models	Fat
Mahalanobis Distance	Fat Milks 2018 View Alerts
Spectral Residual	View OK

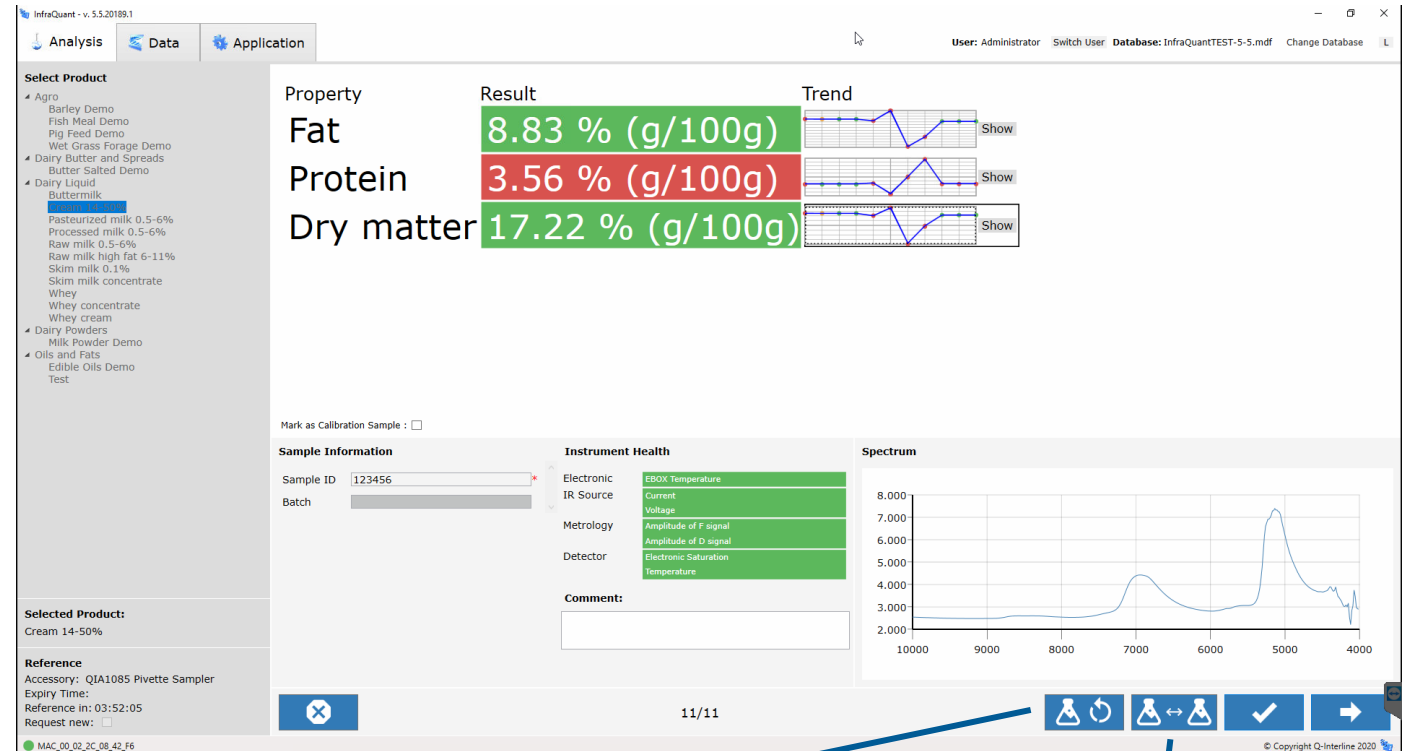


The screenshot shows the 'Reference & Instrument Measurements' page. It displays a comparison of measurements across four categories: Reference method measurement, Instrument measurement, Instrument repeatability measurement, and Sampling repeatability measurement. The measurements are for Fat %, Protein %, and Dry matter % (g/100g).

Measurement Time	Reference method measurement	Instrument measurement	Instrument repeatability measurement	Sampling repeatability measurement
Measured At: 9/10/2020 4:44 PM Due: 9/19/2020		9/10/2020 4:44 PM	9/10/2020 4:44 PM	9/10/2020 4:45 PM
Measurement Comments	Comment: nice sample	Comment: nice sample	Comment: nice sample	Comment: nice sample
Fat % (g/100g)	0.2995	0.3034	0.3003	0.3003
Protein % (g/100g)	3.583	3.549	3.56	3.56
Dry matter % (g/100g)	9.547	9.542	9.546	9.546

# ”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

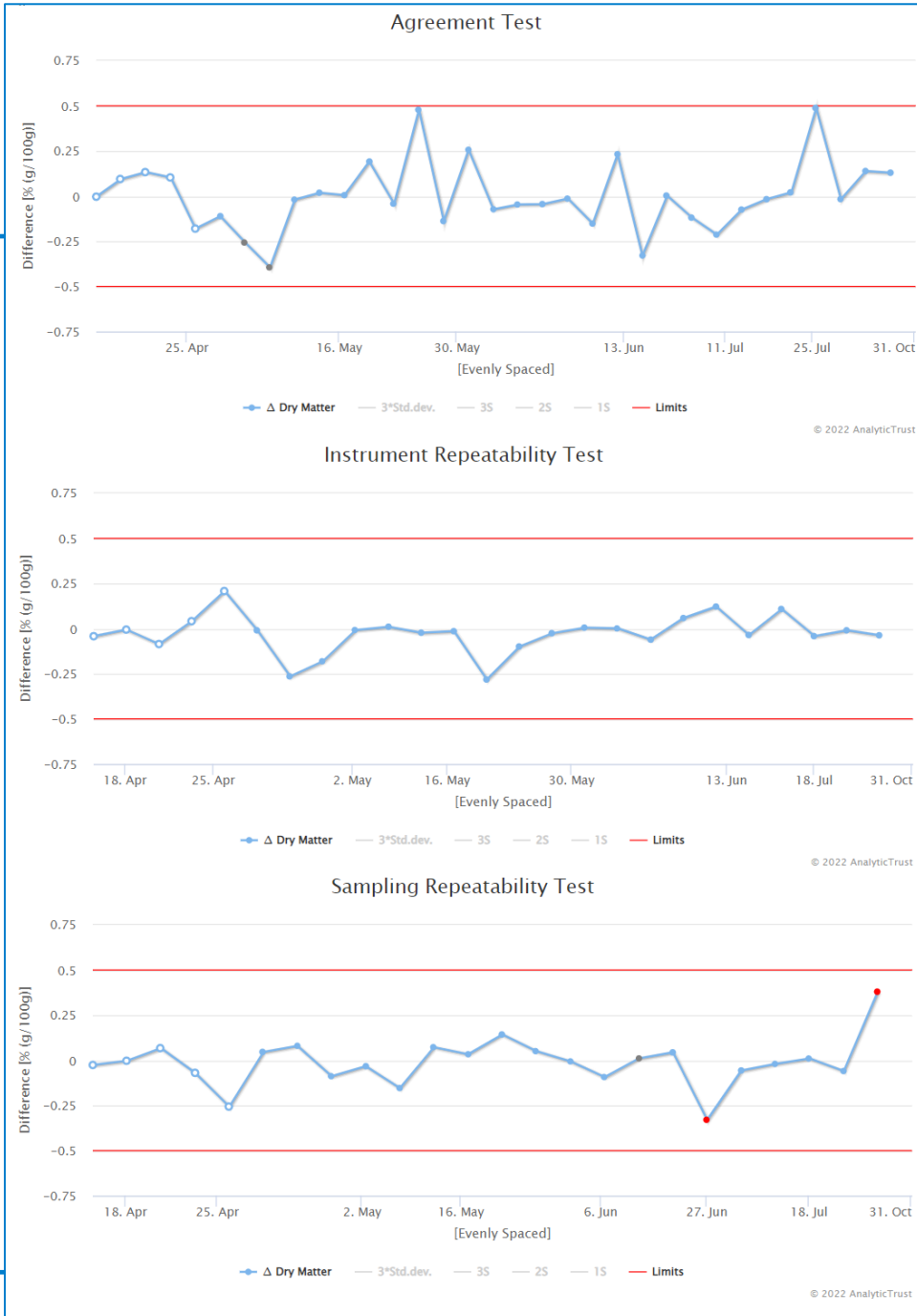
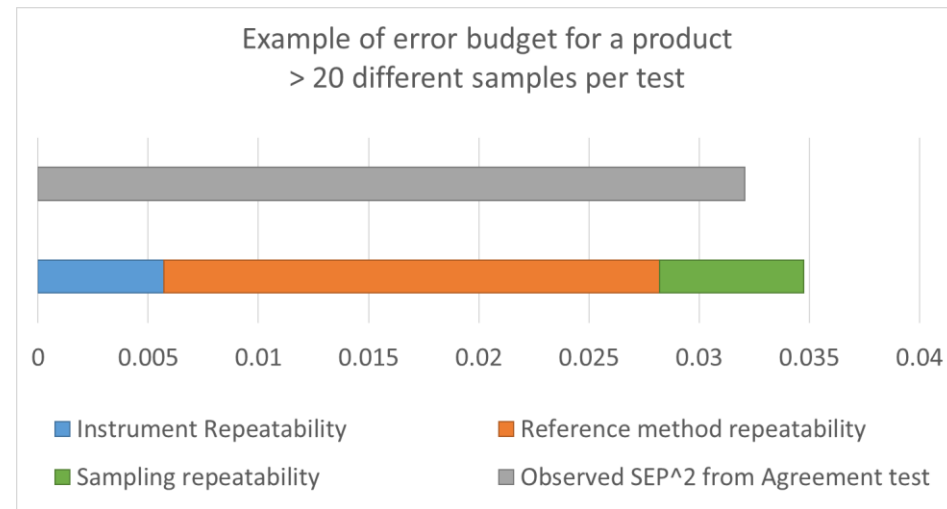


Repeat measurement of the sample

Repeat measurement of another subsample

# 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



# 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

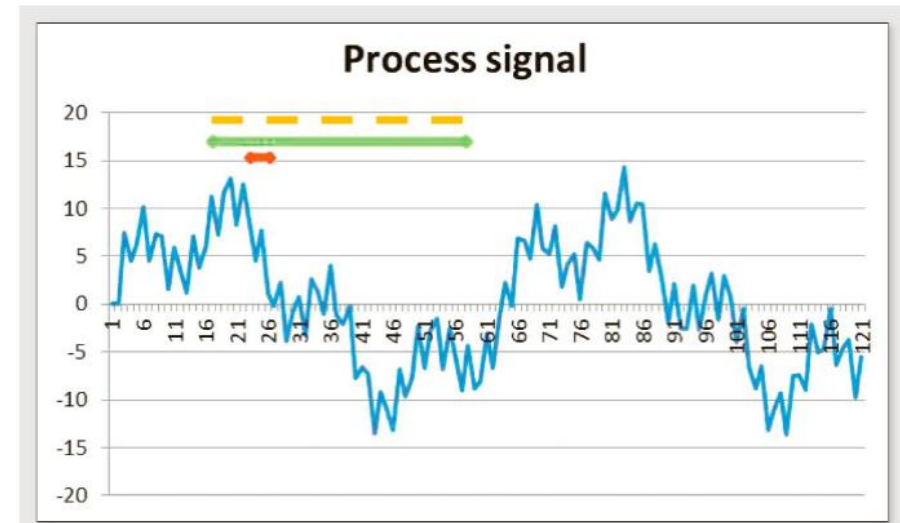
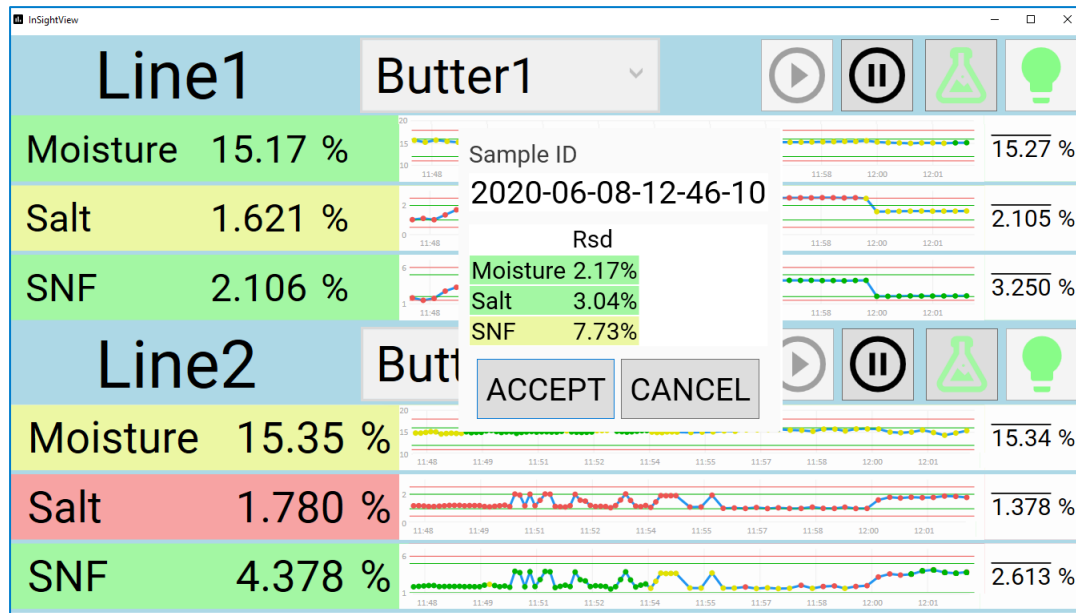


Figure 4 120 sec of a process with relative short term variation of +/- 15%

# ”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



# In summary...

---



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

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



*Value through insight*

SINCE 1998

Thank you



[www.q-interline.com](http://www.q-interline.com)



[LinkedIn.com/company/q-interline](https://www.linkedin.com/company/q-interline)

