



IFA

Institut für Arbeitsschutz der
Deutschen Gesetzlichen Unfallversicherung

Workshop: Measurement Uncertainty for Measurement Methods of Air Monitoring

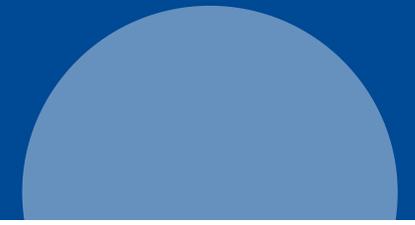
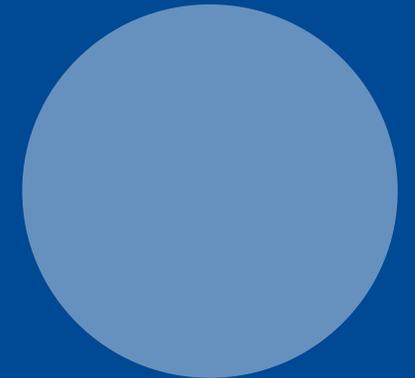
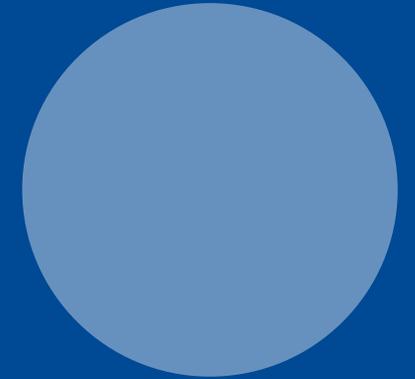
AIRMON 10, Bristol/UK

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Agenda

- **Introduction**
 - What is Measurement Uncertainty?
 - Terms
- **Regulatory Basis**
- **Validation Steps**
- **Calculate the Uncertainty**
 - Mathematical Model
 - Build the Mass Concentration Model
 - Standard Deviations
 - Derive Standard Deviations
- **Implementation into the App**



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Introduction

What is measurement uncertainty?

The true value is principally unknown. The measured value is always an estimate depending on different influences. The uncertainty is a parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand.

Why do we need the measurement uncertainty?

- Customer request
- Regulation requirement (comparison with limit values)
- Comparison with other laboratories, improvement of measurement process

Introduction

Expanded measurement uncertainty:

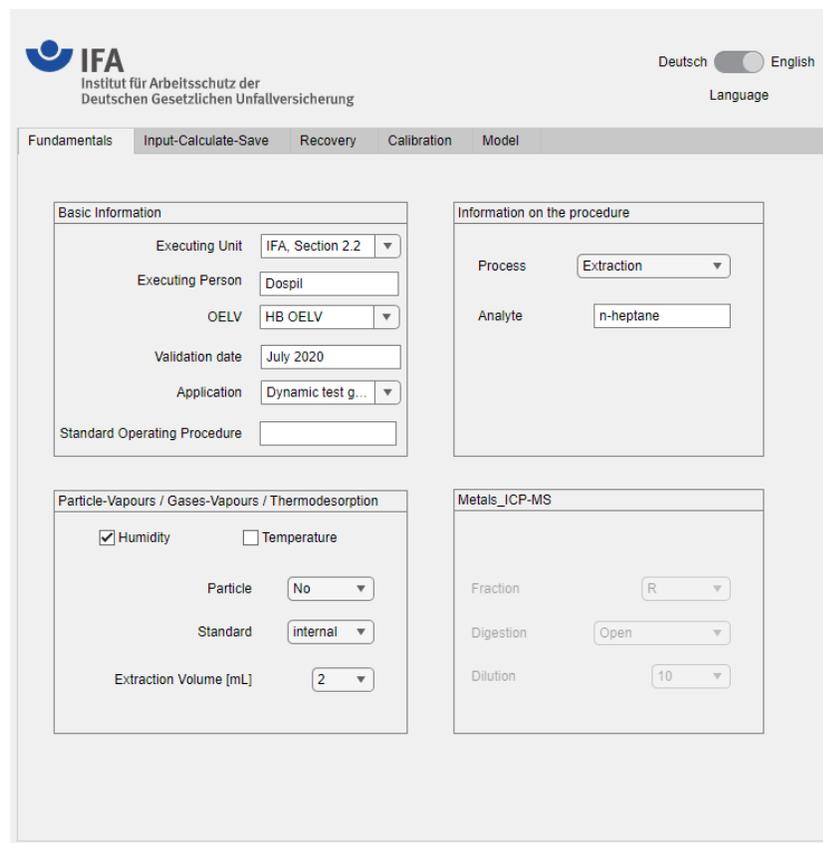
Coverage factor k	Probability
1	68.3 %
1.96	95 %
2	95.45 %
2.6	99 %
3	99.7 %

→ means: one can attribute a certain probability to the expanded uncertainty range.

→ does NOT mean: there is a certain chance that the true value lies within the range of the measurement uncertainty

- ISO 20581: $k = 2$ → approximately 95 % but rounded to a whole number
- In our calculation we use $k = 1.96$

App for the Calculation of the Measurement Uncertainty



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Deutsch English
Language

Fundamentals **Input-Calculate-Save** Recovery Calibration Model

Basic Information

Executing Unit: IFA, Section 2.2
 Executing Person: Dospil
 OELV: HB OELV
 Validation date: July 2020
 Application: Dynamic test g...
 Standard Operating Procedure:

Information on the procedure

Process: Extraction
 Analyte: n-heptane

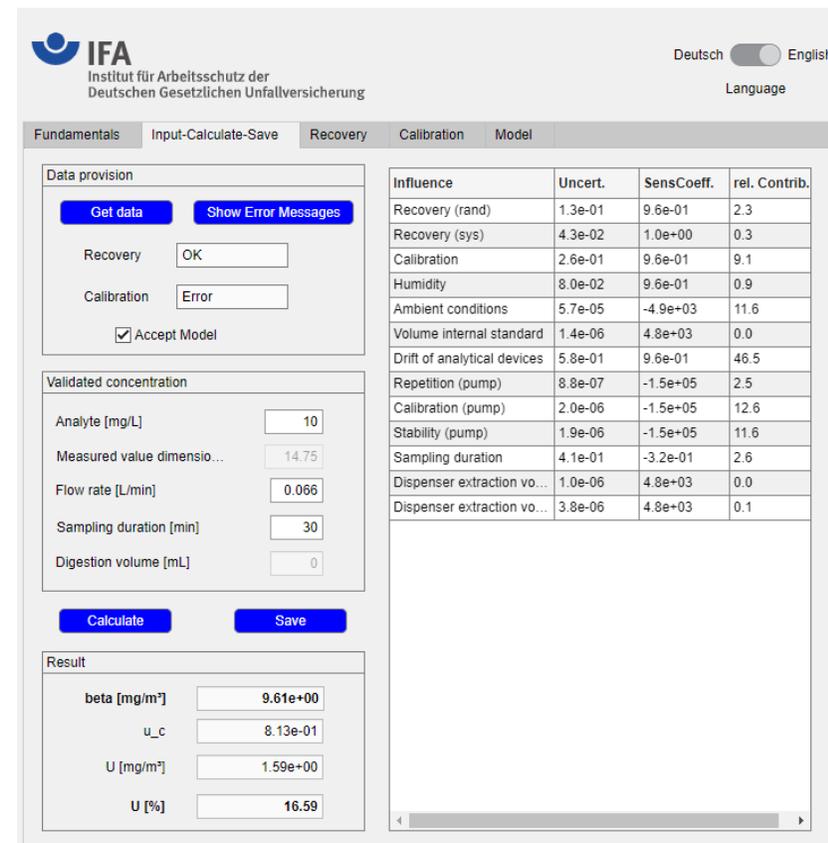
Particle-Vapours / Gases-Vapours / Thermodesorption

Humidity Temperature

Particle: No
 Standard: internal
 Extraction Volume [mL]: 2

Metals_ICP-MS

Fraction: R
 Digestion: Open
 Dilution: 10



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Fundamentals Input-Calculate-Save **Recovery** Calibration Model

Data provision

Get data Show Error Messages

Recovery: OK
 Calibration: Error
 Accept Model

Validated concentration

Analyte [mg/L]: 10
 Measured value dimensio...: 14.75
 Flow rate [L/min]: 0.066
 Sampling duration [min]: 30
 Digestion volume [mL]: 0

Calculate Save

Result

beta [mg/m³]: 9.61e+00
 u_c: 8.13e-01
 U [mg/m³]: 1.59e+00
 U [%]: 16.59

Influence	Uncert.	SensCoeff.	rel. Contrib.
Recovery (rand)	1.3e-01	9.6e-01	2.3
Recovery (sys)	4.3e-02	1.0e+00	0.3
Calibration	2.6e-01	9.6e-01	9.1
Humidity	8.0e-02	9.6e-01	0.9
Ambient conditions	5.7e-05	-4.9e+03	11.6
Volume internal standard	1.4e-06	4.8e+03	0.0
Drift of analytical devices	5.8e-01	9.6e-01	46.5
Repetition (pump)	8.8e-07	-1.5e+05	2.5
Calibration (pump)	2.0e-06	-1.5e+05	12.6
Stability (pump)	1.9e-06	-1.5e+05	11.6
Sampling duration	4.1e-01	-3.2e-01	2.6
Dispenser extraction vo...	1.0e-06	4.8e+03	0.0
Dispenser extraction vo...	3.8e-06	4.8e+03	0.1

Introduction

Uncertainty:

- Part of the norm, determined through experiments
- Imperfection of handling and devices
- Cannot be avoided
- Part of the determination of measurement uncertainty

Error:

- Not part of the norm, lead back to misconduct of handling or device
- Are avoidable
- Need to be minimized or eliminated beforehand

Introduction

Systematic deviation

- This is a known deviation that stays always the same (e.g. instrument offset).
- It can be corrected for, often by including a correction constant.

Random deviation

- This influence can only be described by a random variable.
 - **However**, one has often the situation, that there is a offset for the used instruments, but the instruments are used randomly.
- If the resulting influence is small, one may treat this as a random variable, although it is in principle a systematic deviation.

Example: Extraction volume

Calibration protocol

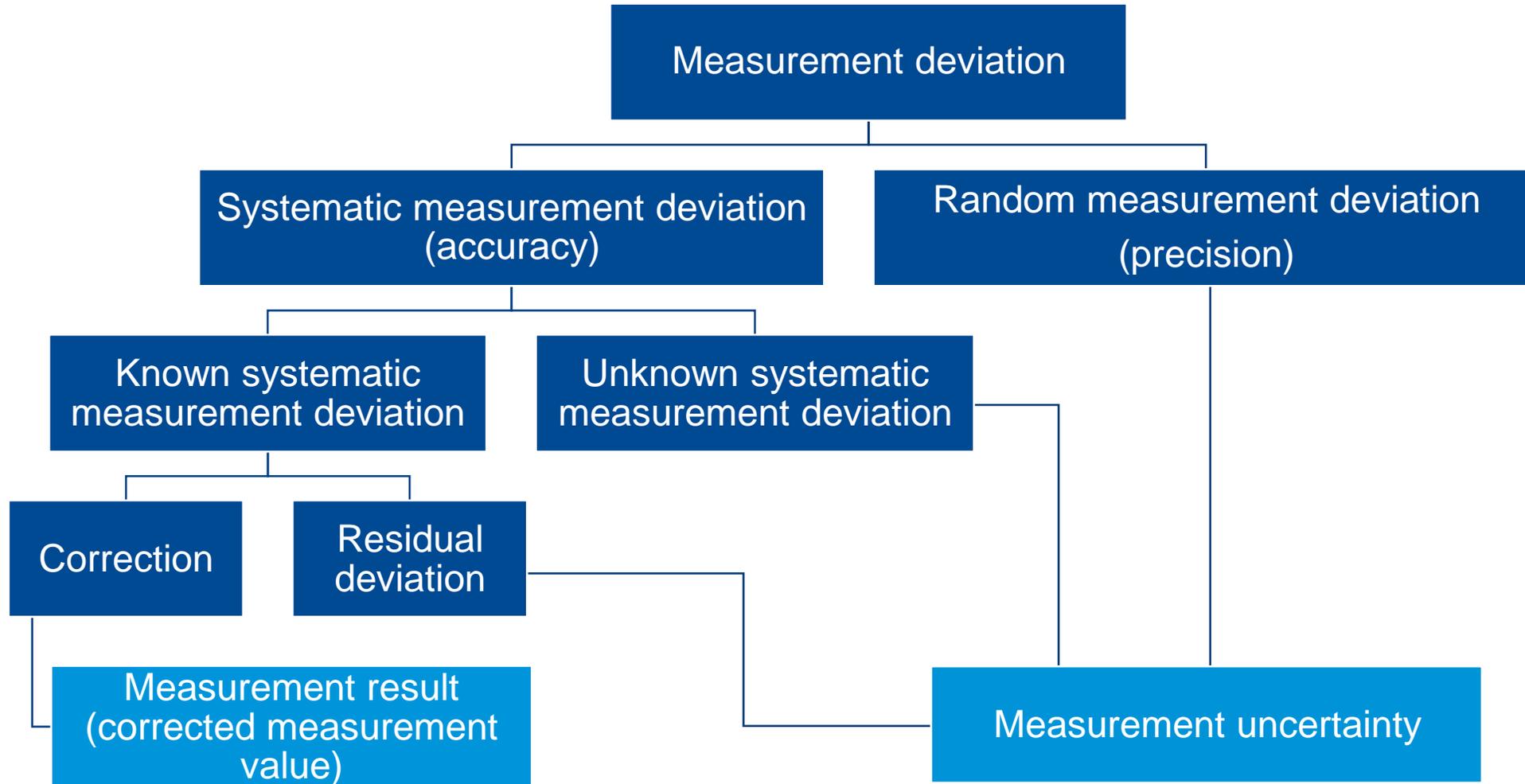
	Actual values		Nominal values	Remarks
Mean value:	2499.60 μL		2500.0 μL	
Systematic deviation:	-0.02 (Es) [%]	\pm	± 0.50 (Es) [%]	OK
Random Deviation:	0.02 (CV) [%]	\pm	± 0.25 (CV) [%]	OK

constant correction e_s

- negative sign \rightarrow always too large
- $e_s = -(2500 \cdot 0.0002)\mu\text{L}$

CV: coefficient of variation

This contains a standard deviation of random variable (s_r)



Regulatory basis

-  ISO 20581: 2016 Workplace air – General requirements for the performance of procedures for the measurement of chemical agents
-  ISO 22065: 2019 Workplace air – Gases and vapours – Requirements for evaluation of measuring procedures using pumped samplers
-  ISO 21832: 2018 Workplace air – Metals and metalloids in airborne particles – Requirements for evaluation of measuring procedures
-  ISO 23861:2020 Workplace air – Chemical agent present as a mixture of airborne particles and vapour – Requirements for evaluation of measuring procedures (draft)
-  DIN 32645: 2008 Chemical analysis – Decision limit, detection limit and determination limit under repeatability conditions – Terms, methods, evaluation

Validation Steps

Experiments	Part of MU
Sampling	✓
Transport	✗ - gases (✓) – metals
Storage (without loss)	✗
Sample preparation	✓
Calibration	✓
Limit of quantification	✗
Recovery	✓
Influence of temperature/humidity (not for metals)	✓

Calculate the uncertainty

The formula

The GUM

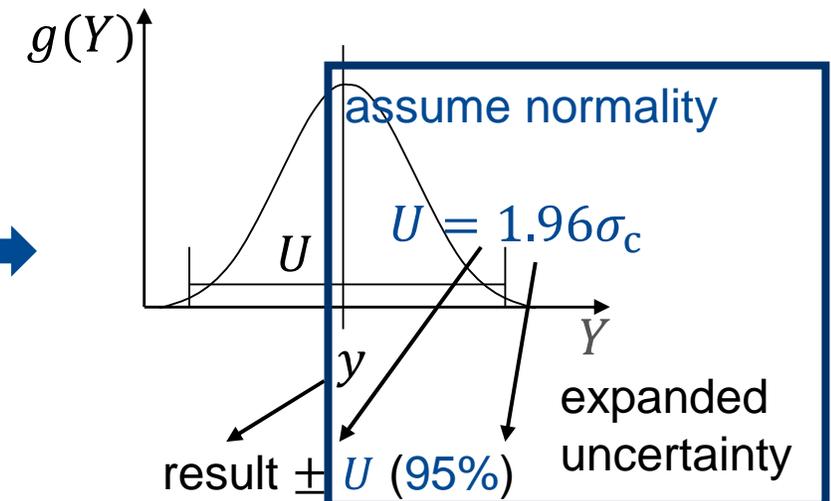
- ISO/IEC Guide 98-1:2009 *Uncertainty of measurement — Part 1: Introduction to the expression of uncertainty in measurement* (Guide to the expression of uncertainty in measurement GUM)
- Influences $\{X_i\}$ affect a measurable quantity $Y = f(\{X_i\})$. The GUM allows to communicate the available information on X_i in a transparent, quantitative way.
- Due to the influences, results vary with a variance σ_c^2 around the measured value y (asymptotically **normal distributed**).

Information on X_i

- influence 1
- ...
- influence i
- ...
- influence n

$$\sigma_c = \sqrt{\sum_i c_i^2 \sigma_i^2}$$

combined uncertainty

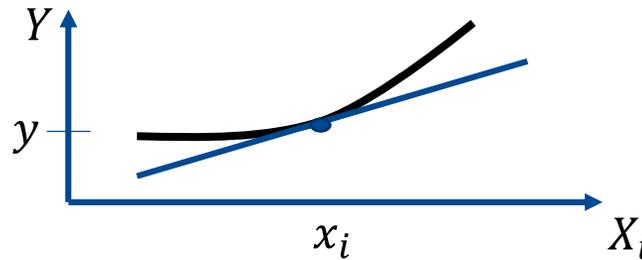


The formula

$$\sigma_c = \sqrt{\sum_i c_i^2 \sigma_i^2}$$

Assumptions/Requirements:

- Normal distribution ($U = 1.96\sigma_c$)
- small effect on Y



Taylor expansion (linear)

$$Y \approx \underbrace{f(\{x_i\})}_y + \sum_i \underbrace{\left(\frac{\delta f}{\delta X_i}\right)}_{c_i} (X_i - x_i)$$



Definition of variance

$$V[Y] = \sigma_c^2 = E[Y - y]^2$$



- **uncorrelated** $\{X_i\}$

$$\sigma_c = \sqrt{\sum_i c_i^2 \sigma_i^2}$$



$$\sigma_c = \sqrt{\sum_i c_i^2 \sigma_i^2 + \sum_{i \neq j} \cancel{c_i c_j \sigma_i \sigma_j \rho_{(X_i, X_j)}}$$

The formula

$$\sigma_c = \sqrt{\sum_i c_i^2 \sigma_i^2}$$

Assumptions/Requirements:

- Normal distribution ($U = 1.96\sigma_c$)
- small effect on Y
- **uncorrelated** $\{X_i\}$

Sensitivity coefficients c_i

- Determine from $Y = f(\{X_i\}) \Rightarrow c_i = \left(\frac{\delta f}{\delta X_i}\right)_{x_i}$
- They account for units.
- They weight the influences:
The larger the exponent of X_i in f , the more important is X_i .



We need the function f (mathematical model)

Standard deviation σ_i

- Derive from information on $\{X_i\}$
- Standard uncertainties u_i are always interpreted as standard deviations σ_i .

Mathematical model

Know and assume

Example: mass concentration (extraction)

How does one get $Y = f(\{X_i\})$?

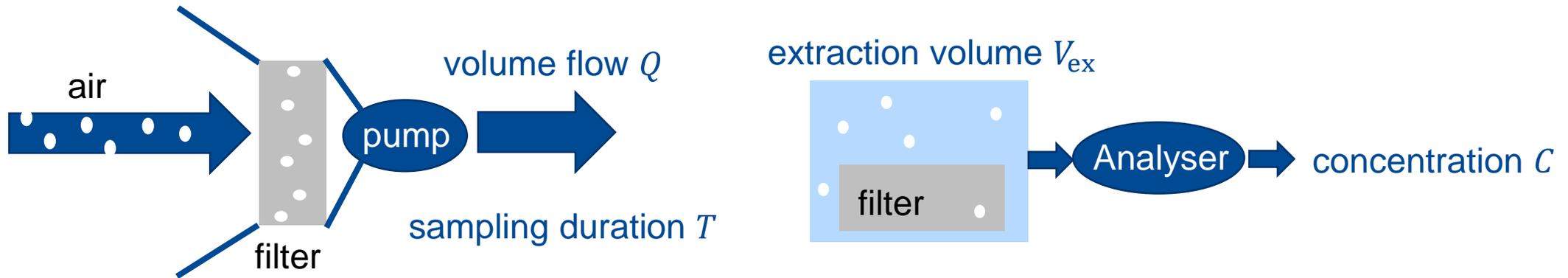
1. The function $Y = f(\{X_i\})$ (mathematical model) is **known**.

2. One can **assume** a functional dependence: $Y = y + \sum_i X_i$

- X_i can be any influence that has to be described.
- X_i is a random variable with expected value $E[X_i] = 0$ and variance $V[X_i] = \sigma_i^2$ (standard deviation σ_i).
- Exponent of X_i is 1 \rightarrow sensitivity coefficients $c_i = 1$

1. Known model for the mass concentration

- What is known for the mass concentration B ? - Generic mathematical model



Sample Preparation



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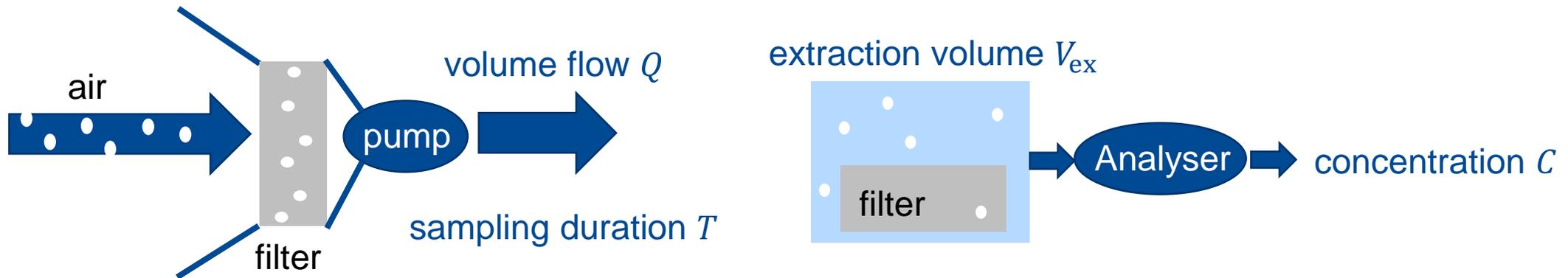
Example: Extraction

- Sampler is opened and transferred into a vial
- Solvent is added
- If needed: internal standard is added
- After a certain extraction time, the extract is filtered and then added into an autosampler vial

Uncertainties: all volumetric instruments

1. Known model for the mass concentration

- What is known for the mass concentration B ? - Generic mathematical model



$$B = \frac{M}{V_{\text{air}}} = \frac{V_{\text{ex}}C}{TQ}$$

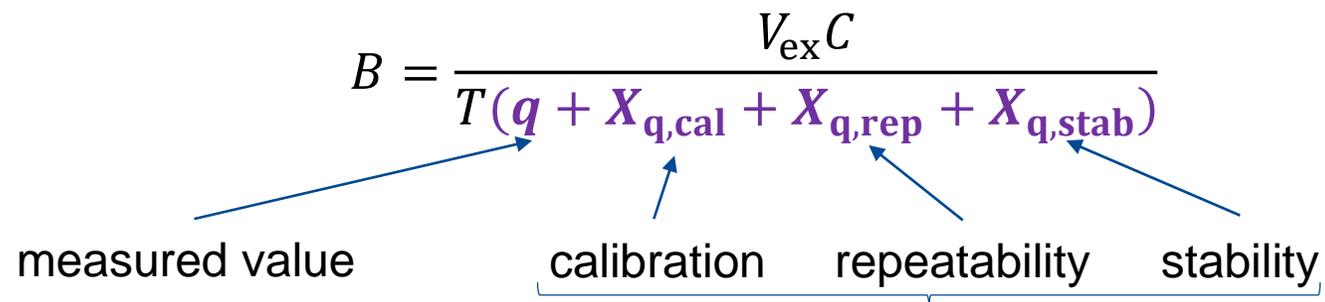
- Volume flow Q is corrected for ambient conditions. Ideal gas: $V_{\text{air}}(p_1, \tau_1) \rightarrow V_{\text{air}}(p_0, \tau_0)$

How does one get $Y = f(\{X_i\})$?

1. The function $Y = f(\{X_i\})$ (mathematical model) is known.

$$B = \frac{V_{\text{ex}} C}{T Q}$$

2. One can **assume** a functional dependence $Y = y + \sum_i X_i$, e. g., for the **volume flow**:

$$B = \frac{V_{\text{ex}} C}{T (q + X_{q,\text{cal}} + X_{q,\text{rep}} + X_{q,\text{stab}})}$$


uncertainty influences mentioned in ISO 22065 and ISO 21832

Sensitivity coefficients for Q

- The $\{X_{q,i}\}$ are variables. The (corrected) measured values v_{ex}, c, t, q are constants.
- With $B = \frac{V_{\text{ex}}C}{T(q+X_{q,\text{cal}}+X_{q,\text{rep}}+X_{q,\text{stab}})} = \frac{V_{\text{ex}}C}{T} \left[\frac{1}{(q+X_{q,\text{cal}}+X_{q,\text{rep}}+X_{q,\text{stab}})} \right]$, one gets:

$$c_{q,i} = \left(\frac{\delta B}{\delta X_{q,i}} \right)_{x_i} = -\beta \frac{1}{q}$$

- All $\{X_{q,i}\}$ have the same $c_{q,i}$, since the inner derivative is always 1.
- $()_{x_i}$ means to take expected/measured value: $\{V_{\text{ex}}; C; T; X_{q,i}\} \rightarrow \{v_{\text{ex}}; c; t; 0\}$

 Proceed in the same way for the other quantities

Build the mass concentration model

Example: Extraction

Sampling duration, ambient conditions, extraction volume

$$B = \frac{(v'_{\text{ex}} + e_s + X_{\text{ex}})}{(t + X_t)(q + X_{q,\text{cal}} + X_{q,\text{rep}} + X_{q,\text{stab}}) + X_{\text{air}}} C$$

- ISO 22065 suggests only one term X_t that is large enough to comprise several influences (calibration of watch, starting/ending delay ...).
- Take one influence X_{air} for the volume $V_{\text{air}} = TQ$ (pressure, temperature measurement equipment, fluctuations during sampling ...).
- Influence of the volumetric instrument X_{ex} .
- Constants:
 - Measured values t, q, v'_{ex}
 - Correction factor $v_{\text{ex}} = v'_{\text{ex}} + e_s$ (systematic correction from calibration protocol).

Sampling duration, ambient conditions, extraction volume

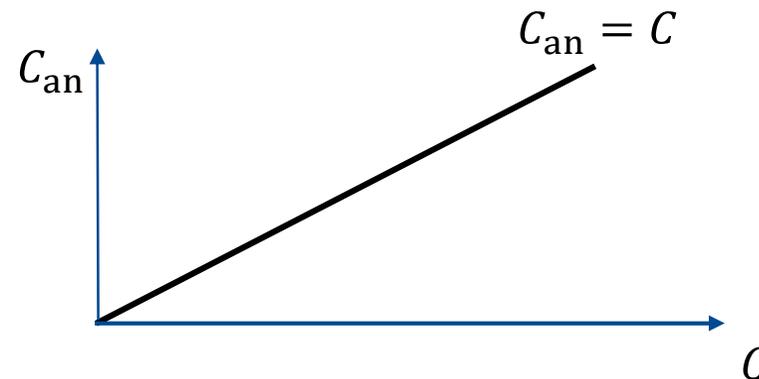
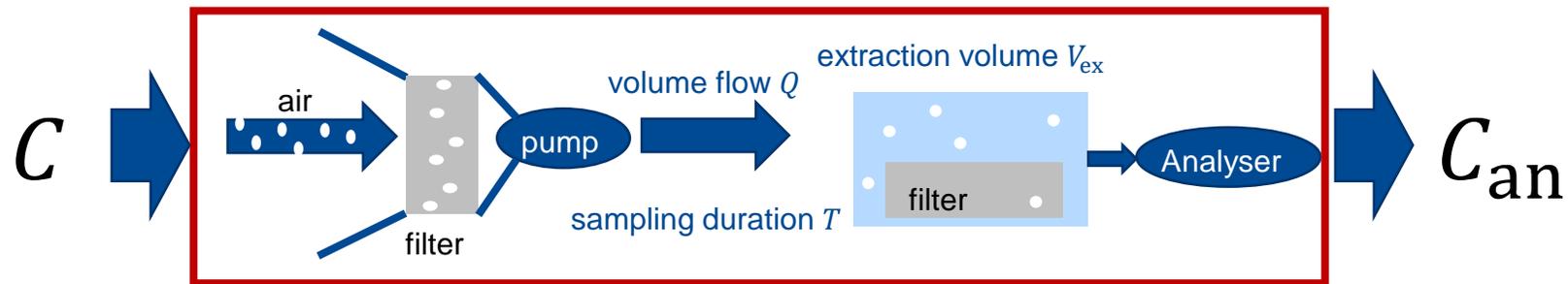
$$B = \frac{(v'_{\text{ex}} + e_s + X_{\text{ex}})}{(t + X_t)(q + X_{q,\text{cal}} + X_{q,\text{rep}} + X_{q,\text{stab}}) + X_{\text{air}}} C$$

Sensitivity coefficient	$c_{q,i}$	c_t	c_{air}	c_{ex}
Formula	$-\beta \frac{1}{q}$	$-\beta \frac{1}{t}$	$-\beta \frac{1}{tq}$	$\beta \frac{1}{v_{\text{ex}}}$
Influences	$X_{q,\text{cal}}, X_{q,\text{rep}}, X_{q,\text{stab}}$	X_t	X_{air}	X_{ex}



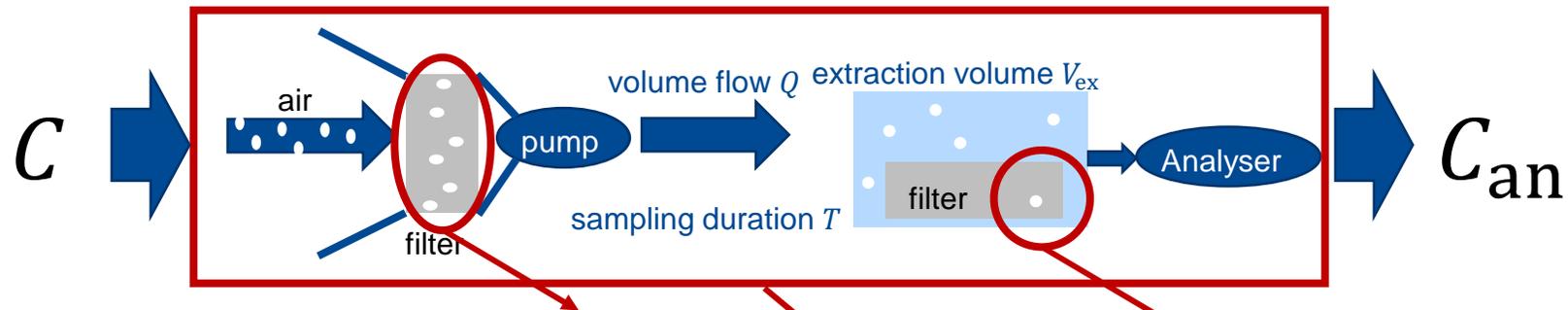
Concentration: **Know** and assume

In an ideal world, the measured concentration in the analyser C_{an} is unaffected by the method.



Concentration: Know and assume

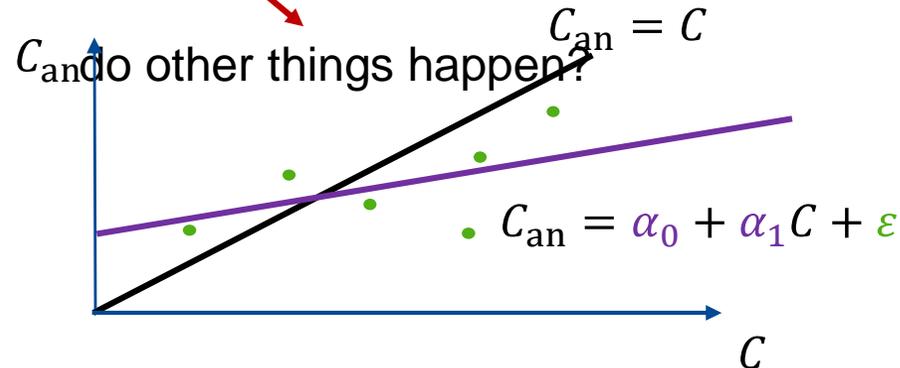
In reality, C_{an} is affected by the method. Supply known concentrations \rightarrow recovery model



do we filter completely?

do we extract completely?

- Linear model – **systematic** effects
 - Offset (intercept, α_0) and proportional effect (slope, α_1)
 - Ideal recovery: $\alpha_0 = 0$ and $\alpha_1 = 1$
 - A **random** effect $\varepsilon \sim \mathcal{N}(0, \sigma_{c,ran}^2)$



Analytics

To taken into account for measurement uncertainty

Calibration / Analyser drift

Recovery of analyte in dependence of concentration

Relative humidity; not for particles

Temperature; not for particles

Analytical Measurement

- **Calibration** of the analytical device via calibration solutions of the analyte in known concentrations
 - Analyser drift: validation of calibration via QC checks
- Uncertainties:
 - Work-day fluctuation of the sensitivity of the analytical device (maximal target-actual-difference of QC checks, e. g. 5 %)



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Recovery



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Is the recovery dependent on the concentration of the analyte?



Is the recovery dependent on the type of analyte?



Experimental determination through validation tests in the laboratory: three different concentration levels with at least 6 replicates at room temperature and average humidity

- Uncertainties: systematic (if there is no correction) and random deviation (precision)

Temperature/Relative Humidity

Do different temperatures and relative humidities influence the recovery of the analyte in the air?

Experimental determination through validation

**high and low humidity at the limits of the measuring range
(n = 6)**

Experimental determination through validation

**high and low temperature at the limits of the measuring range
(n = 6)**

If there is an influence on the recovery, it is part of the measurement uncertainty: Systematic (if there is no correction) and random deviation

Concentration: Know and assume

- Regression analysis:

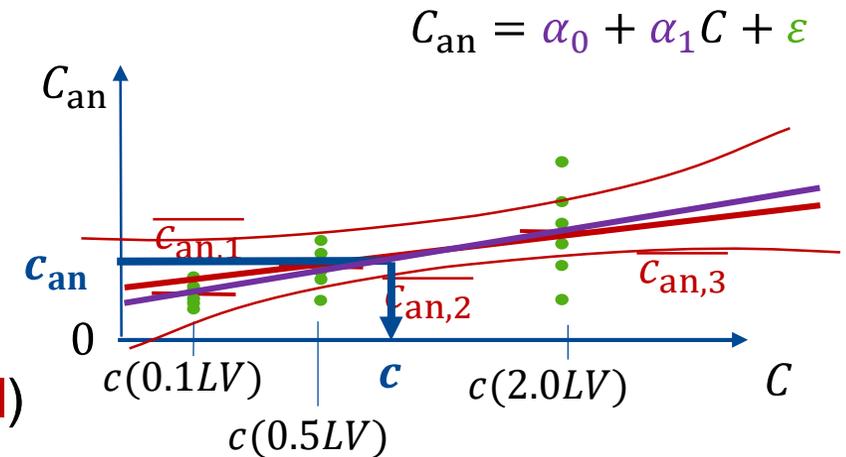
- Truth

$$C_{\text{an}} = \alpha_0 + \alpha_1 C + \varepsilon \quad \xrightarrow{\text{Estimate}} \quad C_{\text{an}} = a_0 + a_1 C + X_{\text{c,est}} + X_{\text{c,ran}}$$

- The estimates a_0 , a_1 have uncertainties (standard errors) \rightarrow uncertainty of regression line (**confidence interval**)
Additional uncertainty term for using regression estimate $X_{\text{c,est}}$
 - We are interested in $C \rightarrow$ inverse regression:

$$C = \frac{C_{\text{an}} + X_{\text{c,ran}} - a_0}{a_1} + X_{\text{c,est}} \quad (\text{symmetric distributions} \rightarrow \text{plus signs})$$

$$B = \frac{V_{\text{ex}}}{TQ} C = \frac{V_{\text{ex}}}{TQ} \left[\frac{1}{a_1} (C_{\text{an}} - a_0) + X_{\text{c,ran}} + X_{\text{c,est}} \right]$$



2022 version changed!
 $X_{\text{c,ran}}$ referred 2022 to C_{an} . Now it refers correctly to C .

Concentration: Know and **assume**

- Now, we plug in the other influences that affect C_{an} as usual: $C_{an} = c_{an} + \sum X_{c,i}$
- The drift of the analyser $X_{c,drift}$, the uncertainty of the calibration function $X_{c,cal}$, the humidity $X_{c,H}$, and temperature $X_{c,\tau}$

$$B = \frac{V_{ex}}{TQ} C = \frac{V_{ex}}{TQ} \left[\frac{1}{a_1} \left(c_{an} + X_{c,drift} + X_{c,cal} + X_{c,H} + X_{c,\tau} - a_0 \right) + X_{c,ran} + X_{c,est} \right]$$

Sensitivity coefficient	$c_{c,i}$	$c_{c,est}$
Formula	$\beta \frac{1}{c_{an} - a_0}$	$\beta \frac{1}{c}$
Influences	$X_{c,drift}, X_{c,cal}, X_{c,H}, X_{c,\tau}$	$X_{c,ran}, X_{c,ran}$



Summary

- We have set up a model for the mass concentration.

$$B = \frac{(v'_{ex} + e_s + X_{ex}) \left[\frac{1}{a_1} (c_{an} + X_{c,drift} + X_{c,cal} + X_{c,H} + X_{c,\tau} - a_0) + X_{c,ran} + X_{c,est} \right]}{(t + X_t)(q + X_{q,cal} + X_{q,rep} + X_{q,stab}) + X_{air}}$$

- Variables: random numbers $\{X_i\}$ colours for different quantities
- Constants: systematic corrections ($e_s, a_{\{0,1\}}$) or measured values (v'_{ex}, c_{an}, t, q)
- One can calculate β , the measured value of the mass concentration:

$$\beta = \frac{v'_{ex} + e_s}{tq} \frac{1}{a_1} (c_{an} - a_0) = \frac{v_{ex}}{tq} \frac{(c_{an} - a_0)}{a_1}$$

Summary

- We have set up a model for the mass concentration.
- We have all sensitivity coefficients for the variables.

Sensitivity coefficient	$c_{q,i}$	c_t	c_{air}	c_{ex}	$c_{c,i}$	$c_{c,est}$
Formula	$-\beta \frac{1}{q}$	$-\beta \frac{1}{t}$	$-\beta \frac{1}{tq}$	$\beta \frac{1}{v_{ex}}$	$\beta \frac{1}{c_{an} - a_0}$	$\beta \frac{1}{c}$
Influences	Calibration, Repeatability, Stability	Duration (all)	Ambient conditions (all)	Extraction volume	Drift, Calibration, Humidity, Temperature	Recovery model, repeatability



Summary

Key approach:

To use the sum assumption allows you to describe otherwise unknown influences.

$$Y = y + \sum_i X_i$$

$$\sigma_c = \sqrt{\sum_i c_i^2 \sigma_i^2}$$

Sensitivity coefficients c_i

- Determine from $Y = f(\{X_i\}) \Rightarrow c_i = \left(\frac{\delta f}{\delta X_i} \right)_{x_i}$



Standard deviation σ_i

- Derive from information on $\{X_i\}$

now

Standard deviations

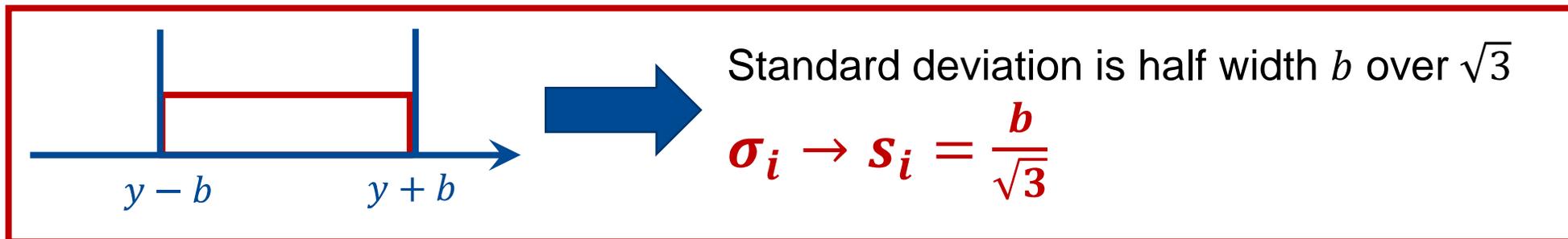
Derived from available information

How does one get the σ_i ?

- We make estimates: $\sigma_i \rightarrow s_i$
- There are three main cases:
 - „Limit of error“ $y \pm b$
 - Known σ_i from other source
 - Known from own measurement (here, regression analysis)

Limit of error

- A given influence changes the measured value y only within fixed boundaries:
 $y \pm b$ (**limit of error**)
- Assume a uniform distribution form based on the principle of maximum entropy.



Example:

How large is the standard deviation for reading off the last digit on a digital display of a scale with the unit 1 g? $\rightarrow s = \frac{0.5}{\sqrt{3}} \text{ g}$

Other source: use as given

- If you find a standard deviation, use it as given.
- Assume normal distribution based on the principle of maximum entropy.
- Interpret the given information
- Example:
Calibration protocol: „The expanded 95 % uncertainty region is ± 4 % of the measured value.“ $\rightarrow s = y \cdot 0.04/1.96$

Derive standard deviations

All sources of information apart from own measurements

Overview – no own measurements

Influence	X_i	Source
Duration (all)	X_t	ISO 22065
Pump calibration	$X_{q,cal}$	ISO 20581 (worst case Table B.1)
Pump repeatability	$X_{q,rep}$	ISO 20581 (worst case Table B.1)
Pump flow stability	$X_{q,stab}$	ISO 13137 (norm requirement)
Extraction volume (rand.)	X_{ex}	Calibration protocol
Ambient conditions	X_{air}	Experience (Limit of error $\pm 5 \%$)
Analyser drift	$X_{c,drift}$	Experience (Limit of error $\pm 10 \%$)
Calibration	$X_{c,cal}$	Calibration measurement
Humidity, Temperature, Concentration (est./rand.)	$X_{c,\{H,\tau,ran,est\}}$	Recovery measurement

Extraction volume (random) – use as given

- There is information on the random influence of the volumetric instrument in the calibration protocol

	Actual values
Mean value:	2499.60 μL
Systematic deviation:	-0.02 (Es) [%]
Random Deviation:	0.02 (CV) [%]

- CV: coefficient of variation:

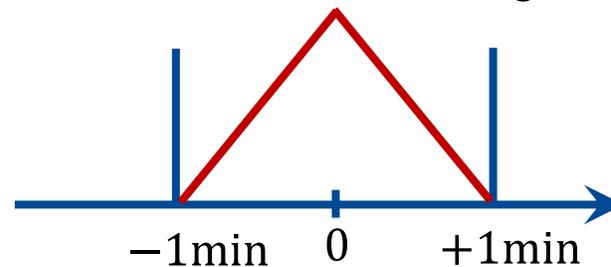
$$\frac{s_r}{\bar{V}} 100\% = 0.02\% \rightarrow s_r = \frac{2499.6 \cdot 0.02}{100} \mu\text{L} \approx 0.5 \mu\text{L}$$

Influence	X_i	c_i	s_i
Extraction volume (rand.)	X_{ex}	$\beta \frac{1}{v_{\text{ex}}}$	0.5 μL



Duration – use as given

- Guideline and discussion, e. g., in ISO 22065
 - Measurement is started/ended within 0.5 min before/after the true start/end of the measurement. → assume ± 1 min and neglect other terms (reading error ...)



- Standard proposes triangular distribution. → Use $s_i = \frac{1}{\sqrt{6}} \text{ min} \approx 0.408 \text{ min}$

Influence	X_i	c_i	s_i
Duration (all)	X_t	$-\beta \frac{1}{t}$	0.408 min



Volume flow stability – limit of error

- ISO 20581 on **flow stability**: „ISO 13137 requires that the flow rate is maintained to within $\pm 5\%$.”
- Use limit of error ($b = q \cdot 0.05$): $s_{q,stab} = \frac{q \cdot 0.05}{\sqrt{3}}$

Influence	X_i	c_i	s_i
Pump flow stability	$X_{q,stab}$	$-\beta \frac{1}{q}$	$\frac{q \cdot 0.05}{\sqrt{3}}$



Analyser drift – limit of error

- „Experience shows that the analyser drift changes the measured concentration within $\pm 10\%$.“
- Limit of error, half width $b = c_{\text{an}} \cdot 0.10 \rightarrow s_{\text{an}} = \frac{c_{\text{an}} \cdot 0.10}{\sqrt{3}}$

Influence	X_i	c_i	s_i
Analyser drift	$X_{\text{c,drift}}$	$\beta \frac{1}{c_{\text{an}} - a_0}$	$\frac{c_{\text{an}} \cdot 0.10}{\sqrt{3}}$



Overview – no own measurements

Influence	X_i	Source	
Duration (all)	X_t	ISO 22065	✓
Pump calibration	$X_{q,cal}$	ISO 20581 (worst case Table B.1)	
Pump repeatability	$X_{q,rep}$	ISO 20581 (worst case Table B.1)	
Pump flow stability	$X_{q,stab}$	ISO 13137 (norm requirement)	✓
Extraction volume (rand.)	X_{ex}	Calibration protocol	✓
Ambient conditions	X_{air}	Experience (Limit of error $\pm 5\%$)	
Analyser drift	$X_{c,drift}$	Experience (Limit of error $\pm 10\%$)	✓

Overview – no own measurements

Missing standard deviations are found in the same way

X_i	Source			
X_t	ISO 22065	✓	use given uncertainty	
$X_{q,cal}$	ISO 20581 (worst case Table B.1)	→	5.2 %	→ $s_{q,cal} = q \cdot 0.052$
$X_{q,rep}$	ISO 20581 (worst case Table B.1)	→	2.3 %	→ $s_{q,rep} = q \cdot 0.023$
$X_{q,stab}$	ISO 13137 (norm requirement)	✓		
X_{ex}	Calibration protocol	✓		
X_{air}	Experience (Limit of error $\pm 5\%$)	→	same as drift	→ $s_{air} = \frac{tq \cdot 0.05}{\sqrt{3}}$
$X_{c,drift}$	Experience (Limit of error $\pm 10\%$)	✓		

Summary – other source

Key approach:

To use the limit of error approach allows you to describe your own experience.

$$s_i = \frac{b}{\sqrt{3}}$$

With the table, one can derive the combined standard deviation (up to the missing terms $X_{c,\{H,T,ran,est,cal\}}$):

$$s_c = \sqrt{\sum_i c_i^2 s_i^2} \rightarrow B = \beta \pm 1.96 s_c$$

Could be dealt with in a spread sheet

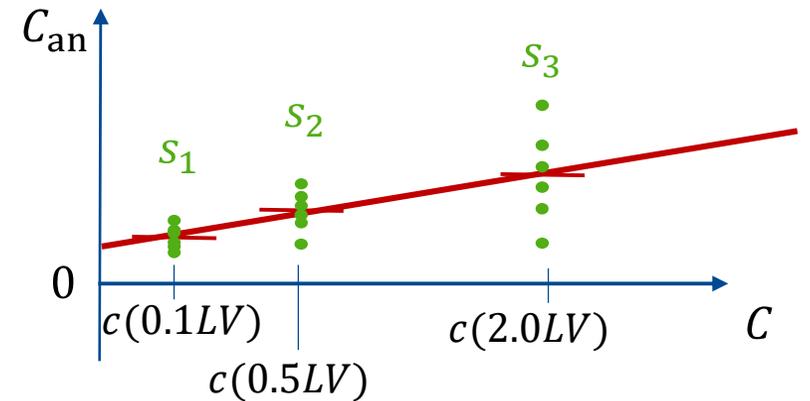
Influence	X_i	c_i	s_i
Duration (all)	X_t	$-\beta \frac{1}{t}$	0,408 min
Pump calibration	$X_{q,cal}$	$-\beta \frac{1}{q}$	$q \cdot 0.052$
Pump repeatability	$X_{q,rep}$		$q \cdot 0.023$
Pump flow stability	$X_{q,stab}$		$\frac{q \cdot 0.05}{\sqrt{3}}$
Extraction volume (rand.)	X_{ex}	$\beta \frac{1}{v_{ex}}$	0.5µl
Ambient conditions	X_{air}	$-\beta \frac{1}{k_{air} \cdot tq}$	$\frac{tq \cdot 0.05}{\sqrt{3}}$
Analyser drift	$X_{c,drift}$	$\beta \frac{1}{c_{an} - a_0}$	$\frac{c_{an} \cdot 0.10}{\sqrt{3}}$

Derive standard deviations

Regression analyses

Recovery/calibration – non-constant variance

- Homoscedasticity: ε has constant variance
 $C_{\text{an}} = \alpha_0 + \alpha_1 C + \varepsilon$ with $\varepsilon \sim \mathcal{N}(0, \sigma_{\varepsilon, \text{ran}}^2)$
- Heteroscedasticity: ε has **not** a constant variance
- Variance s_i^2 increases with c .



- You cannot do ordinary least squares fit (OLS) for the estimates a_0, a_1
- Do **weighted regression** (Draper & Smith 1998):
 - Determine s_i
 - Weight the dependent values y with $w_i = \frac{1}{s_i^2}$
 (Supply a vector with the w_i to the regression routine)

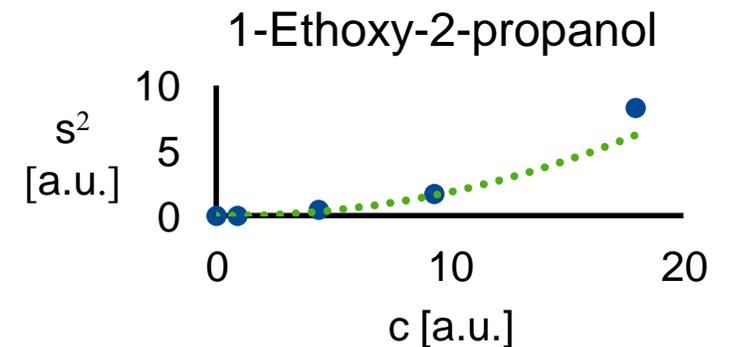
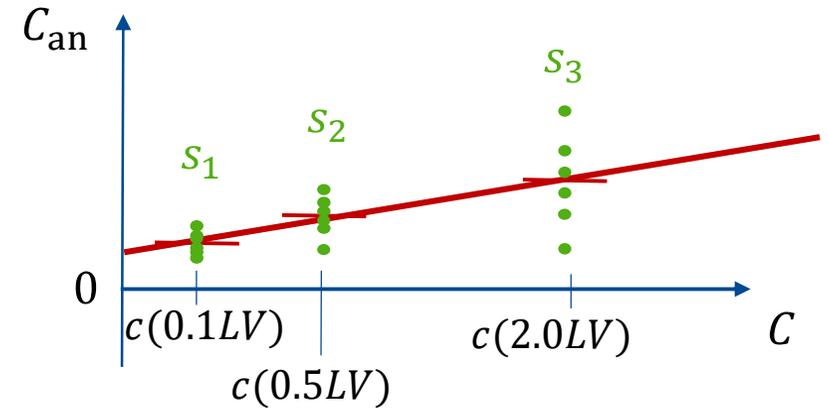
Draper N. R., Smith H., Applied Regression Analysis (1998) 3rd edition, Wiley.

Concentration random

- Variation around the regression line $X_{c,ran}$

$$B = \frac{V_{ex}}{TQ} \left[\frac{1}{a_1} (C_{an} - a_0) + X_{c,ran} + X_{c,est} \right]$$

- Heteroscedasticity: $C_{an} = \alpha_0 + \alpha_1 C + \varepsilon$
Variance s_i^2 is surprisingly often quadratic in c : $\varepsilon(0, k_\varepsilon c^2)$
- Determine k with fit: $s_i^2 = k_\varepsilon c^2$



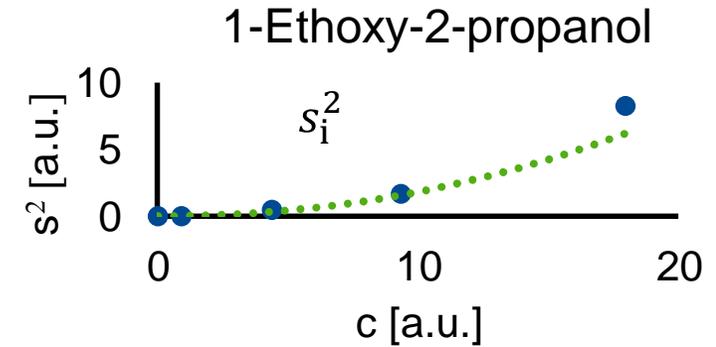
2022 version changed!

$X_{c,ran}$ referred 2022 to C_{an} .

Now it refers correctly to C .

Concentration random

1. Determine s_i standard deviations
2. Regression coefficient for recovery variance k_ε
Fit: $s_i^2 = k_\varepsilon c_i^2 \rightarrow s_{c,ran} = \sqrt{k_\varepsilon c^2}$
3. Check coefficient of determination $R^2 > 0.95$.
If not, try $s_i^2 = k_\varepsilon c$.
4. Take k_ε and calculate s



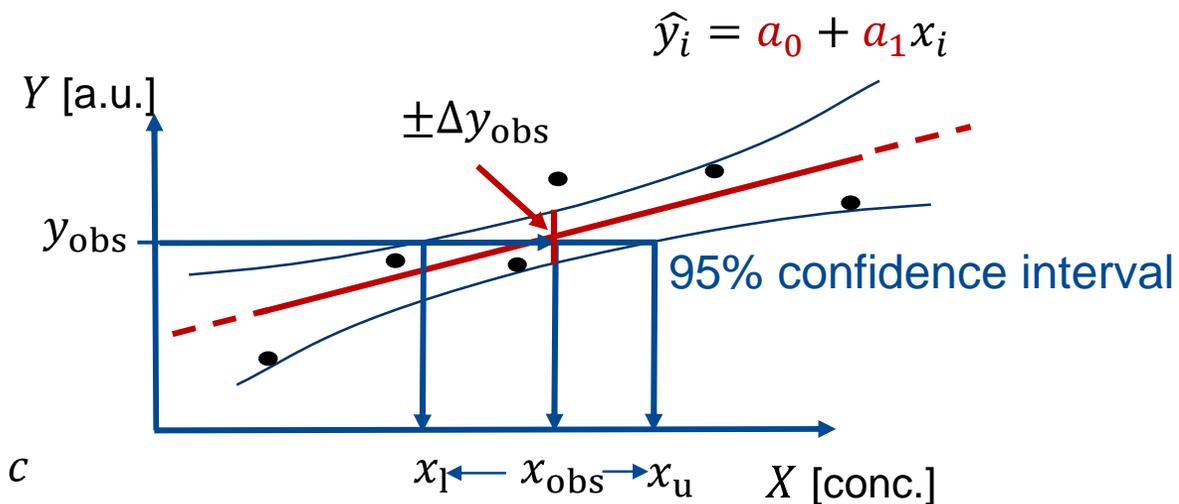
Influence	X_i	c_i	s_i
Concentration (random)	$X_{c,ran}$	$\beta \frac{1}{c}$	$\sqrt{k_\varepsilon c (c_{in})^2}$



Concentration estimate

- The uncertainty of the regression line is largest on the boundaries of the covered range.
 → If we leave this range, we may observe a severe increase in the uncertainty.
- We derive desired quantities x_{obs} by inverse regression from measured quantities y_{obs} :
 $y_{\text{obs}} \rightarrow x_{\text{obs}}$; calibration: $\text{area} \rightarrow c_{\text{an}}$; recovery: $c_{\text{an}} \rightarrow c$
- The uncertainty of x_{obs} due to the inverse regression is given by a „fiducial limit“

$$x_l \leq x_{\text{obs}} \leq x_u$$
- Solve $y_{\text{obs}} = \hat{y}_i \pm \Delta y_{\text{obs}} = (a_0 + a_1 x) \pm \Delta y_{\text{obs}}$.
 This determines $x_{l,u}$.

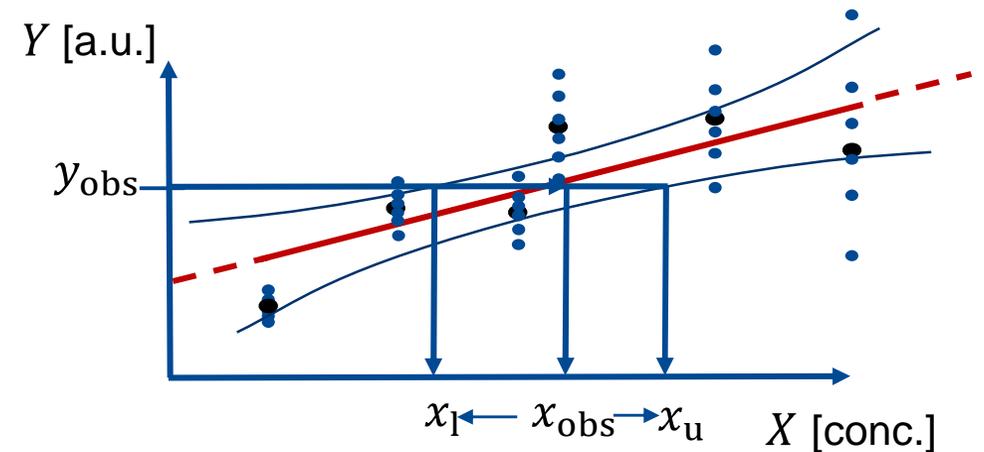


The fiducial limit is not a confidence interval.
 It can be treated as a limit of error: $s = \frac{x_u - x_l}{2\sqrt{3}}$

Calibration/recovery – heteroscedasticity

- Do weighted regression. Weight the dependent values y_i with $w_i = \frac{1}{s_i^2} \rightarrow$ weighted $\Delta y_{\text{obs},w}$
- Solve $y_{\text{obs}} = \hat{y}_i \pm \Delta y_{\text{obs},w}$ for $x_{l,u}$
- Construct the uncertainty limit of error:

$$s = \frac{x_u - x_l}{2\sqrt{3}}$$



Influence	X_i	c_i	s_i
Calibration	$X_{c,\text{cal}}$	$\beta \frac{1}{c_{\text{an}} - a_0}$	$s_{c,\text{cal}} = \frac{x_u - x_l}{2\sqrt{3}}$ (Calibration data)
Concentration (est.)	$X_{c,\text{est}}$	$\beta \frac{1}{c}$	$s_{c,\text{est}} = \frac{x_u - x_l}{2\sqrt{3}}$ (Recovery data)



Recovery – humidity and temperature

- Include humidity H and temperature τ in the linear recovery model $f_{\text{rec}}(C, H, \tau)$:

$$C_{\text{an}} = \alpha_0 + \alpha_1 C + \underbrace{\alpha_H CH + \alpha_T C\tau}_{X_{C,H} + X_{C,\tau}} + \varepsilon(\sigma(C))$$

- In principle, H and τ are correlated. However, τ affects mainly the filter capacity (ISO 22065). Conditions do not cover interaction of H and τ .
- Recovery conditions cover „worst case ranges“ → Transfer $\alpha_H CH$, $\alpha_T C\tau$ into $X_{C,H}$, $X_{C,\tau}$
- What is the worst case range of C_{an} depending on H and τ ?
→ Worst case range – limit of error

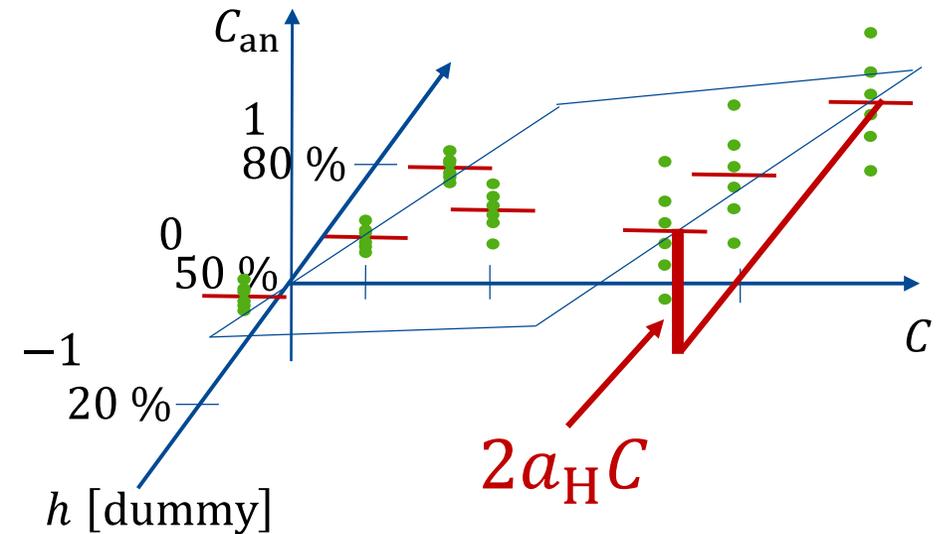
Recovery – humidity and temperature

What is the worst case range of C_{an} depending on H ?

- $\hat{C}_{an} = a_0 + a_1 C$
 $\rightarrow a_1$ is the change in \hat{C}_{an} if C changes ± 1 unit
- Use dummies $h = \{-1, 0, 1\} \leftrightarrow \{20\%, 50\%, 80\%\}$
 $\hat{C}_{an} = a_0 + a_1 C + a_H C h$
 $\rightarrow a_H C$ is the change in \hat{C}_{an} if h changes ± 1
- Consider standard errors $s(a_{H,\tau})$ of $a_{\{H,\tau\}}$

$$S_{H,T} = \frac{(a_{H,\tau} + t_{n-1,0.975} \cdot s(a_{H,\tau})) c}{\sqrt{3}}$$

Worst case change $\pm a_H C$



Influence	X_i	c_i	s_i
Humidity, Temperature	$X_{c,\{H,\tau\}}$	$\beta \frac{1}{c_{an} - a_0}$	$\frac{(a_{\{H,T\}} + t_{v,1-\alpha/2} \cdot s(a_{\{H,T\}})) c}{\sqrt{3}}$



2022 version changed!

$X_{c,ran}$ referred 2022 to C_{an} .

Now it refers correctly to C .

Summary

- Make measurements v'_{ex}, c_{an}, t, q
take corrections into account ($e_s, a_{\{0,1\}}$)
- Build the model ($Y = y + \sum_i X_i$)
→ Get the $\{c_i\}$ from the mathematical model.
- Get the $\{s_i\}$:
Information of regression, other sources ($\frac{b}{\sqrt{3}}$)
→ App is needed for regression
- Declare 95 % expanded uncertainty:

$$s_c = \sqrt{\sum_i c_i^2 s_i^2} \rightarrow B = \beta \pm 1.96 s_c$$

$$B = \frac{(v'_{ex} + e_s + X_{ex}) \left[\frac{1}{a_1} (c_{an} + X_{c,drift} + X_{c,cal} + X_{c,H} + X_{c,\tau} - a_0) + X_{c,ran} + X_{c,est} \right]}{(t + X_t)(q + X_{q,cal} + X_{q,rep} + X_{q,stab}) + X_{air}}$$

Influence	X_i	c_i	s_i
Duration (all)	X_t	$-\beta \frac{1}{t}$	0,408 min
Pump calibration	$X_{q,cal}$	$-\beta \frac{1}{q}$	$q \cdot 0.052$
Pump repeatability	$X_{q,rep}$		$q \cdot 0.023$
Pump flow stability	$X_{q,stab}$		$\frac{q \cdot 0.05}{\sqrt{3}}$
Extraction volume (rand.)	X_{ex}	$\beta \frac{1}{v_{ex}}$	0.5µl
Ambient conditions	X_{air}	$-\beta \frac{1}{tq}$	$\frac{tq \cdot 0.05}{\sqrt{3}}$
Analyser drift	$X_{c,drift}$	$\beta \frac{1}{c_{an} - a_0}$	$\frac{c_{an} \cdot 0.10}{\sqrt{3}}$
Concentration (ran.) (Recovery data)	$X_{c,ran}$	$\beta \frac{1}{c}$	$\sqrt{k_\epsilon c(c_{in})}$
Calibration (Calibration data)	$X_{c,cal}$	$\beta \frac{1}{c_{an} - a_0}$	$s_{c,cal} = \frac{x_u - x_l}{2\sqrt{3}}$
Concentration (est.) (Recovery data)	$X_{c,est}$	$\beta \frac{1}{c}$	$s_{c,est} = \frac{x_u - x_l}{2\sqrt{3}}$
Humidity, Temperature (Recovery data)	$X_{c,\{H,T\}}$	$\beta \frac{1}{c_{an} - a_0}$	$\frac{(a_{\{H,T\}} + t_{v,1-\alpha/2} \cdot s(a_{\{H,T\}})) c}{\sqrt{3}}$

Implementation into the App

Example: Extraction

Model data – Everything, except for own measurements

Table: Influence, Parameters, Sensitivity coefficients and example

Influence	X_i	c_i	s_i
Duration (all)	X_t	$-\beta \frac{1}{t}$	0.408 min
Pump calibration	$X_{q,cal}$	$-\beta \frac{1}{q}$	$q \cdot 0.052$
Pump repeatability	$X_{q,rep}$		$q \cdot 0.023$
Pump flow stability	$X_{q,stab}$		$\frac{q \cdot 0.05}{\sqrt{3}}$
Extraction vol. (rand.)	X_{ex}	$-\beta \frac{1}{v_{ex}}$	0.5 μ L
Extraction vol. (sys. corr)	e_s	-	-0.000005 L
Ambient conditions	X_{air}	$-\beta \frac{1}{tq}$	$\frac{tq \cdot 0.05}{\sqrt{3}}$
Analyser drift	$X_{c,drift}$	$\beta \frac{1}{c_{an} - a_0}$	$\frac{c_{an} \cdot 0.10}{\sqrt{3}}$

Table: Model data sheet

information
unit_beta
unit_Vol
t_{tot}
q_{cal}
q_{rep}
q_{stab}
$V_{ex_rand_3}$
$V_{ex_corr_3}$
c_{drift}

Implementation into the App using Model data

- 1) Supply the app with the sensitivity coefficients c_i
- 2) Account for units, such that $\beta = 1 \frac{\text{mg}}{\text{m}^3}$

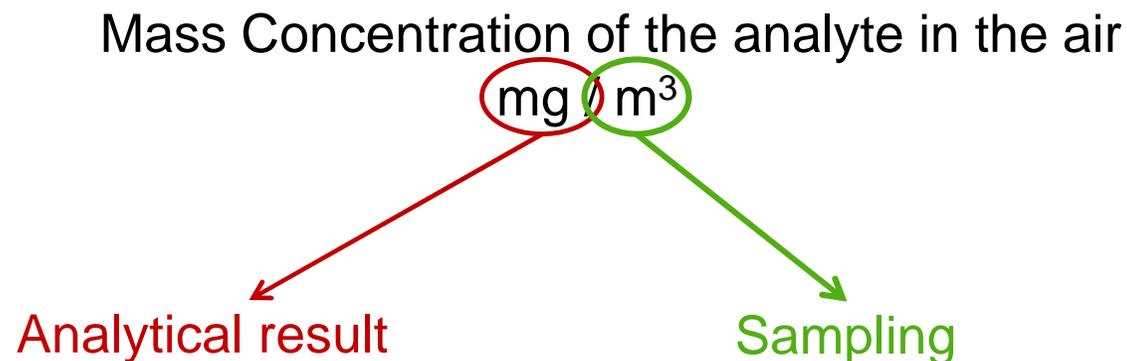


Table: Model data sheet

information	Indicator	value	percentage
unit_beta		1	
unit_Vol		0.001	
t_tot	1	0.408	
q_cal	2	0.030	5.2
q_rep	2	0.013	2.3
q_stab	2	0.029	5
V_ex_corr_3	1	-0.000005	
V_ex_rand_3	1	0.000005	
c_drift	2	0.058	10

Implementation into the App using Model data

- 1) Supply the app with the sensitivity coefficients c_i
- 2) Account for units, such that $\beta = 1 \frac{\text{mg}}{\text{m}^3}$
- 3) Be aware of parameter designation
 - Letter/Text before underscore determines the c_i for value
- 4) Determine the indicator
 - Indicator 1 = absolute value
 - Indicator 2 = relative value, multiply with $t, q, c \dots$
- 5) Determine extraction volume
 - Last number in $V_ex_corr_3$ and $V_ex_rand_3$ determines extraction volume

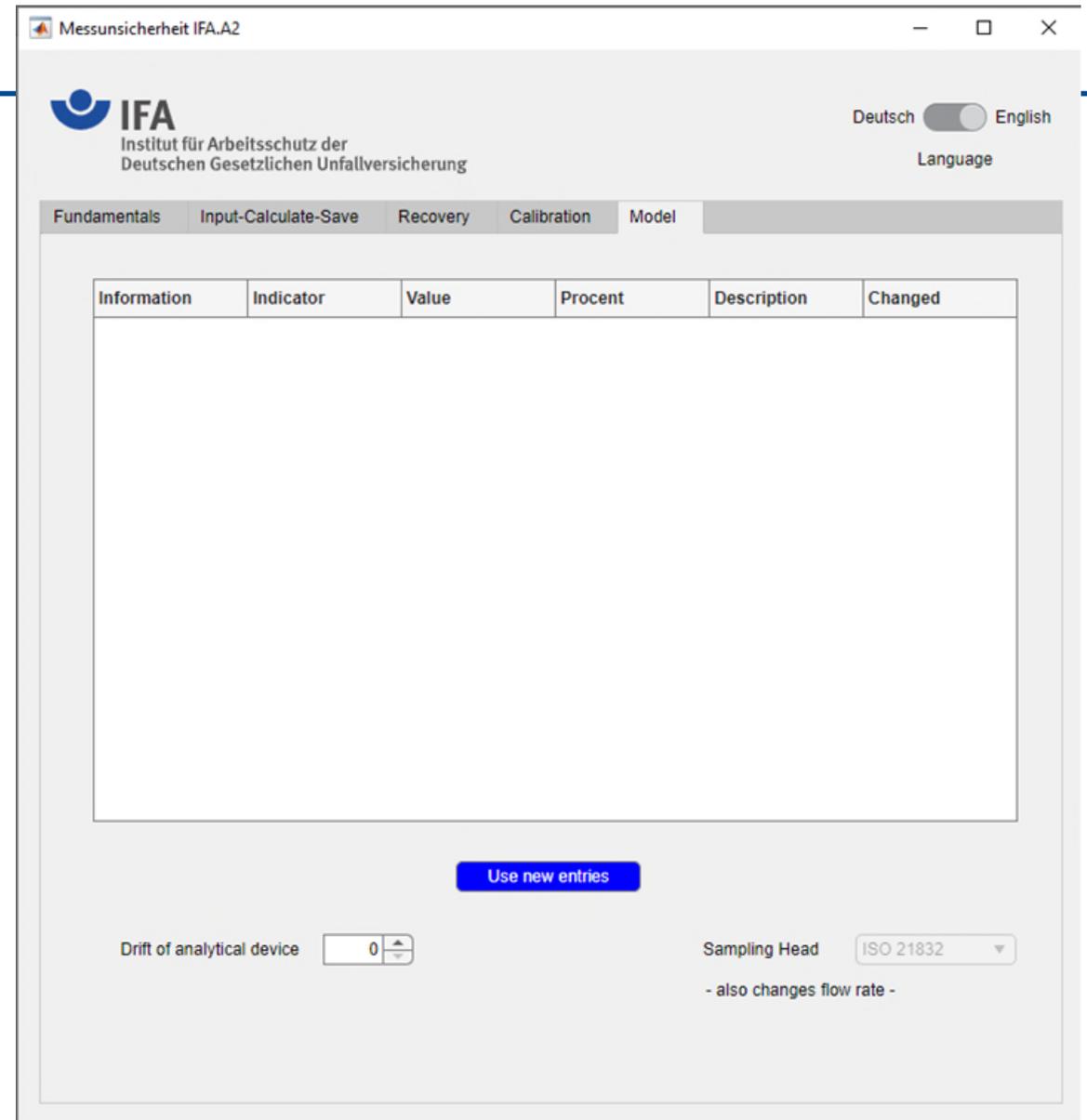
Table: Model data sheet

information	Indicator	value	percentage
unit_beta		1	
unit_Vol		0.001	
t_tot	1	0.408	
q_cal	2	0.030	5.2
q_rep	2	0.013	2.3
q_stab	2	0.029	5
V_ex_corr_3	1	-0.000005	
V_ex_rand_3	1	0.000005	
c_drift	2	0.058	10

App Design

Five Datasheets

- Fundamentals:
 - Information about Method, Analyte, Validation
- Input-Calculate-Save:
 - Data Input, validated concentration, Calculation and saving of results
- Recovery:
 - Recovery Data and Parameters of Regression
- Calibration:
 - Calibration points, measured signals, Parameters of Regression
- Model:
 - Model Data and change options



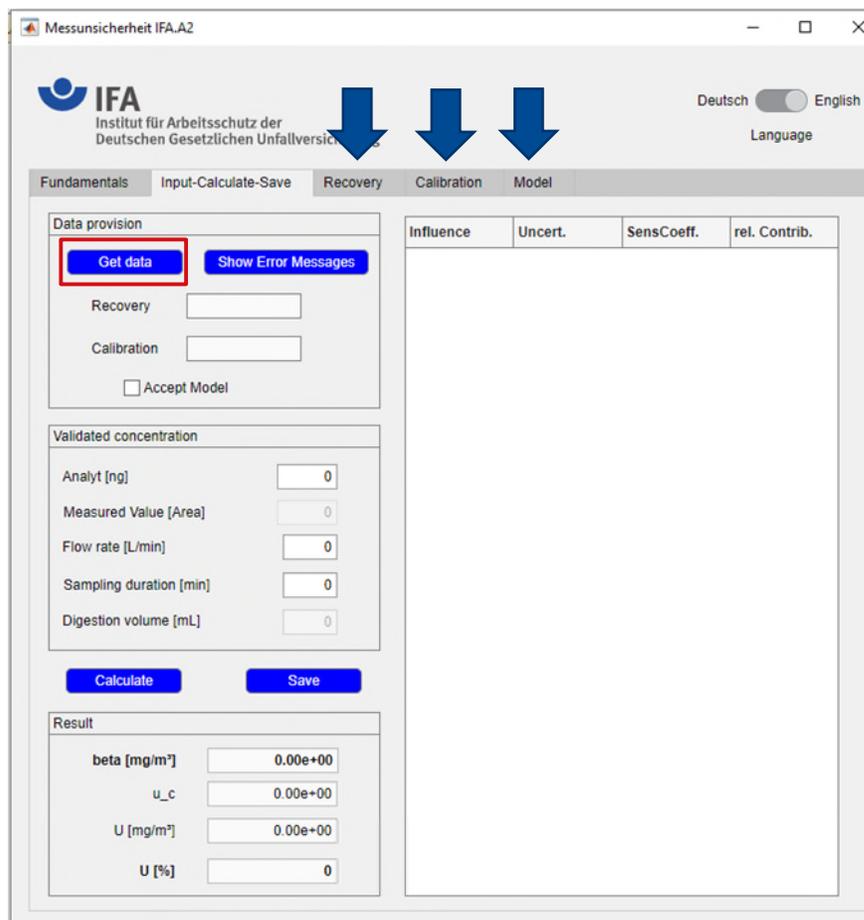
Data input and Model Data in App

Calibration Data

x_i	\bar{y}_i , Mittelwert	$y_{i,1}$	$y_{i,2}$	$y_{i,3}$
9.840	14.352	13.861	14.695	14.500
49.220	70.206	69.465	71.679	69.473
98.440	132.330	127.148	136.263	133.580
196.880	278.543	265.935	283.262	286.431
295.320	402.588	392.999	398.304	416.460
393.750	531.178	541.398	524.663	527.474
492.190	660.305	662.501	619.434	698.980

Temp./Hum. Recovery Data

$x_{BG,20}$	$x_{1,20}$	$x_{2,20}$	$x_{1,80}$	$x_{2,80}$
21.000	22.000	19.000	84.000	80.000
19.000	19.100	201.800	18.900	200.400
$\mu\text{g}/\text{m}^3$	$\mu\text{g}/\text{m}^3$	$\mu\text{g}/\text{m}^3$	$\mu\text{g}/\text{m}^3$	$\mu\text{g}/\text{m}^3$
20.326	20.326	211.803	20.377	208.227
20.258	20.258	211.684	20.540	211.020
20.308	20.308	211.364	19.999	211.930
19.976	19.976	212.559	19.928	212.083
20.341	20.341	209.893	19.570	211.152
20.259	20.259	209.172	19.489	210.682



Model Data

information	indicator	value	percentage
unit_beta		1	
unit_Vol		0.001	
t_tot	1	0.408	
q_cal	2	0.030	5.2
q_rep	2	0.013	2.3
q_stab	2	0.029	5
V_ex_corr_3	1	-0.000005	
V_ex_rand_3	1	0.000005	
c_drift	2	0.058	10

Recovery Data

x_1	x_2	x_3
19.100	47.500	198.100
$\mu\text{g}/\text{m}^3$	$\mu\text{g}/\text{m}^3$	$\mu\text{g}/\text{m}^3$
19.239	50.145	214.005
19.501	49.690	210.950
19.245	50.032	212.336
19.516	49.649	207.206
19.417	49.998	209.606
19.447	50.176	208.290