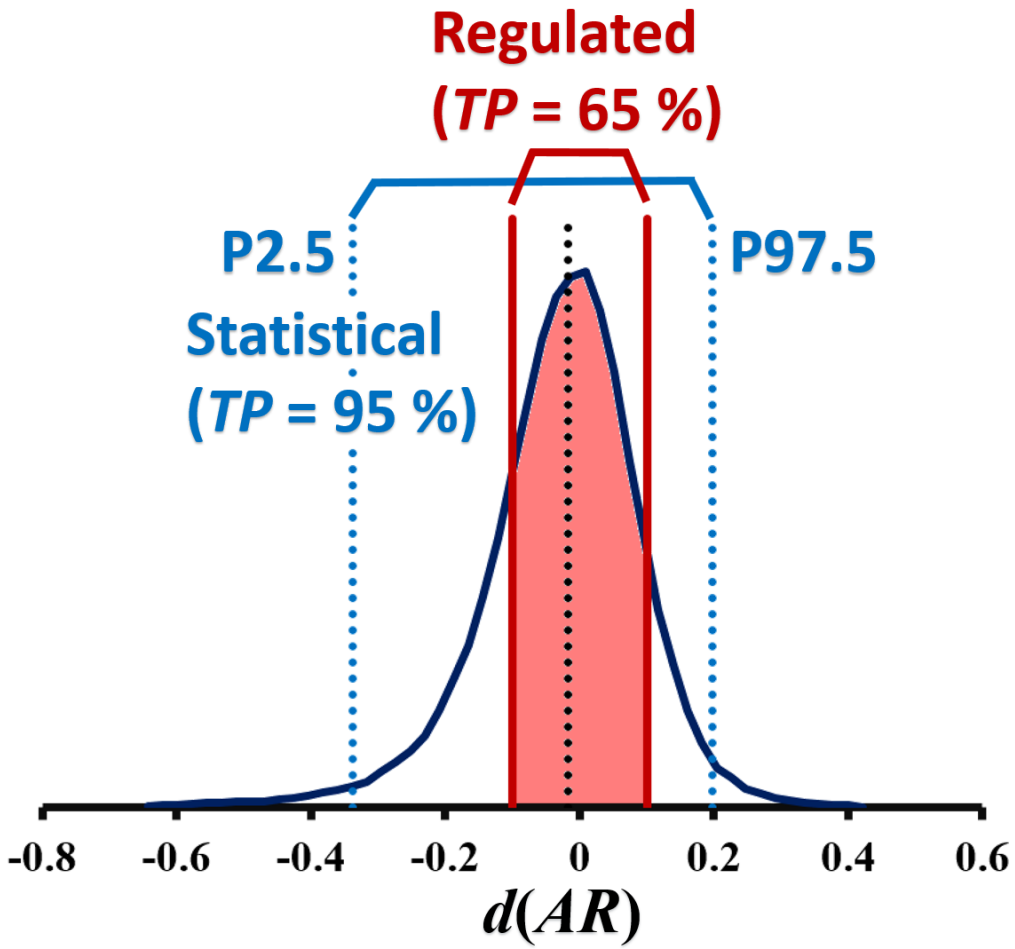
Traceability and uncertainty of qualitative targeted and non-targeted analysis

Ricardo Bettencourt da Silva
CQE@FCUL – Universidade de Lisboa

Tartu, 20 May 2019



rjsilva@fc.ul.pt

FCT

Outline

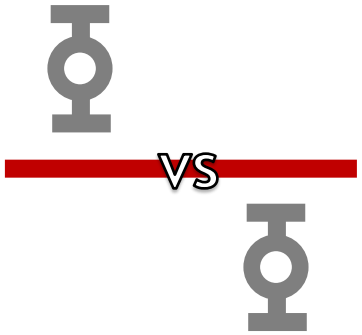
1. Qualitative analyses specificities
2. Qualitative analysis traceability
3. Qualitative analysis uncertainty
4. Targeted analysis
5. Non-targeted analysis
6. Example – Doping analysis by GC-MS/MS
7. Conclusions

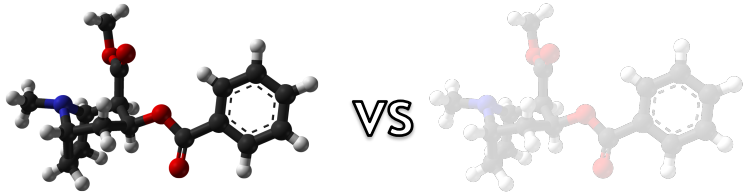
rjsilva@fc.ul.pt

1. Qualitative analyses specificities

The chemical characterization of an item can involve:

- the quantification of a chemical parameter (measurement[1])
- the determination of a qualitative property (examination[1,2])
  - Compliance/non-compliance with a quantitative limit
  - Presence/absence of a property





1 - JCGM 200, International Vocabulary of Metrology - Basic and General Concepts and Associated Terms (VIM 3rd edition), BIPM, 2012.
2 - G. Nordin, R. Dybkaer, U. Forsum, X. Fuentes-Arderiu, F. Pontet, Vocabulary on nominal property, examination, and related concepts for clinical laboratory sciences (IFCC-IUPAC Recommendations 2017), Pure Appl. Chem. 90 (2018) 913-935.

rjsilva@fc.ul.pt

1. Qualitative analyses specificities

Quantitative parameter:

- **Measurement[1]:**

2.41 (6.10)
metrological traceability
property of a **measurement result** whereby the result can be related to a reference through a documented unbroken chain of **calibrations**, each contributing to the **measurement uncertainty**

Define the reference for the measurement

2.26 (3.9)
measurement uncertainty
uncertainty of measurement
uncertainty
non-negative parameter characterizing the dispersion of the **quantity values** being attributed to a **measurand**, based on the information used

Quantify measurement quality
(confidence interval for the measurand)

1 – JCGM 200, International Vocabulary of Metrology – Basic and General Concepts and Associated Terms (VIM 3rd edition), BIPM, 2012.

rjsilva@fc.ul.pt

1. Qualitative analyses specificities

Qualitative parameter:

- **Examination[2]:**

3.21 examination traceability → Define the reference for the examination

property of an *examination result* (3.4) whereby it can be related to a reference through a documented unbroken chain of *examination calibrations* (4.3), each contributing to the *examination uncertainty* (3.9)

3.9 examination uncertainty → Quantify examination quality *(probability of result being correct)*

fraction of *examined values* (3.5) that is different from a *reference nominal property value* (3.3) among all the examined values provided

2 - G. Nordin, R. Dybkaer, U. Forsum, X. Fuentes-Arderiu, F. Pontet, Vocabulary on nominal property, examination, and related concepts for clinical laboratory sciences (IFCC-IUPAC Recommendations 2017), Pure Appl. Chem. 90 (2018) 913-935.

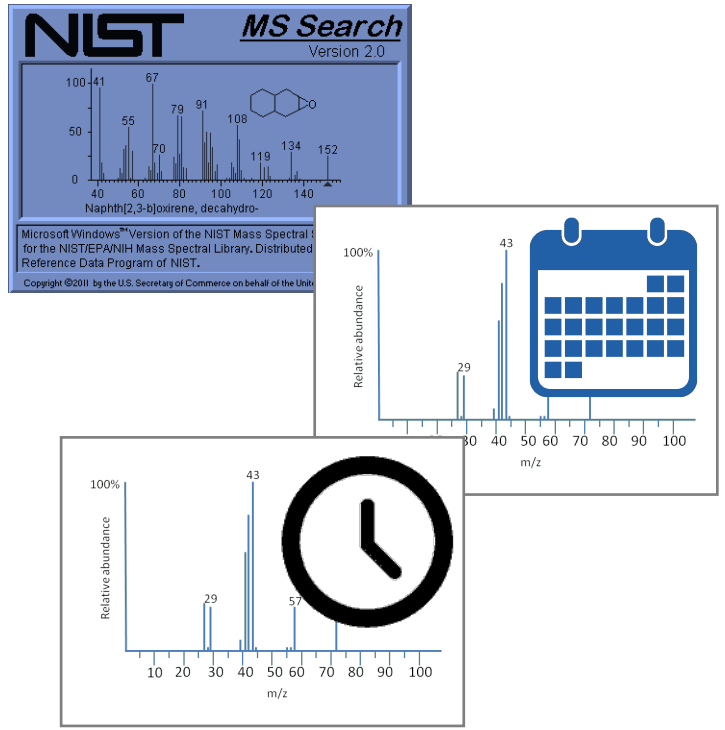
rjsilva@fc.ul.pt

2. Qualitative analysis traceability

Example of references types:

The identification of trace levels of compounds can be performed by GC-MS using:

- **Ref. 1: Mass spectrum obtained on other equipment and ionization conditions**
- **Ref. 2: Mass spectrum obtained in the used equipment in another day**
- **Ref. 3: Mass spectrum obtained immediately before sample analysis**



rjsilva@fc.ul.pt

2. Qualitative analysis traceability

Although m/z scale must be calibrated, abundances are reported in arbitrary units and a reference for a nominal property is also a nominal property.

Ref. 1: Result is traceable to mass spectrum X of the library Y

Ref. 2: Result is traceable to mass spectrum X obtained from reference substance Y in conditions A and day B

Ref. 3: Result is traceable to mass spectrum X obtained from reference substance Y in equivalent conditions (…)

Mass spectra collection conditions and used reference substance must be described with adequate detail.

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

The most trivial way of reporting qualitative analysis uncertainty:

Positive result:

- **True positive result rate (*TP*)**
- **False positive result rate (*FP*)**

Negative result:

- **True negative result rate (*TN*)**
- **False negative result rate (*FN*)**

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

The most trivial way of reporting qualitative analysis uncertainty:

Positive result:

- **True positive result rate (*TP*)**
- **False positive result rate (*FP*)**

Negative result:

- **True negative result rate (*TN*)**
- **False negative result rate (*FN*)**

$$TP + FN = 1$$

$$TN + FP = 1$$

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

The most trivial way of reporting qualitative analysis uncertainty:

These metrics can be combined in likelihood ratios, *LR*:

Positive result:

- True positive result rate **(*TP*)**
- False positive result rate **(*FP*)**

$$LR(+) = \frac{TP}{FP}$$

Negative result:

- True negative result rate **(*TN*)**
- False negative result rate **(*FN*)**

$$LR(-) = \frac{TN}{FN}$$

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

The most trivial way of reporting qualitative analysis uncertainty:

These metrics can be combined in likelihood ratios, *LR*:

Positive result:

- True positive result rate (*TP*)
- False positive result rate (*FP*)

$$LR(+) = \frac{TP}{FP}$$

A $LR(+)$ of 10^6 indicate that the positive result is 10^6 more likely true that false

Negative result:

- True negative result rate (*TN*)
- False negative result rate (*FN*)

$$LR(-) = \frac{TN}{FN}$$

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

(…) when a positive result is reported after the convergence of two or more independent evidences (e.g. (a) retention time and (b) mass spectrum)):

$$LR(+:a;b)=LR(+:a)\cdot LR(+:b)$$

where $LR(+:a)$ and $LR(+:b)$ are the likelihood ratios from both independent evidences.

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

(…) when a positive result is reported after the convergence of two or more independent evidences (e.g. (a) retention time and (b) mass spectrum)):

$$LR(+:a;b)=LR(+:a)\cdot LR(+:b)$$

It can be defined target values for the $LR(+:a;b)$[3]:

Value of likelihood ratio	Verbal equivalent
>1 to 10	Weak support for proposition
10 to 100	Moderate support
100 to 1000	Moderately strong support
1000 to 10,000	Strong support
10,000 to 1,000,000	Very strong
>1,000,000	Extremely strong

3 – Association of Forensic Science Providers, Science and Justice 49 (2009) 161-164.

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

(…) if it is known the probability of analysed item result being positive, $P(+)$:

$$P = \frac{O}{O+1}$$

where P is the probability of positive result being correct and[4,5]:

$$O = \frac{P(+)}{1-P(+)} LR(+)$$

In many cases, it is difficult to have sound estimates of $P(+)$.

4 - S. L. R. Ellison, S. Gregory, W. A. Hardcastle, Analyst 123 (1998) 1155-1161.
5 - R. B. Silva, Talanta 150 (2016) 553-567.

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

Challenges:

When identification criteria are probabilistic, the confidence level, *cl*, defines the *TP*:

$$TP = cl$$

If *FP* is defined experimentally, many blank tests need to be performed.

If *FP* is 1 %, 299 tests must be performed to have a 95 % chance of observing at least one false positive result[6].

6 – S. D. Ferrara, L. Tedeschi, G. Frison, G. Brusini, F. Castagna, B. Bernadelli, D. Soregaroli, J.Anal.Toxicol. 18 (1994) 278-291.

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

Challenges:

For a positive result:

***TP* and *FP* can be estimated by:**

- **Statistical modelling: Analytical or Simulation**
- **Experimentation**
- **Inference from available indirect information *[more subjective]***

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

Example 1: Statistical modelling - Analytical

- **Criteria for identification by chromatography:**

Agreement between analyte retention time observed in a daily calibrator, t_r(C), and in the sample, t_r(S).

$$|t_r(C) - t_r(S)| \leq t\sqrt{2}s_r$$

where s_r is the repeatability standard deviation and t the t value of the Student's t-distribution for 95 % confidence level and the degrees of freedom of s_r.

$$TP = 95\ \%$$

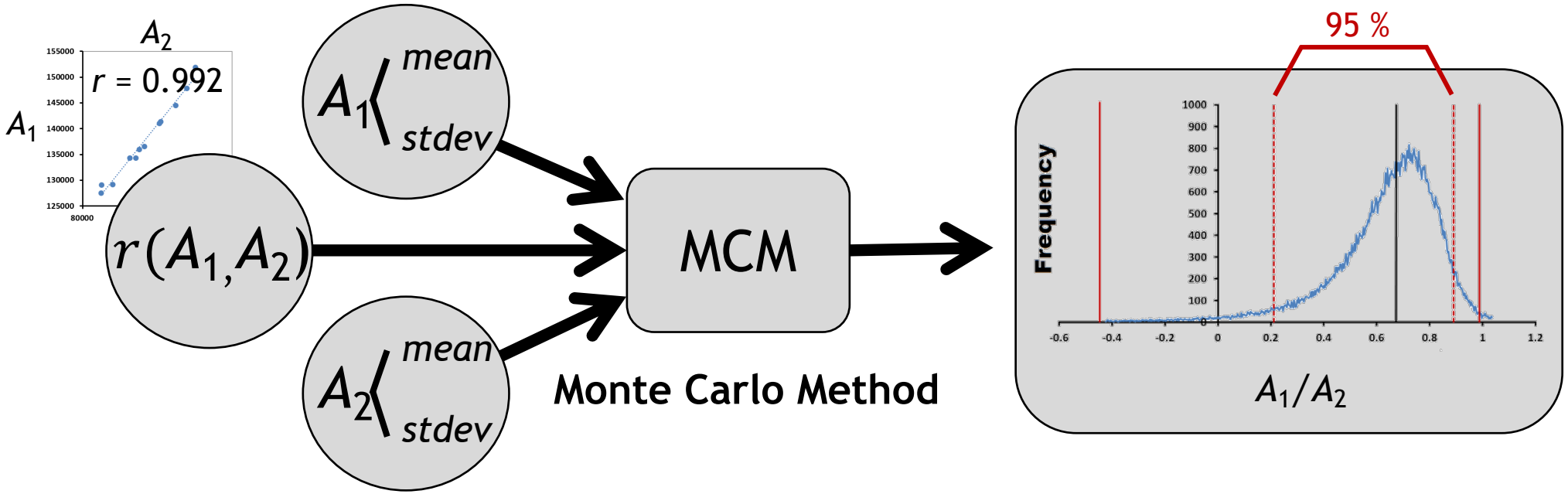
rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

Example 2: Statistical modelling - Simulation

- Criteria for identification by mass spectrometry:

The ratio of characteristic ion abundances of a mass spectra has an asymmetric distribution[5] (...)



5 - R. B. Silva, Talanta 150 (2016) 553-567.

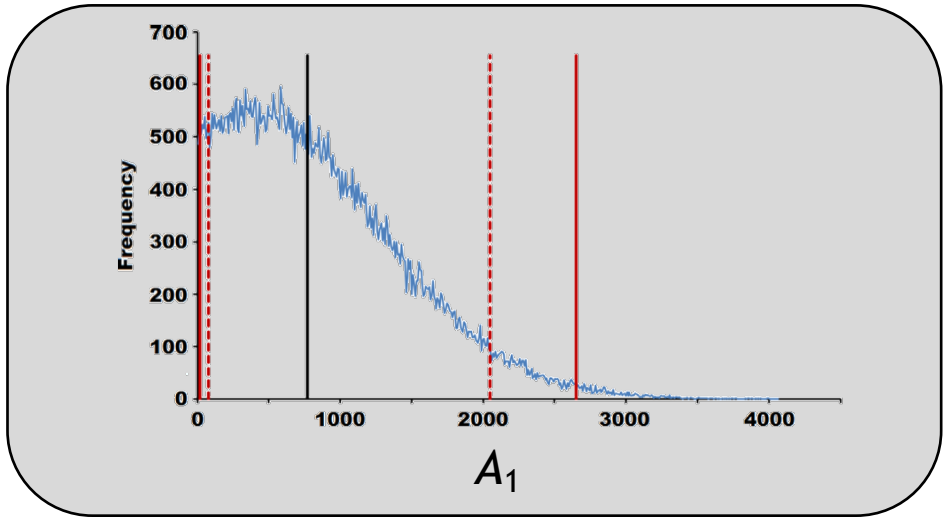
rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

Example 3: Statistical modelling to estimate *FP*

- Criteria for identification by GC-MS:

The simulation of blank signals by taking the mean and standard deviation of the signal noise truncated below zero: (…)



(…) allow estimating the change of signal noise producing a false positive (…)

5 - R. B. Silva, Talanta 150 (2016) 553-567.

rjsilva@fc.ul.pt

3. Qualitative analysis uncertainty

Example 4: Experimentation

● Criteria for identification by chromatography:
Define a criteria for the retention time, RT (e.g. maximum difference between the RT observed in a calibrator and the sample of 0.1 min) and analyse samples with known presence and absence of the analyte to estimate *TP* and *FP*.

This approach requires a large number of experimental tests
(not feasible for newly developed and selective procedures)

rjsilva@fc.ul.pt

4. Targeted analysis

Ideally, in targeted analysis, statistically sound identification criteria should be considered defining the *TP*.

The *FP* can be estimated experimentally if *FP* is larger than 10 %, or estimated from modelling or analyst's experience.

rjsilva@fc.ul.pt

5. Non-targeted analysis

TP **and** ***FP*** **can be estimated from worst-case signal modelling or analyst's experience (…)**

rjsilva@fc.ul.pt

6. Example – Doping analysis by GC-MS/MS

The World Antidoping Agency, WADA, defined minimum identifiable levels[6,7] and identification criteria[8] for the analysis of doping substances or their metabolite in urine samples by GC-MS and LC-MS analysis.

Retention time criterion:

$$|t_r(\mathrm{C}) - t_r(\mathrm{S})| \leq 0.1 t_r(\mathrm{C}) \text{ or } 0.1 \text{ min}$$

Relative retention time criterion:

$$\left|t_{Rr}(\mathrm{C}) - t_{Rr}(\mathrm{S})\right| \leq 0.005 t_{Rr}(\mathrm{C}) \text{ or } 0.01 t_{Rr}(\mathrm{C})$$

6 - WADA - LEG, Minimum Required Performance Levels for Detection and Identification of Non-Threshold Substances, TD2015MRPL, WADA, 2015.
7 - WADA – LEG, Decision limits for the confirmatory quantification of threshold substances, TD2014DL, WADA, 2014.
8 - WADA – LEG, Minimum Criteria for Chromatographic-Mass Spectrometric Confirmation of the Identity of Analytes for Doping Control Purposes, TD2015IDCR, WADA, 2015.

rjsilva@fc.ul.pt

6. Example – Doping analysis by GC-MS/MS

The World Antidoping Agency, WADA, defined minimum identifiable levels[6,7] and identification criteria[8] for the analysis of doping substances or their metabolite in urine samples by GC-MS and LC-MS analysis.

Ion abundances ratio criteria:

AR (% of the base peak)	Identification criterion
50 to 100	$\lvert AR(C) - AR(S)\rvert \leq 10\ \%$
25 to 50	$\lvert AR(C) - AR(S)\rvert \leq 0.2 \cdot AR(C)$
1 to 25	$\lvert AR(C) - AR(S)\rvert \leq 5\ \%$
AR(C) and *AR*(S) are the abundance ratios of the analyte observed in the calibrator (Positive Control) and sample, respectively.	

6 - WADA - LEG, Minimum Required Performance Levels for Detection and Identification of Non-Threshold Substances, TD2015MRPL, WADA, 2015.

7 - WADA – LEG, Decision limits for the confirmatory quantification of threshold substances, TD2014DL, WADA, 2014.

8 - WADA – LEG, Minimum Criteria for Chromatographic-Mass Spectrometric Confirmation of the Identity of Analytes for Doping Control Purposes, TD2015IDCR, WADA, 2015.

rjsilva@fc.ul.pt

6. Example – Doping analysis by GC-MS/MS

The World Antidoping Agency, WADA, defined minimum identifiable levels[6,7] and identification criteria[8] for the analysis of doping substances or their metabolite in urine samples by GC-MS and LC-MS analysis.

These criteria are strict to avoid false positive results (….)

(…) however, drives to high false negative result rates?

!?

6 - WADA - LEG, Minimum Required Performance Levels for Detection and Identification of Non-Threshold Substances, TD2015MRPL, WADA, 2015.
7 - WADA – LEG, Decision limits for the confirmatory quantification of threshold substances, TD2014DL, WADA, 2014.
8 - WADA – LEG, Minimum Criteria for Chromatographic-Mass Spectrometric Confirmation of the Identity of Analytes for Doping Control Purposes, TD2015IDCR, WADA, 2015.

rjsilva@fc.ul.pt

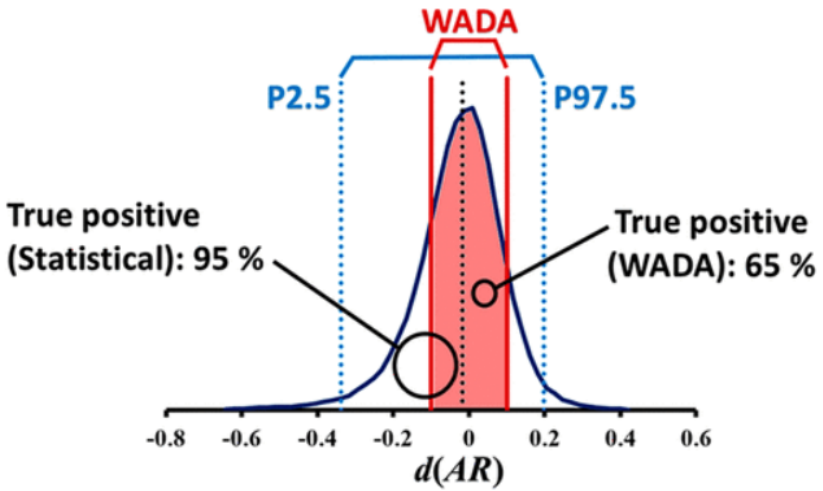
6. Example – Doping analysis by GC-MS/MS

(…)

Narciso et al[9] defined statistically sound criteria for the identification of doping substances in urine samples by GC-MS/MS and assessed the WADA's criteria.

The criteria were estimated from Monte Carlo simulations based on experimentally estimated dispersion and correlation of identification parameters.

The false negative results rates were checked experimentally.



9 - J. Narciso, S. Luz, R. B. Silva, Anal. Chem (2019) in press (DOI 10.1021/acs.analchem.9b00560).

rjsilva@fc.ul.pt

6. Example – Doping analysis by GC-MS/MS

(...)

Analyte	Conc.	$d(t_{Rr})$		$d(AR)$	
		WADA *TP* (%)	Statistical *FP* (%)	WADA *TP* (%)	WADA *FP* (%)
19-Norandrosterone[a]	L/4	100.00	21.1	57.9	0.012
	L/2	99.99	1.7	65.2	0.012
	L	100.00	0.001	66.6	0.012
	2L	100.00	0.001	77.3	0.008
19-Noretiocholanolone [a]	MRPL/4	99.97	0.001	82.5	0.017
	MRPL/2	99.95	0.001	74.4	0.013
	MRPL	99.96	0.001	91.7	0.010
	2MRPL	99.95	0.001	93.8	0.012
5β-Tetrahydromethyltestosterone[b]	MRPL/4	100.00	0.001	1.9	0.002
	MRPL/2	100.00	0.057	19.0	0.002
	MRPL	100.00	0.001	49.7	0.003
	2MRPL	100.00	0.001	12.4	0.001
6β-Hydroxymethandienone[b]	MRPL/4	99.42	0.001	25.7	0.001
	MRPL/2	99.24	0.703	50.2	0.001
	MRPL	99.33	0.001	82.6	0.001
	2MRPL	99.30	0.001	83.7	0.001
Epimetendiol[b]	MRPL/4	100.00	0.001	80.7	0.001
	MRPL/2	100.00	0.001	91.4	0.001
	MRPL	100.00	0.001	99.1	0.001
	2MRPL	100.00	0.001	99.1	0.001
Carboxy-tetrahydrocannabinol[c]	L/4	99.97	0.001	97.1	0.003
	L/2	99.96	0.001	98.2	0.005
	L	99.96	0.001	98.9	0.008
	2L	99.96	0.001	98.8	0.007

Analyte	Conc.	$d(t_{Rr})$		$d(AR)$	
		WADA *TP* (%)	Statistical *FP* (%)	WADA *TP* (%)	WADA *FP* (%)
Amiloride	MRPL/4	100.00	7.5	58.18	0.001
	MRPL/2	100.00	0.001	65.42	0.001
	MRPL	100.00	0.001	81.91	0.001
	2MRPL	100.00	0.001	86.23	0.001
Canrenone	MRPL/4	97.62	0.001	97.43	0.001
	MRPL/2	97.30	0.001	96.84	0.001
	MRPL	97.30	0.001	97.57	0.001
	2MRPL	97.29	0.001	98.33	0.001
Triamterene	MRPL/4	100.00	0.001	92.36	0.001
	MRPL/2	99.99	0.001	94.97	0.001
	MRPL	99.99	0.001	95.70	0.001
	2MRPL	100.00	0.001	98.11	0.001
Carphedon	MRPL/4	100.00	0.001	92.39	0.001
	MRPL/2	100.00	0.001	94.07	0.001
	MRPL	100.00	0.001	96.97	0.001
	2MRPL	100.00	0.001	97.82	0.001
Modafinil	MRPL/4	99.94	0.26	23.75	0.005
	MRPL/2	99.99	0.009	38.33	0.005
	MRPL	100.00	0.001	49.60	0.004
	2MRPL	100.00	0.001	48.01	0.001
Octopamine	MRPL/4	100.00	52.6	39.91	0.001
	MRPL/2	100.00	9.5	50.08	0.001
	MRPL	100.00	0.001	83.03	0.001
	2MRPL	100.00	0.001	81.47	0.001

[a] – metabolite of nandrolone, [b] – metabolite of methandienone, [c] – metabolite of tetrahydrocannabinol and [T] - threshold value.

9 - J. Narciso, S. Luz, R. B. Silva, Anal. Chem (2019) in press (DOI 10.1021/acs.analchem.9b00560).

rjsilva@fc.ul.pt

6. Example – Doping analysis by GC-MS/MS

(...)

Analyte	Conc.	$d(t_{Rr})$ WADA *TP* (%)	$d(t_{Rr})$ Statistical *FP* (%)	*d*(*AR*) WADA *TP* (%)	*d*(*AR*) WADA *FP* (%)
19-Norandrosterone[a]	L/4	100.00	21.1	57.9	0.012
	L/2	99.99	1.7	65.2	0.012
	L	100.00	0.001	66.6	0.012
	2L	100.00	0.001	77.3	0.008
19-Noretiocholanolone [a]	MRPL/4	99.97	0.001	82.5	0.017
	MRPL/2	99.95	0.001	74.4	0.013
	MRPL	99.96	0.001	91.7	0.010
	2MRPL	99.95	0.001	93.8	0.012
5β-Tetrahydromethyltestosterone[b]	MRPL/4	100.00	0.001	1.9	0.002
	MRPL/2	100.00	0.057	19.0	0.002
	MRPL	100.00	0.001	49.7	0.003
	2MRPL	100.00	0.001	12.4	0.001
6β-Hydroxymethandienone[b]	MRPL/4	99.42	0.001	25.7	0.001
	MRPL/2	99.24	0.703	50.2	0.001
	MRPL	99.33	0.001	82.6	0.001
	2MRPL	99.30	0.001	83.7	0.001
Epimetendiol[b]	MRPL/4	100.00	0.001	80.7	0.001
	MRPL/2	100.00	0.001	91.4	0.001
	MRPL	100.00	0.001	99.1	0.001
	2MRPL	100.00	0.001	99.1	0.001
	L/4	99.97	0.001	97.1	0.003
Carboxy-tetrahydrocannabinol[c]	L/2	99.96	0.001	98.2	0.005
	L	99.96	0.001	98.9	0.008
	2L	99.96	0.001	98.8	0.007

Analyte	Conc.	$d(t_{Rr})$ WADA *TP* (%)	$d(t_{Rr})$ Statistical *FP* (%)	*d*(*AR*) WADA *TP* (%)	*d*(*AR*) WADA *FP* (%)
Amiloride	MRPL/4	100.00	7.5	58.18	0.001
	MRPL/2	100.00	0.001	65.42	0.001
	MRPL	100.00	0.001	81.91	0.001
	2MRPL	100.00	0.001	86.23	0.001
Canrenone	MRPL/4	97.62	0.001	97.43	0.001
	MRPL/2	97.30	0.001	96.84	0.001
	MRPL	97.30	0.001	97.57	0.001
	2MRPL	97.29	0.001	98.33	0.001
Triamterene	MRPL/4	100.00	0.001	92.36	0.001
	MRPL/2	99.99	0.001	94.97	0.001
	MRPL	99.99	0.001	95.70	0.001
	2MRPL	100.00	0.001	98.11	0.001
Carphedon	MRPL/4	100.00	0.001	92.39	0.001
	MRPL/2	100.00	0.001	94.07	0.001
	MRPL	100.00	0.001	96.97	0.001
	2MRPL	100.00	0.001	97.82	0.001
Modafinil	MRPL/4	99.94	0.26	23.75	0.005
	MRPL/2	99.99	0.009	38.33	0.005
	MRPL	100.00	0.001	49.60	0.004
	2MRPL	100.00	0.001	48.01	0.001
Octopamine	MRPL/4	100.00	52.6	39.91	0.001
	MRPL/2	100.00	9.5	50.08	0.001
	MRPL	100.00	0.001	83.03	0.001
	2MRPL	100.00	0.001	81.47	0.001

[a] – metabolite of nandrolone, [b] – metabolite of methandienone, [c] – metabolite of tetrahydrocannabinol and [T] - threshold value.

9 - J. Narciso, S. Luz, R. B. Silva, Anal. Chem (2019) in press (DOI 10.1021/acs.analchem.9b00560).

rjsilva@fc.ul.pt

6. Example – Doping analysis by GC-MS/MS

(...)

Analyte	Conc.	$d(t_{Rr})$ WADA *TP* (%)	$d(t_{Rr})$ Statistical *FP* (%)	*d(AR)* WADA *TP* (%)	*d(AR)* WADA *FP* (%)
19-Norandrosterone[a]	L/4	100.00	21.1	57.9	0.012
	L/2	99.99	1.7	65.2	0.012
	L	100.00	0.001	66.6	0.012
	2L	100.00	0.001	77.3	0.008
19-Noretiocholanolone [a]	MRPL/4	99.97	0.001	82.5	0.017
	MRPL/2	99.95	0.001	74.4	0.013
	MRPL	99.96	0.001	91.7	0.010
	2MRPL	99.95	0.001	93.8	0.012
5β-Tetrahydromethyltestosterone[b]	MRPL/4	100.00	0.001	1.9	0.002
	MRPL/2	100.00	0.057	19.0	0.002
	MRPL	100.00	0.001	49.7	0.003
	2MRPL	100.00	0.001	12.4	0.001
6β-Hydroxymethandienone[b]	MRPL/4	99.42	0.001	25.7	0.001
	MRPL/2	99.24	0.703	50.2	0.001
	MRPL	99.33	0.001	82.6	0.001
	2MRPL	99.30	0.001	83.7	0.001
Epimetendiol[b]	MRPL/4	100.00	0.001	80.7	0.001
	MRPL/2	100.00	0.001	91.4	0.001
	MRPL	100.00	0.001	99.1	0.001
	2MRPL	100.00	0.001	99.1	0.001
Carboxy-tetrahydrocannabinol[c]	L/4	99.97	0.001	97.1	0.003
	L/2	99.96	0.001	98.2	0.005
	L	99.96	0.001	98.9	0.008
	2L	99.96	0.001	98.8	0.007

Analyte	Conc.	$d(t_{Rr})$ WADA *TP* (%)	$d(t_{Rr})$ Statistical *FP* (%)	*d(AR)* WADA *TP* (%)	*d(AR)* WADA *FP* (%)
Amiloride	MRPL/4	100.00	7.5	58.18	0.001
	MRPL/2	100.00	0.001	65.42	0.001
	MRPL	100.00	0.001	81.91	0.001
	2MRPL	100.00	0.001	86.23	0.001
Canrenone	MRPL/4	97.62	0.001	97.43	0.001
	MRPL/2	97.30	0.001	96.84	0.001
	MRPL	97.30	0.001	97.57	0.001
	2MRPL	97.29	0.001	98.33	0.001
Triamterene	MRPL/4	100.00	0.001	92.36	0.001
	MRPL/2	99.99	0.001	94.97	0.001
	MRPL	99.99	0.001	95.70	0.001
	2MRPL	100.00	0.001	98.11	0.001
Carphedon	MRPL/4	100.00	0.001	92.39	0.001
	MRPL/2	100.00	0.001	94.07	0.001
	MRPL	100.00	0.001	96.97	0.001
	2MRPL	100.00	0.001	97.82	0.001
Modafinil	MRPL/4	99.94	0.26	23.75	0.005
	MRPL/2	99.99	0.009	38.33	0.005
	MRPL	100.00	0.001	49.60	0.004
	2MRPL	100.00	0.001	48.01	0.001
Octopamine	MRPL/4	100.00	52.6	39.91	0.001
	MRPL/2	100.00	9.5	50.08	0.001
	MRPL	100.00	0.001	83.03	0.001
	2MRPL	100.00	0.001	81.47	0.001

[a] – metabolite of nandrolone, [b] – metabolite of methandienone, [c] – metabolite of tetrahydrocannabinol and [T] - threshold value.

9 - J. Narciso, S. Luz, R. B. Silva, Anal. Chem (2019) in press (DOI 10.1021/acs.analchem.9b00560).

rjsilva@fc.ul.pt

7. Conclusion

- The performance of qualitative analyses should be monitored

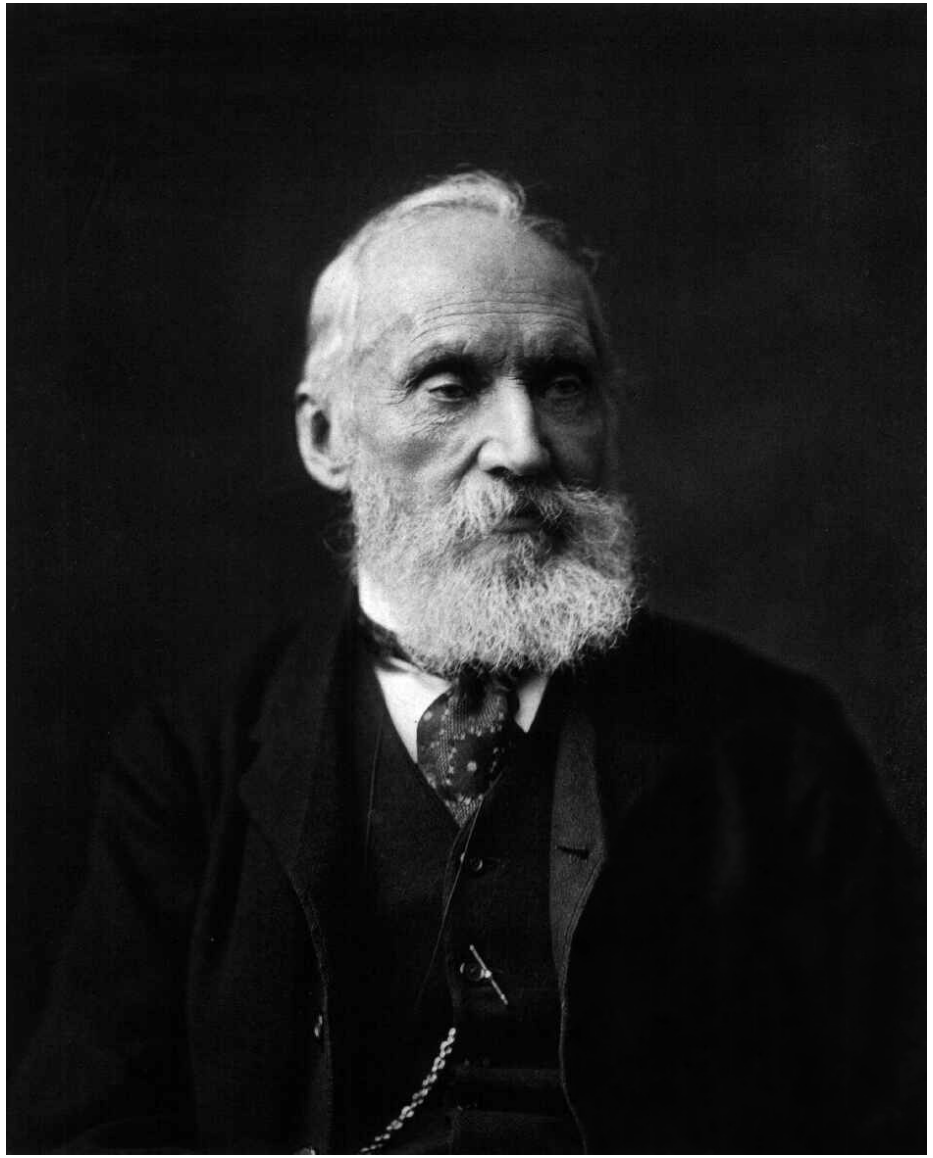
- Qualitative analyses should be based on adequate references

- If sound estimates of false results rates are available, it is useful to report qualitative analysis results with uncertainty

- The likelihood ratio is a convenient way of reporting result uncertainty

- It is necessary to know how good a positive result is but also how likely a positive is identified…

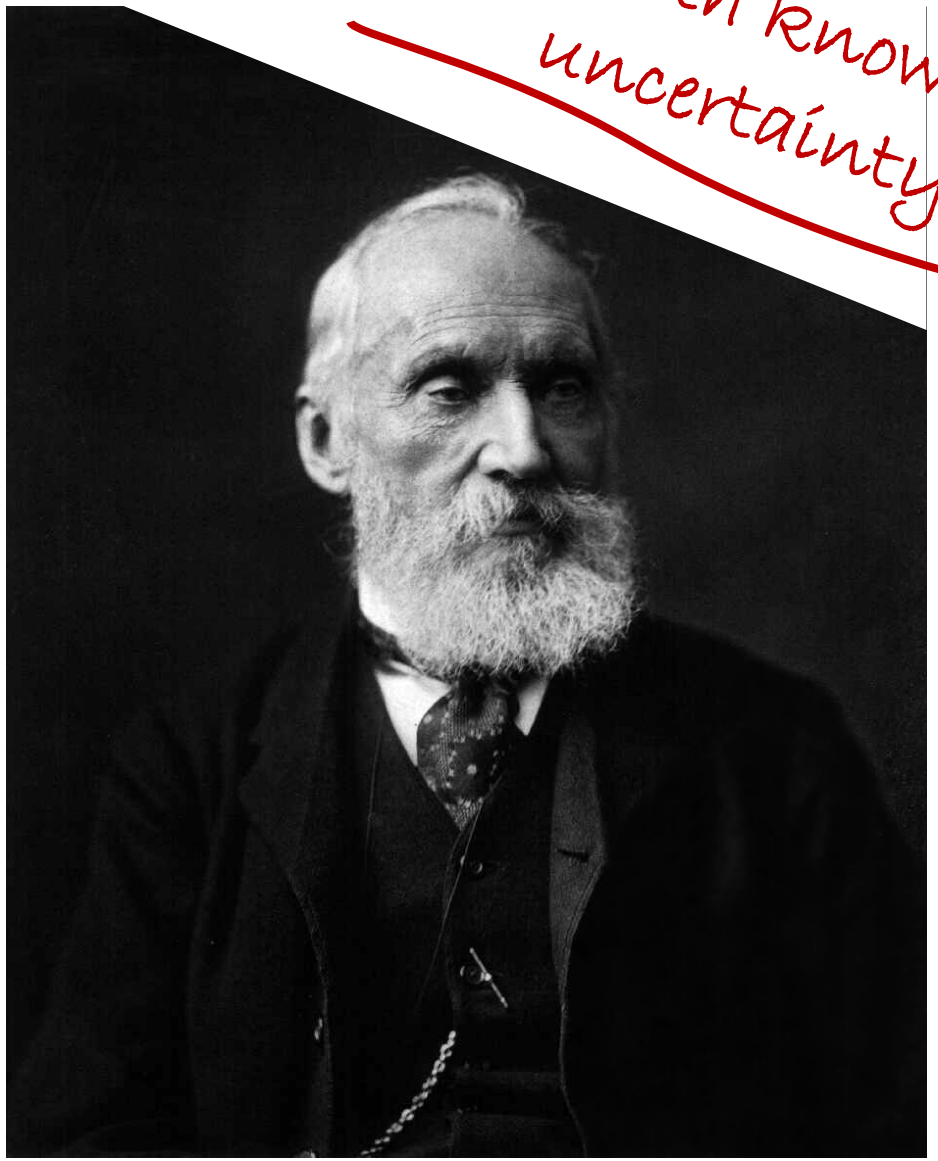
rjsilva@fc.ul.pt



To measure
is to know.
If you can not
measure it,
you can not
improve it.

- Lord Kelvin -

rjsilva@fc.ul.pt



With known uncertainty

To measure or to examine
is to know.
If you can not or to examine
measure it,
you can not
improve it.

- Lord Kelvin -

rjsilva@fc.ul.pt

With known uncertainty

To measure or to examine is to know.

If you can not measure it, or to examine you can not improve it.

Thank you for your attention!

rjsilva@fc.ul.pt