Analysis Report

Bruker IVDr Quantification in URine B.I.Quant-UR ne™

Sample ID:	Demo_Urine_03
Measuring Date:	04-Dec-2019 13:04:59
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Quantification Method Version:	Quant-UR NE.1.1.0

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RESEARCH USE ONLY: This is no clinical diagnostic analysis report. Must not be used for clinical (medical or IVD) diagnosis or for patient management! Additional concentration range information (95% range) provided numerically or graphically in this report must not be used for clinical diagnostic interpretation.

Application of B.I.Quant-UR NE 1.1.0 requires use of Bruker's B.I.Methods SOP for urine.

Summary

The following metabolites were found with concentrations outside the 95% range of Bruker Quant-UR NE.1.1.0 urine metabolite concentration database:

Alcohols and derivatives: Isopropanol (66 mmol/mol Crea),
Amines and derivatives: Dimethylamine (29 mmol/mol Crea),
Purine, Pyridine and Pyrimidine derivatives: 1,3-Dimethyluric acid (< 13 mmol/mol Crea), 4-Pyridoxic acid (< 6 mmol/mol Crea), Caffeine (< 8 mmol/mol Crea).

Further detailed information is provided on the following pages.

Contents

1 Targeted Analysis

1.1 Creatinine

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/L
Creatinine	2.1	0.3	2.138	100 ●	0.041	0-12

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.2 Alcohols and derivatives

Compound	Conc. mmol/L	Conc. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{mmol}{mol\ Crea}$
Ethanol	< 1.8	< 840	840	0.000	0 ○	0.622	≤ 840
Isopropanol	0.14	66	9	0.141	100 ●	0.025	≤ 9
Methanol	< 0.19	< 91	91	0.045	65 ○	0.032	≤ 400
Propylene glycol	< 0.10	< 45	45	0.000	0 ○	0.101	≤ 1200

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.3 Amines and derivatives

Compound	Conc. mmol/L	Conc. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{mmol}{mol\ Crea}$
1-Methylguanidine	< 0.21	< 98	98	0.066	78 ○	0.051	≤ 160
Dimethylamine	0.06	29	8	0.061	100 ●	0.001	38-160
Trimethylamine	< 0.01	< 2	2	0.002	97 ●	0.000	≤ 6
Tyramine	< 0.18	< 86	86	0.000	0 ○	0.083	≤ 86

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.4 Amino acids and derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
1-Methylhistidine	< 0.82	< 380	380	0.000	0 ○	0.021	≤ 380
2-Furoylglycine	< 0.08	< 39	39	0.000	0 ○	0.027	≤ 39
3-Aminoisobutyric acid	< 0.64	< 300	300	0.000	0 ○	0.253	≤ 390
3-Methylcrotonylglycine	< 0.13	< 60	60	0.000	0 ○	0.214	≤ 60
4-Aminobutyric acid	< 0.04	< 17	17	0.000	0 ○	0.032	≤ 20
5-Aminopentanoic acid	< 0.37	< 170	170	0.000	0 ○	0.217	≤ 170
Alanine	0.11	50	14	0.107	100 ●	0.003	27-350
Arginine	< 10.0	< 4800	4800	0.269	27 ○	0.769	≤ 4800
Argininosuccinic acid	< 0.21	< 99	99	0.000	0 ○	0.272	≤ 99
Betaine	< 0.10	< 44	44	0.042	100 ●	0.006	≤ 1200
Citrulline	< 1.7	< 780	780	0.209	33 ○	0.683	≤ 780
Creatine	< 0.11	< 50	50	0.005	100 ●	0.041	≤ 680
Cystine	< 0.16	< 75	75	0.000	0 ○	0.980	≤ 75
DL-Alloisoleucine	< 0.10	< 47	47	0.000	0 ○	0.059	≤ 47
DL-Tyrosine	< 0.09	< 43	43	0.000	0 ○	0.046	≤ 43
Glutamic acid	< 0.70	< 330	330	0.000	0 ○	0.424	≤ 330
Glutamine	< 1.8	< 830	830	0.000	0 ○	2.977	≤ 830
Glycine	0.34	160	30	0.339	100 ●	0.011	87-1900
Guanidinoacetic acid	< 0.20	< 93	93	0.117	33 ○	0.156	≤ 190
Isobutyrylglycine	< 0.06	< 29	29	0.000	0 ○	0.034	≤ 29
L-Homocystine	< 0.35	< 170	170	0.000	0 ○	0.075	≤ 170
L-Isoleucine	< 0.10	< 47	47	0.000	0 ○	0.015	≤ 47
L-Pyroglutamic acid	0.08	37	5	0.080	56 ○	0.079	≤ 44
L-Tryptophan	< 0.10	< 49	49	0.014	98 ●	0.011	≤ 49
Leucine	< 0.03	< 13	13	0.011	32 ○	0.009	≤ 40
Methionine	< 0.03	< 13	13	0.000	0 ○	0.088	≤ 22
N,N-Dimethylglycine	< 0.03	< 15	15	0.022	99 ●	0.002	≤ 220
N-Acetylaspartic acid	< 0.10	< 48	48	0.000	0 ○	0.130	≤ 48
N-Acetylglutamate	< 0.09	< 42	42	0.000	0 ○	0.086	≤ 42
N-Acetylphenylalanine	< 0.19	< 87	87	0.000	0 ○	0.075	≤ 87
N-Acetyltyrosine	< 2.3	< 1100	1100	0.000	0 ○	0.366	≤ 1100
N-Isovaleroylglycine	0.00	2	2	0.004	83 ○	0.002	≤ 5
Phenylalanine	< 0.26	< 120	120	0.040	27 ○	0.034	≤ 120
Proline betaine	< 0.05	< 24	24	0.045	80 ○	0.026	≤ 120
Propionylglycine	< 0.01	< 2	2	0.000	0 ○	0.046	≤ 2
Sarcosine	< 0.01	< 5	5	0.000	0 ○	0.001	≤ 25
Taurine	< 0.52	< 250	250	0.389	99 ●	0.046	≤ 910
Tiglylglycine	< 0.16	< 74	74	0.000	0 ○	0.056	≤ 74
Valine	0.01	5	5	0.011	94 ●	0.004	≤ 24

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.5 Benzene and substituted derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
2-Hydroxyphenylacetic acid	< 0.02	< 10	10	0.000	0 ○	0.106	≤ 10
3-Phenyllactic acid	< 0.18	< 85	85	0.000	0 ○	0.300	≤ 85
4-Aminohippuric acid	< 3.5	< 1700	1700	0.000	0 ○	0.062	≤ 1700
4-Ethylphenol	< 0.02	< 8	8	0.000	0 ○	0.064	≤ 8
4-Hydroxyhippuric acid	< 2.1	< 980	980	0.000	0 ○	0.043	≤ 980
4-Hydroxyphenylacetic acid	< 0.08	< 36	36	0.000	0 ○	0.127	≤ 69
4-Hydroxyphenyllactic acid	< 1.00	< 470	470	0.000	0 ○	0.259	≤ 470
Benzoic acid	< 0.03	< 12	12	0.000	0 ○	0.013	≤ 12
D-Mandelic acid	< 0.01	< 4	4	0.000	0 ○	0.058	≤ 43
Hippuric acid	< 0.10	< 49	49	0.000	0 ○	0.072	≤ 510
Phenylacetic acid	< 1.00	< 470	470	0.002	93 ●	0.004	≤ 470
Phenylpyruvic acid	< 0.18	< 85	85	0.018	92 ●	0.008	≤ 85
Pyrocatechol	< 0.37	< 170	170	0.000	0 ○	0.072	≤ 170
Syringic acid	< 0.02	< 10	10	0.012	91 ●	0.013	≤ 23

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.6 Carboxylic acids

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
5-Aminolevulinic acid	< 0.01	< 3	3	0.004	65 ○	0.020	≤ 3
Acetic acid	< 0.02	< 10	10	0.010	98 ●	0.001	≤ 790
Citric acid	0.91	420	46	0.906	100 ●	0.065	≤ 1400
E-Glutaconic acid	< 0.27	< 130	130	0.000	0 ○	0.019	≤ 130
Ethylmalonic acid	< 0.04	< 20	20	0.000	0 ○	0.192	≤ 42
Formic acid	< 0.20	< 92	92	0.048	100 ●	0.002	≤ 660
Fumaric acid	< 0.01	< 2	2	0.002	95 ●	0.000	≤ 40
Glutaric acid	< 0.14	< 67	67	0.004	11 ○	0.029	≤ 67
Imidazole	< 0.08	< 38	38	0.013	56 ○	0.009	≤ 38
Lactic acid	< 0.10	< 45	45	0.060	93 ●	0.037	≤ 410
Maleic acid	< 0.01	< 7	7	0.001	94 ●	0.000	≤ 10
Methylmalonic acid	< 0.02	< 10	10	0.007	0 ○	0.041	≤ 20
Propionic acid	< 0.16	< 76	76	0.000	0 ○	0.046	≤ 76
Succinic acid	0.02	11	8	0.024	99 ●	0.001	9-360
Tartaric acid	< 0.10	< 45	45	0.003	93 ●	0.002	≤ 60
Trigonelline	< 0.07	< 33	33	0.006	58 ○	0.007	≤ 33
Xanthurenic acid	< 0.04	< 18	18	0.009	34 ○	0.008	≤ 18

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.7 Cosmetics, vitamines, drugs and drug metabolites

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
Choline	< 0.20	< 94	94	0.000	0 ○	0.053	≤ 94
D-Panthenol	< 0.04	< 19	19	0.000	0 ○	0.228	≤ 19
L-Ascorbic acid	< 0.57	< 270	270	0.000	0 ○	0.123	≤ 270
Pantothenic acid	< 0.04	< 20	20	0.011	100 ●	0.058	≤ 50
Paracetamol	< 0.11	< 50	50	0.000	0 ○	0.073	≤ 50
Paracetamol-glucuronide	< 3.2	< 1500	1500	0.000	0 ○	0.074	≤ 1500

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.8 Fatty acids and derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
2-Hydroxy-4-methylvaleric acid	< 0.08	< 37	37	0.000	0 ○	0.013	≤ 37
2-Hydroxyisovaleric acid	< 0.01	< 4	4	0.001	58 ○	0.003	≤ 4
2-Methylsuccinic acid	< 0.07	< 34	34	0.000	0 ○	0.068	≤ 34
3-Hydroxy-3-methylglutaric acid	< 0.23	< 110	110	0.000	0 ○	0.313	≤ 110
3-Hydroxyisovaleric acid	< 0.04	< 18	18	0.016	99 ●	0.003	≤ 33
3-Hydroxyvaleric acid	< 0.01	< 6	6	0.000	0 ○	0.072	≤ 8
3-Methylglutaconic acid	< 0.04	< 17	17	0.016	66 ○	0.008	≤ 26
Butyric acid	< 0.06	< 26	26	0.000	0 ○	0.253	≤ 34
Citraconic acid	< 0.18	< 86	86	0.000	0 ○	0.099	≤ 86
L-Citramalic acid	< 1.2	< 560	560	0.047	9 ○	0.467	≤ 560
Pimelic acid	< 0.16	< 74	74	0.000	0 ○	0.205	≤ 74
Thymol	< 0.37	< 170	170	0.000	0 ○	0.222	≤ 170

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.9 Hydroxy acids and derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
3-Hydroxyglutaric acid	< 0.09	< 41	41	0.000	0 ○	0.059	≤ 44
3-Hydroxypropionic acid	< 0.20	< 93	93	0.004	0 ○	0.063	≤ 93
D-Galactonic acid	< 0.28	< 130	130	0.129	98 ●	0.018	≤ 130
D-Gluconic acid	< 0.41	< 190	190	0.094	89 ●	0.022	≤ 550
Glycolic acid	< 0.40	< 190	190	0.155	94 ●	0.057	≤ 480
Malic acid	< 0.17	< 81	81	0.000	0 ○	0.697	≤ 250

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.10 Keto acids and derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
2-Ketobutyric acid	< 0.11	< 54	54	0.000	0 ○	0.087	≤ 54
2-Oxoglutaric acid	< 0.33	< 160	160	0.052	36 ○	0.081	≤ 590
2-Oxoisocaproic acid	< 0.01	< 5	5	0.000	0 ○	0.015	≤ 10
2-Oxoisovaleric acid	< 0.01	< 4	4	0.000	0 ○	0.038	≤ 4
3-Hydroxybutyric acid	< 0.21	< 97	97	0.000	0 ○	0.172	≤ 100
3-Methyl-2-oxovaleric acid	< 0.04	< 19	19	0.012	94 ●	0.128	≤ 19
4-Hydroxyphenylpyruvic acid	< 0.10	< 45	45	0.000	0 ○	0.065	≤ 45
Acetoacetic acid	< 0.01	< 5	5	0.005	0 ○	0.010	≤ 28
Acetoine	< 0.02	< 9	9	0.000	0 ○	0.008	≤ 9
Acetone	< 0.03	< 14	14	0.007	98 ●	0.001	≤ 110
DL-Kynurenin	< 1.7	< 790	790	0.000	0 ○	0.141	≤ 790
Oxaloacetic acid	< 0.09	< 44	44	0.004	0 ○	0.031	≤ 210
Pyruvic acid	< 0.03	< 13	13	0.009	98 ●	0.002	≤ 41
Succinylacetone	< 0.87	< 410	410	0.000	0 ○	0.160	≤ 410

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.11 Purine, Pyridine and Pyrimidine derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
1,3-Dimethyluric acid	< 0.03	< 13	13	0.001	90	0.005	20-150
1-Methyladenosine	< 0.02	< 9	9	0.000	0	0.045	≤ 9
1-Methylhydantoin	< 0.10	< 49	49	0.041	96	0.010	≤ 370
1-Methylnicotinamide	< 0.10	< 46	46	0.021	83	0.013	≤ 120
4-Pyridoxic acid	< 0.01	< 6	6	0.010	0	0.017	11-92
Adenine	< 0.03	< 13	13	0.003	0	0.011	≤ 20
Adenosine	< 2.0	< 950	950	0.000	0	0.329	≤ 950
Allantoin	< 0.04	< 19	19	0.018	95	0.004	≤ 120
Allopurinol	< 0.04	< 18	18	0.007	69	0.008	≤ 23
Caffeine	< 0.02	< 8	8	0.000	0	0.022	21-450
Cytosine	< 0.02	< 9	9	0.000	0	0.197	≤ 9
Dihydrothymine	< 0.92	< 430	430	0.000	0	0.028	≤ 560
Dihydrouracil	< 0.28	< 130	130	0.000	0	0.576	≤ 130
Inosine	< 0.04	< 17	17	0.000	0	0.029	≤ 17
Neopterin	< 0.04	< 17	17	0.004	64	0.003	≤ 17
Orotic acid	< 0.01	< 5	5	0.003	30	0.003	≤ 6
Oxypurinol	< 0.04	< 19	19	0.019	97	0.007	≤ 37
Quinolinic acid	< 0.08	< 38	38	0.000	0	0.136	≤ 38
Theobromine	< 0.17	< 81	81	0.027	91	0.028	≤ 150
Thymine	< 0.01	< 4	4	0.001	85	0.000	≤ 4
Uracil	0.03	13	8	0.027	0	0.076	≤ 110
Uridine	< 0.03	< 15	15	0.000	0	0.519	≤ 15

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

1.12 Sugars and derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
D-Galactose	< 0.18	< 85	85	0.000	0	0.032	≤ 1400
D-Glucose	< 0.16	< 76	76	0.068	88	0.015	≤ 810
D-Lactose	< 0.20	< 96	96	0.020	85	0.012	≤ 850
D-Mannitol	< 0.91	< 430	430	0.255	0	0.864	≤ 430
D-Mannose	< 0.04	< 20	20	0.000	0	0.014	≤ 310
D-Xylose	< 1.8	< 840	840	0.000	0	0.207	≤ 840
Galactitol	< 0.64	< 300	300	0.492	92	0.143	≤ 300
Glycerol	< 1.7	< 790	790	0.000	0	1.060	≤ 790
L-Fucose	< 0.64	< 300	300	0.153	0	0.101	≤ 460
L-Threonic acid	< 0.38	< 180	180	0.000	0	0.846	≤ 180
Myo-Inositol	< 5.4	< 2500	2500	0.000	0	1.446	≤ 2500

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

2 Non-Targeted Analysis

2.1 Univariate analysis

Result: There are no detected deviations in univariate verification analysis.

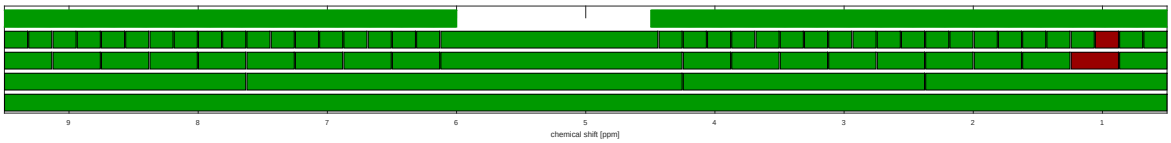
2.2 Multivariate analysis

Result: Multivariate analysis detected significant deviations in the following chemical shift regions (in ppm):

- 0.876 - 1.054
- 0.876 - 1.242

2.3 Spectroscopical overview

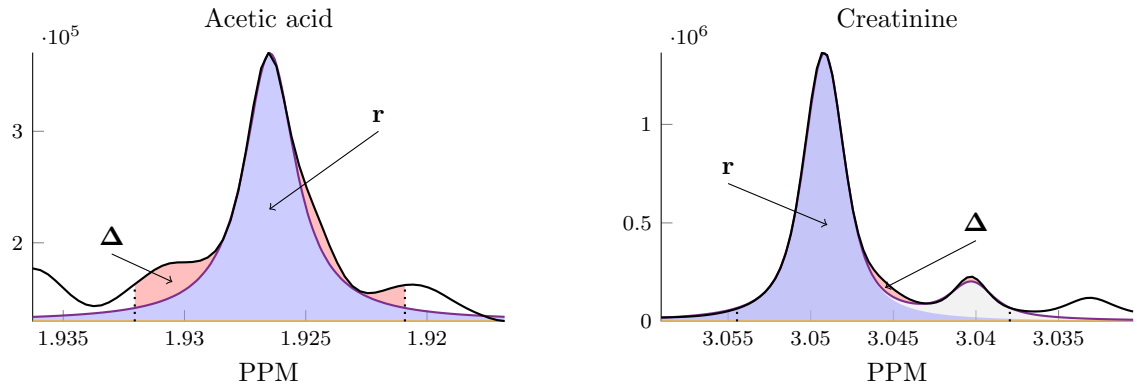
The following figure shows if any ppm region in the spectrum is affected by any significant deviations from the reference data. Each stripe represents an individual verification model. Chemical shifts or chemical shift regions with deviations from the reference are colored red. At the top, results of the univariate analysis are presented while the following stripes represent the multivariate analysis for different subdivisions of the entire spectrum.



3 Explanations

This section contains the definition of the parameters used above. In the section 3.1 a short manual, how to interpret the results, is presented. The section 3.3 contains the exact definitions of the parameters $\mathbf{r}$, ρ and $\mathbf{\Delta}$.

3.1 How to read the result



(a) Single signal fitting.

(b) Simultaneous fitting of two signals.

Figure 1: Examples of fitting.

In the figure 1(a), the black line, the blue line and the yellow line represent the original spectrum, the calculated signal fit and its baseline, respectively.

The blue area relates to the metabolite concentration to be determined and the red area represents a residue.

In case of the signal overlap a different approach is used: two or more overlapping signals are being fitted simultaneously. The most iconic example of such signals are the ones generated by $\mathrm{CH_3}$ groups of Creatinine and Creatine. In such a case, the blue line and the grey area relate the sum of all fitted signals. The blue area corresponds to the concentration of the metabolite of interest (cf. figure 1(b)).

3.2 Result parameters

a) **Conc.** is the final result concentration of the metabolite,

b) **LOD** is the *limit of detection* of the given metabolite,

c) $\mathbf{r}$ is the *raw concentration* i.e. the concentration equivalent of the resulting signal fit prior to comparing to **LOD** (relates to the blue area, cf. α)),

d) ρ is the correlation of lineshape metabolite signal with calculated fit characterizing the match between metabolite signal and fit (cf. β)). Depending on the value of ρ, the following *flag* is displayed:

- ●, if the correlation is 95%,

- 🟡, if the correlation is in between 85% and 95%,
- ○, if the correlation is less than 85%,

e) **Δ** is the concentration equivalent of the difference between metabolite signal and calculated fit (residue corresponding to the the red area, cf. γ)).

3.3 Detailed definitions

Let s, f and b denote the functions describing the *raw spectra*, *fitted curve* and *(fitted) baseline* respectively. These functions are chosen such that $s \approx f + b$. Moreover, let I be a relevant PPM interval and P_N be the proton number for given metabolite/signal.

α) $\mathbf{r}$ (*raw concentration*) is defined as

$$\mathbf{r} = \frac{1}{P_N} \int_{\mathbb{R}} f(\xi)\, \mathrm{d}\xi.$$

β) ρ is the *correlation* of the functions s and $f + b$, i.e.

$$\rho = \max\left(0, \mathrm{corr}\left(\overline{s}, \overline{f+b}\right)\right),$$

where $\overline{s}$, $\overline{f+b}$ are numerical representations of the functions s and $f+b$ on sufficiently fine mesh of the interval I.

γ) **Δ** is the the area between the raw signal s and the fitted data $f + b$ on the interval I expressed in the terms of the concentration, i.e.

$$\mathbf{\Delta} = \frac{1}{P_N} \int_I |s(\xi) - f(\xi) - b(\xi)|\, \mathrm{d}\xi.$$