Estimating errors in clinical MRS

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transact

Transforming Magnetic Resonance Spectroscopy into a Clinical Tool

MARIE CURIE ACTIONS

PEOPLE

2nd Transact Workshop

16/18-06-2014, Bern University Hospital, CH

Quality issues in clinical MR Spectroscopy

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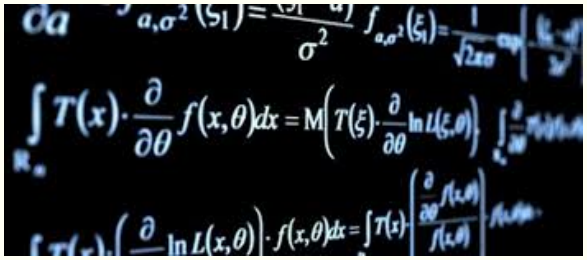
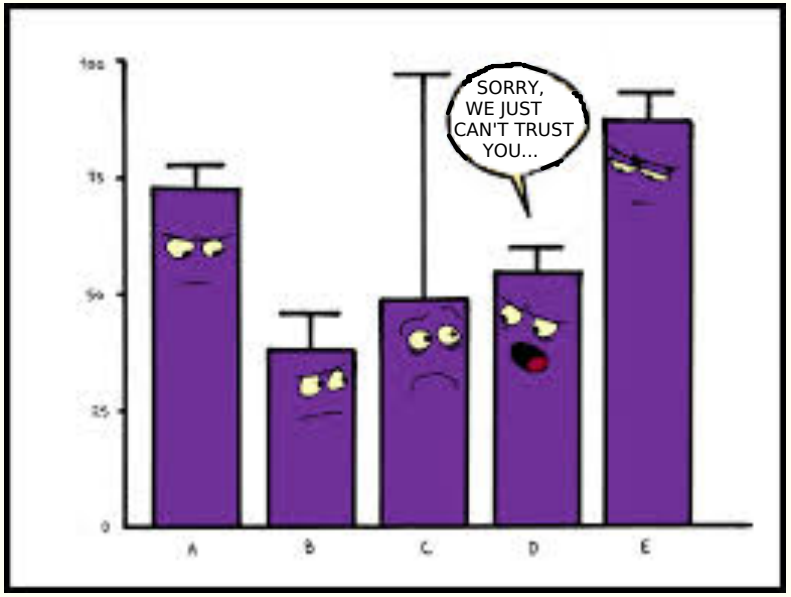
Needed: Awareness of how to estimate errors

Metabolite concentrations to be estimated in vivo.

Error bars on concentrations must be reliable: Not trivial.

MRS uses CRB





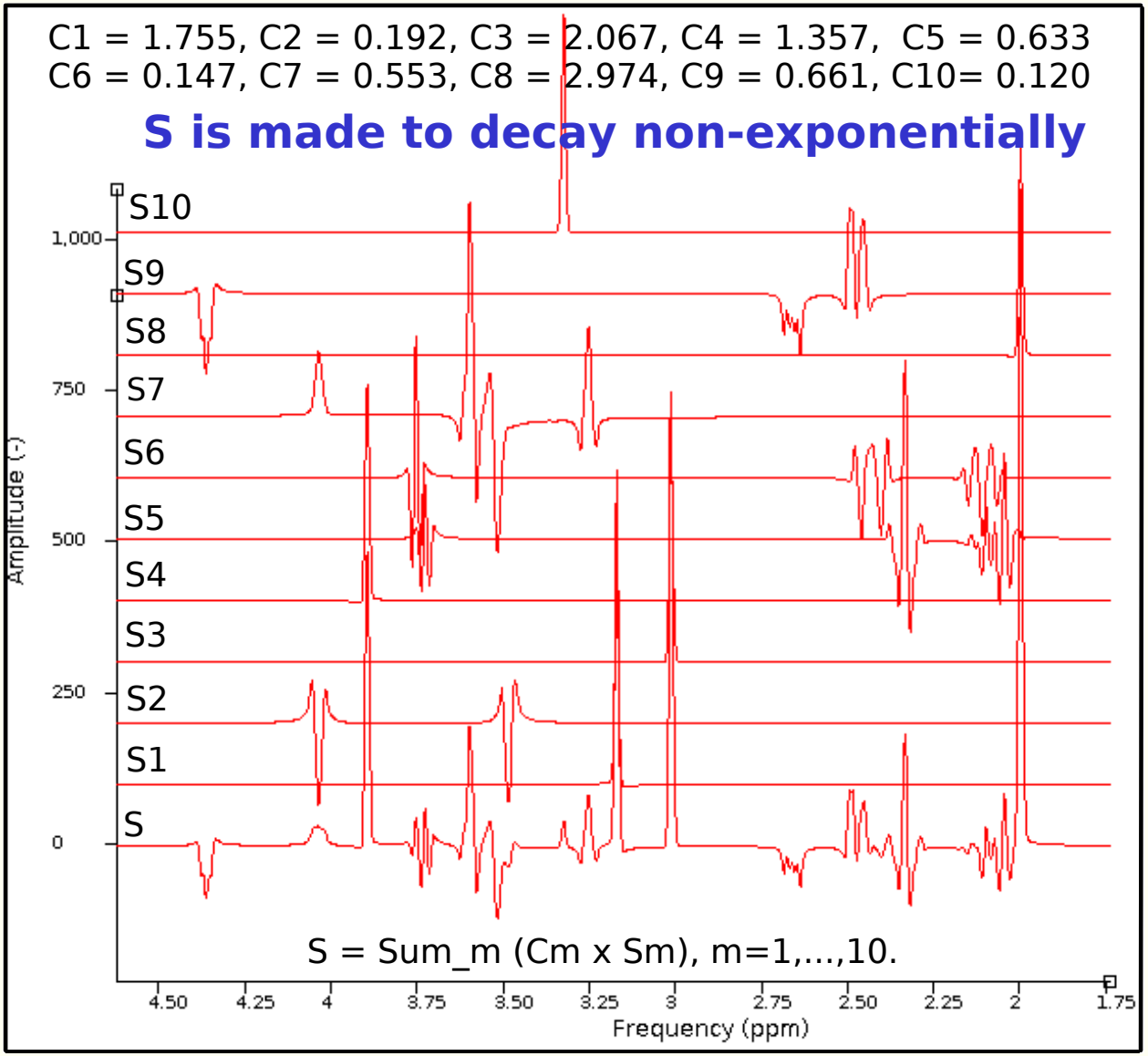
MONTE-CARLO SIMULATION: HOW TO DO I

From 10 metabolites with signals/spectra S1, . . . , S10, and concentrations C1, . . . , C10, make a signal S.

Make **100 noisy versions** of S. p5

For each version, estimate C1,. . .,C10 with, *e.g.*, QUEST, **approximating** the **form** of the decay of S with, *e.g.*, $e^{\alpha t}$.

11.7 T. Signal database by R. de Beer.



The 100 sets of estimated C1,. . .,C10 yield distribution of errors.

Reminder: spectrum = FFT[signal].

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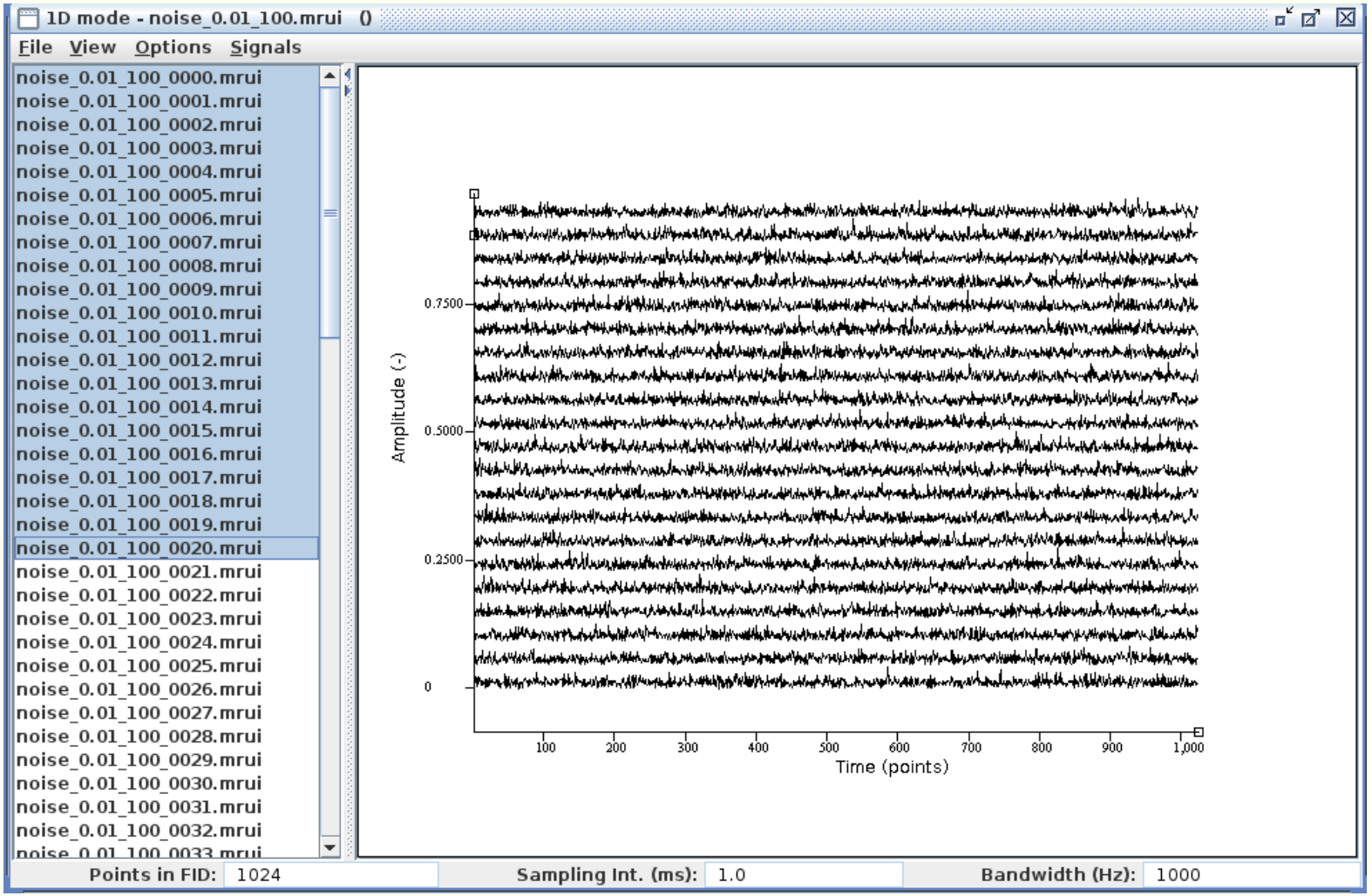
MONTE-CARLO SIMULATION: HOW TO DO II

Noise realisations



Each **noise-realisation** has equal stdev, σ, and mean, μ $(= 0)$.

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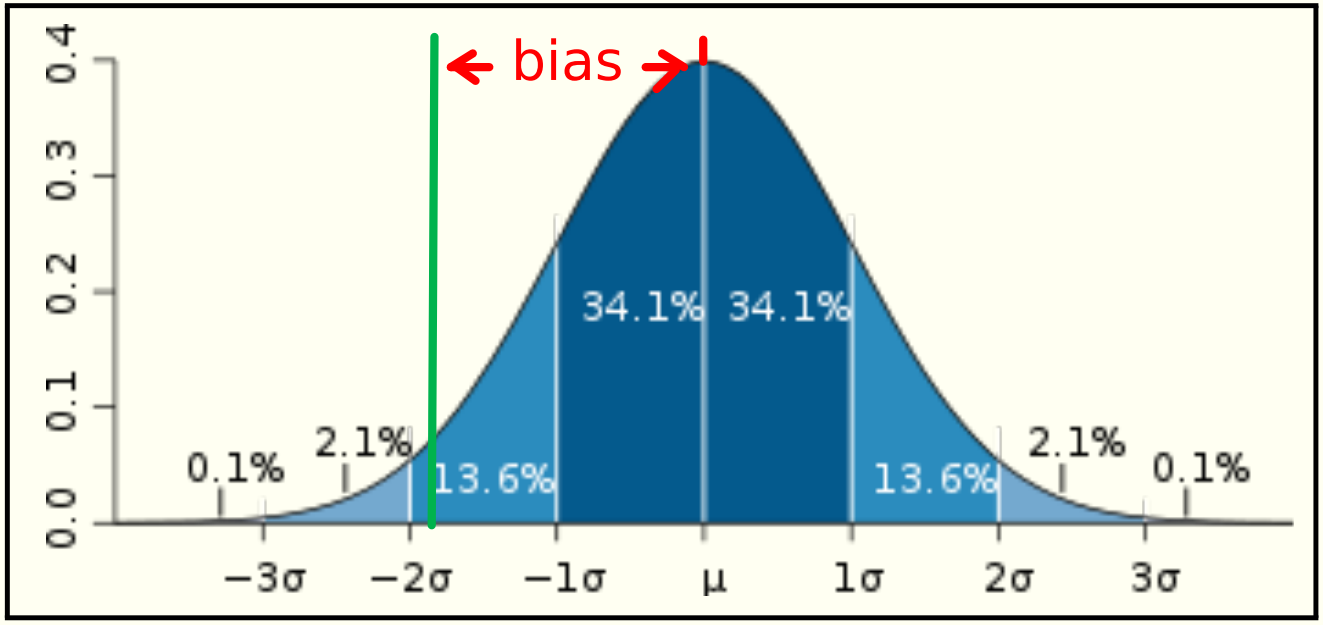
MONTE-CARLO SIMULATION: RESULT



Distribution of estimated values of a parameter.

- A Monte-Carlo simulation yields σ, μ, bias for each estimated (= fitted) parameter. ☺
- Bias (= $\mu -$ true value) is caused by, *e.g.*, *incorrectness* of a model function, or *sub*-optimality of the used parameter-estimator. gotoslide4
- ☞ In simulations, the **true values** are, of course, known. Not so in the clinic.

MONTE-CARLO: USEFUL IN THE CLINIC?

- ☞ In clinics, only a single measurement is available.
- ☞ Monte-Carlo simulations are less of an option.

ALTERNATIVE NEEDED IN CLINICAL ROUTINE:
Harald Cramér
Radhakrishna Rao

anno 2012

MRS uses pragmatic error-estimation (JMR, 1986)

CRB – Cramér-Rao (lower) Bound –

Contained in jMRUI, LCModel, etc.

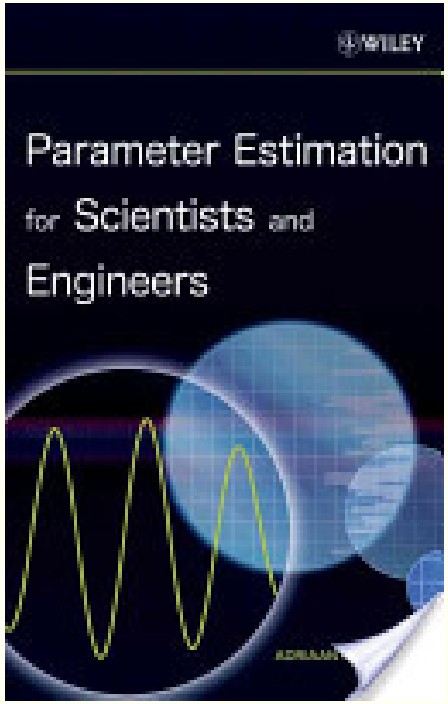
CRB I. Theory & Computation

- **CRB considered as 'black box' with input and output**

jmrui-provided, invisible for user: **Input** → jmrui-computation: **Cramer Rao Lower Bounds** → jmrui-provided results-file: **Output**

- **Info on Theory & Computation**

A. van den Bos :



D. Graveron-Demilly : Quantification in magnetic resonance spectroscopy based on semi-parametric approaches. Magn Reson Mater Phy 27:113-130, 2014, and references therein.

Google

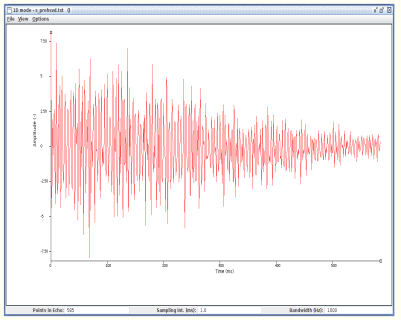
CRB II. Input for CRB-computation. Exact vs In Vivo.

1. **Exact model function of the MRS-signal,**

e.g.: $s(t) = \overbrace{\text{decay}(t)}^{\text{in vivo} \rightarrow \text{problematic}} \times \sum_{m=1}^{10} c_m \, s_m(t).$

- *In vivo*: $\text{decay}(t) \overset{?}{\approx} \underbrace{e^{\alpha t}, e^{\beta t^2}, e^{\alpha t + \beta t^2}}_{\text{surrogate model}}$, etc.

Noisy signal



2. **Exact concentrations, decay-parameters.**
   - *In vivo*: parameters estimated.

3. **Exact pdf of the noise.**
   - *In vivo*: Consensus: Gaussian pdf assumed.
   - *In vivo*: σ, μ estimated.

Gaussian pdf

$$f(x; \mu, \sigma) = \frac{e^{-(x-\mu)^2/2\sigma^2}}{\sqrt{2\pi\sigma^2}},$$

with

$x =$ noise.

N.B. CRB $\propto \sigma$.

Individual values $\sigma(t)$ of the actual noise realisation do NOT enter the CRB computation (estimation).

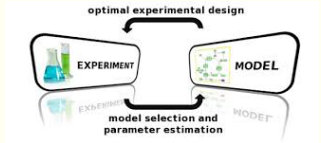
CRB III. Output of CRB-computation

- **Standard deviation of each estimated parameter.**
- **Correlations between estimated parameters.**

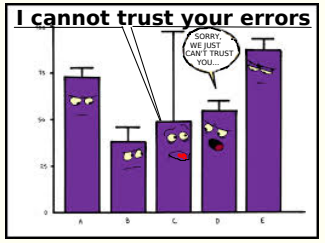
Remarks

- **Parametric case: Model function correct and complete. No Bias. Application of CRB warranted and highly recommended.**

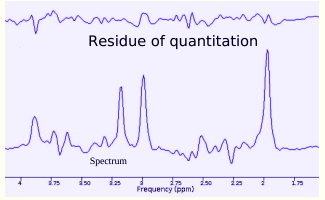
- **CRB's and correlations are useful for experimental design and cost estimation.**



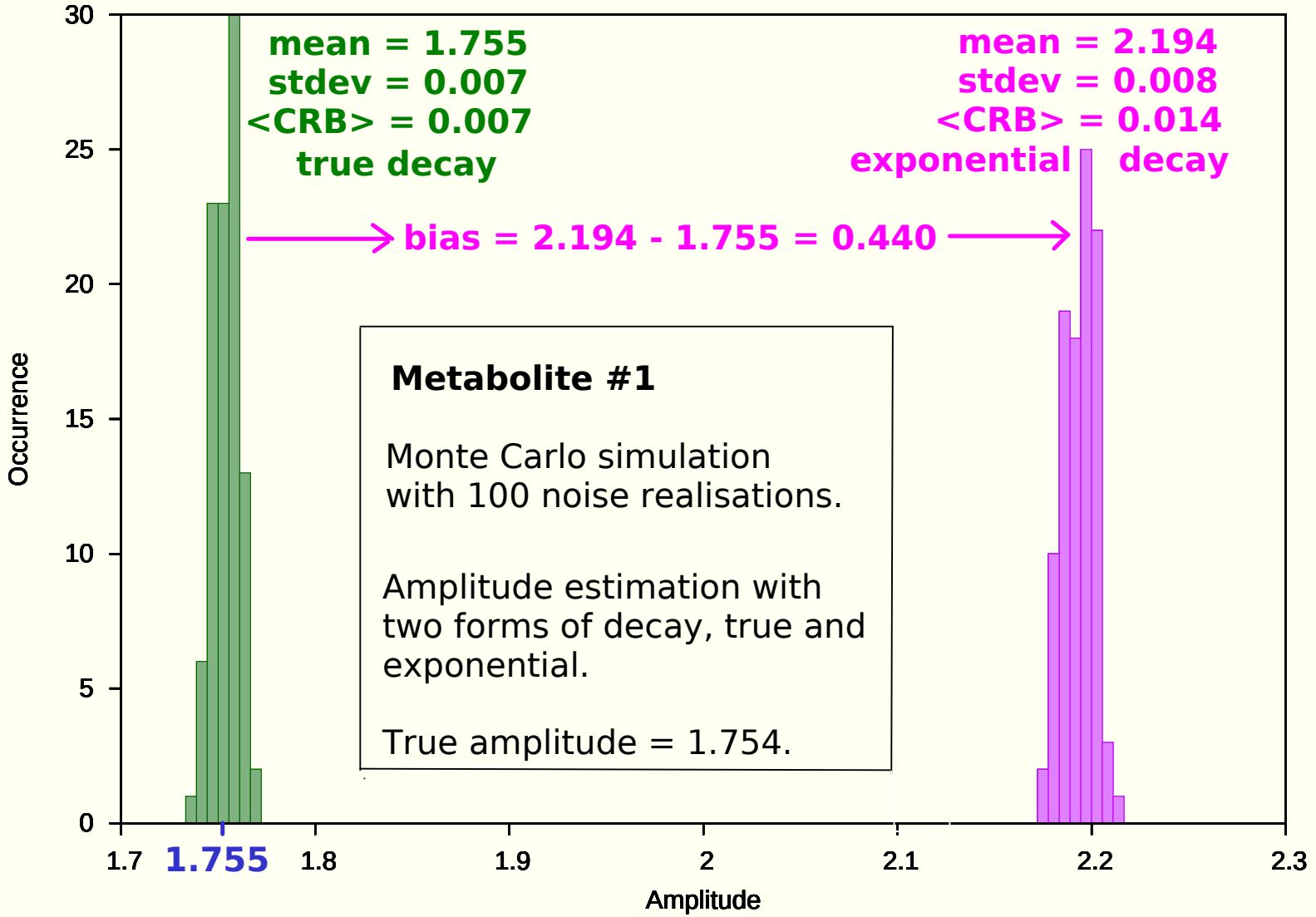
- **Semi-parametric case: Model function supplemented with 'surrogate' model function. Bias incurred, unknowingly. CRB may lead clinicians & others astray.**



- **How to judge semiparametric model function? From residue? Statistics package 'R'?**



Results: Monte-Carlo simulation I



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Mean and stdev of Monte-Carlo simulation versus CRB.

Results: Monte-Carlo simulation II

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Table: Results for true form of the decay, *i.e.*, parametric case.

m	$\mu_{c_m}{}^{\dagger}$	c_m^{true}	bias_{c_m}	$\sigma_{c_m}{}^{\ddagger}$	$\mu_{\text{CRB}_{c_m}}{}^{\dagger}$
1	1.7541	1.7550	-0.0008	0.0069	0.0071
2	0.1923	0.1921	0.0002	0.0081	0.0093
3	2.0665	2.0673	-0.0008	0.0073	0.0074
4	1.3582	1.3563	0.0019	0.0067	0.0070
5	0.6330	0.6330	-0.0000	0.0055	0.0059
6	0.1472	0.1472	-0.0000	0.0072	0.0069
7	0.5523	0.5527	-0.0004	0.0036	0.0042
8	2.9743	2.9742	0.0001	0.0084	0.0083
9	0.6611	0.6609	0.0003	0.0062	0.0069
10	0.1208	0.1199	0.0009	0.0060	0.0063

†) μ stands for mean, ‡) σ stands for standard deviation.

Mean and stdev of Monte-Carlo simulation versus CRB.

Results: Monte-Carlo simulation III

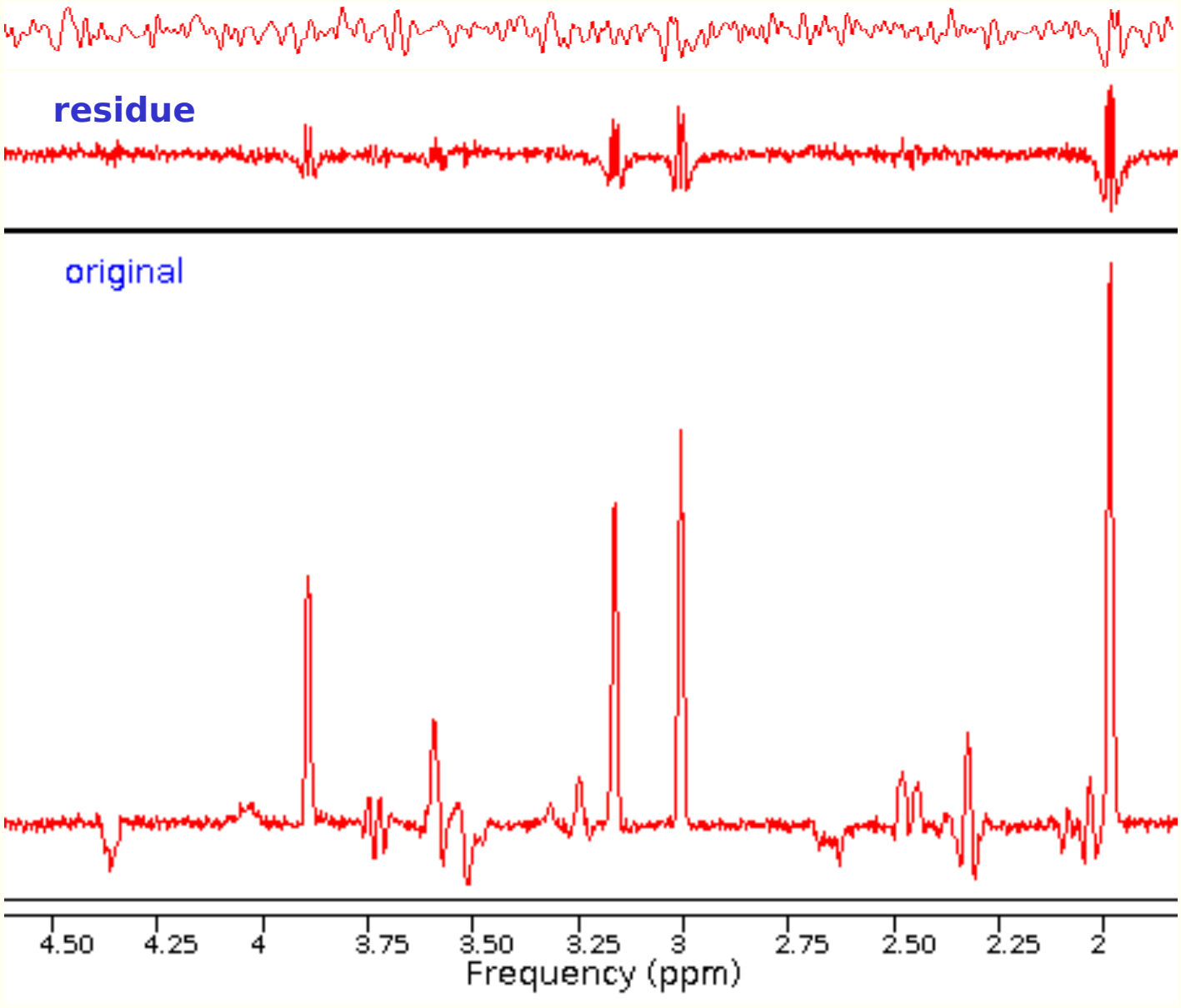
Table: Results for exponential decay, *i.e.*, semi-parametric case.

m	$\mu_{c_m}{}^{\dagger}$	c_m^{true}	bias_{c_m}	$\sigma_{c_m}{}^{\ddagger}$	$\mu_{\text{CRB}_{c_m}}{}^{\dagger}$	$\sigma_{\text{CRB}_{c_m}}{}^{\ddagger}$
1	2.1937	1.7550	0.4387	0.0080	0.0143	0.00009
2	0.2288	0.1921	0.0367	0.0111	0.0217	0.00014
3	2.5850	2.0673	0.5176	0.0079	0.0143	0.00010
4	1.6943	1.3563	0.3380	0.0078	0.0139	0.00009
5	0.8960	0.6330	0.2630	0.0074	0.0137	0.00009
6	0.1980	0.1472	0.0508	0.0097	0.0156	0.00011
7	0.7104	0.5527	0.1577	0.0046	0.0091	0.00006
8	3.7260	2.9742	0.7517	0.0088	0.0160	0.00010
9	0.7762	0.6609	0.1153	0.0075	0.0136	0.00009
10	0.1446	0.1199	0.0247	0.0076	0.0133	0.00009

†) μ stands for mean, ‡) σ stands for standard deviation.

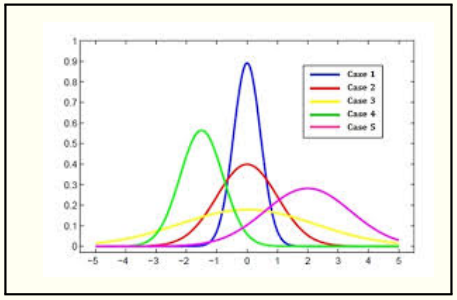
Mean and stdev of Monte-Carlo simulation versus CRB.

Residue of the quantitation



SUMMARY

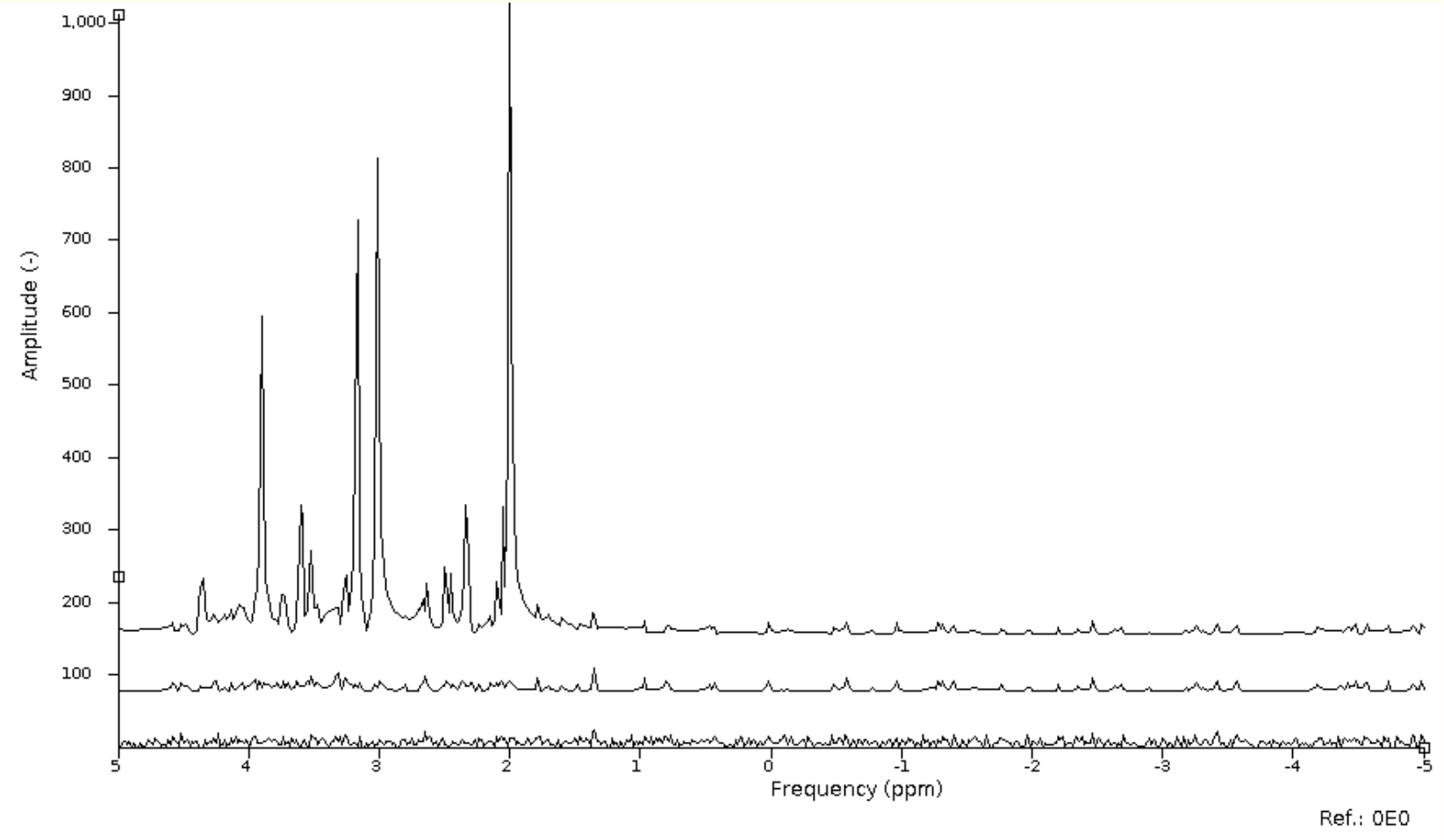
- Cramér-Rao :
  - Parametric case: Ideal. ☞
  - Semi-parametric case: Bias. CRB too low.
- Monte-Carlo :
  - Provides crucial insight, especially in semi-parametric estimation.
  - Simulation of 'real-world' signals may be difficult.
  - Not applicable in clinical routine.



RECOMMENDATIONS

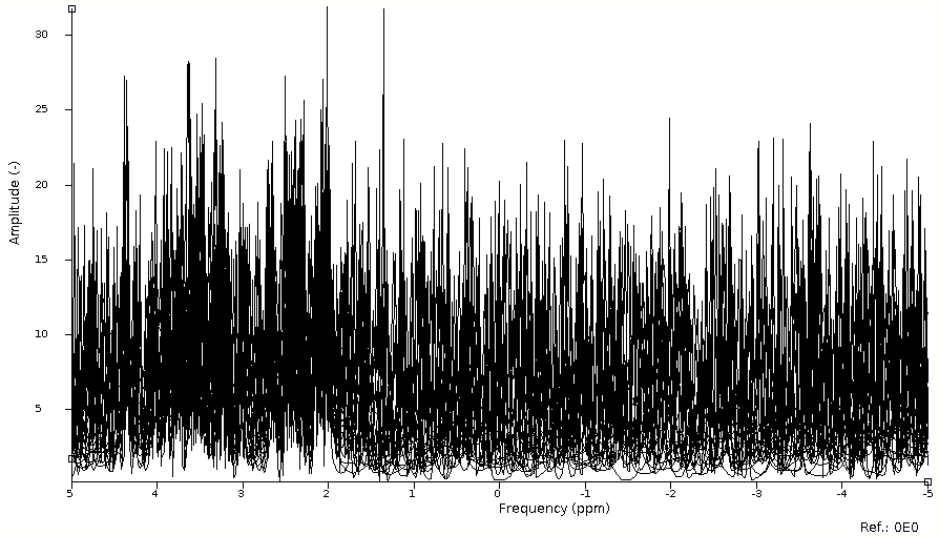
- ☞ Dramatic increase of SNR: 'hp', etc.
- ☞ Spectral editing.
- ☞ Denoising ?

DENOISING, 'SVD-truncation' I



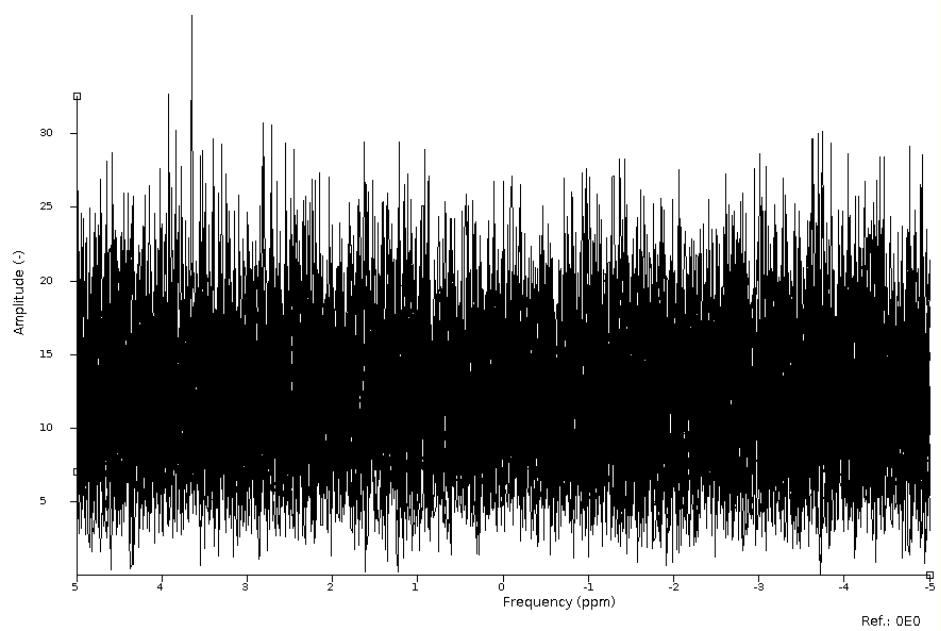
Single noise realisation shown. Absolute values.
Upper: FFT of denoised signal, 11.7 T.
Middle: FFT of denoised signal minus noiseless, true signal.
Lower: FFT of original noise.

DENOISING, 'SVD-truncation' II



Superimposed FFTs of 20 denoised signals from which the true, noiseless signal has been subtracted, i.e., only noise and signal deformation remain. Absolute values.

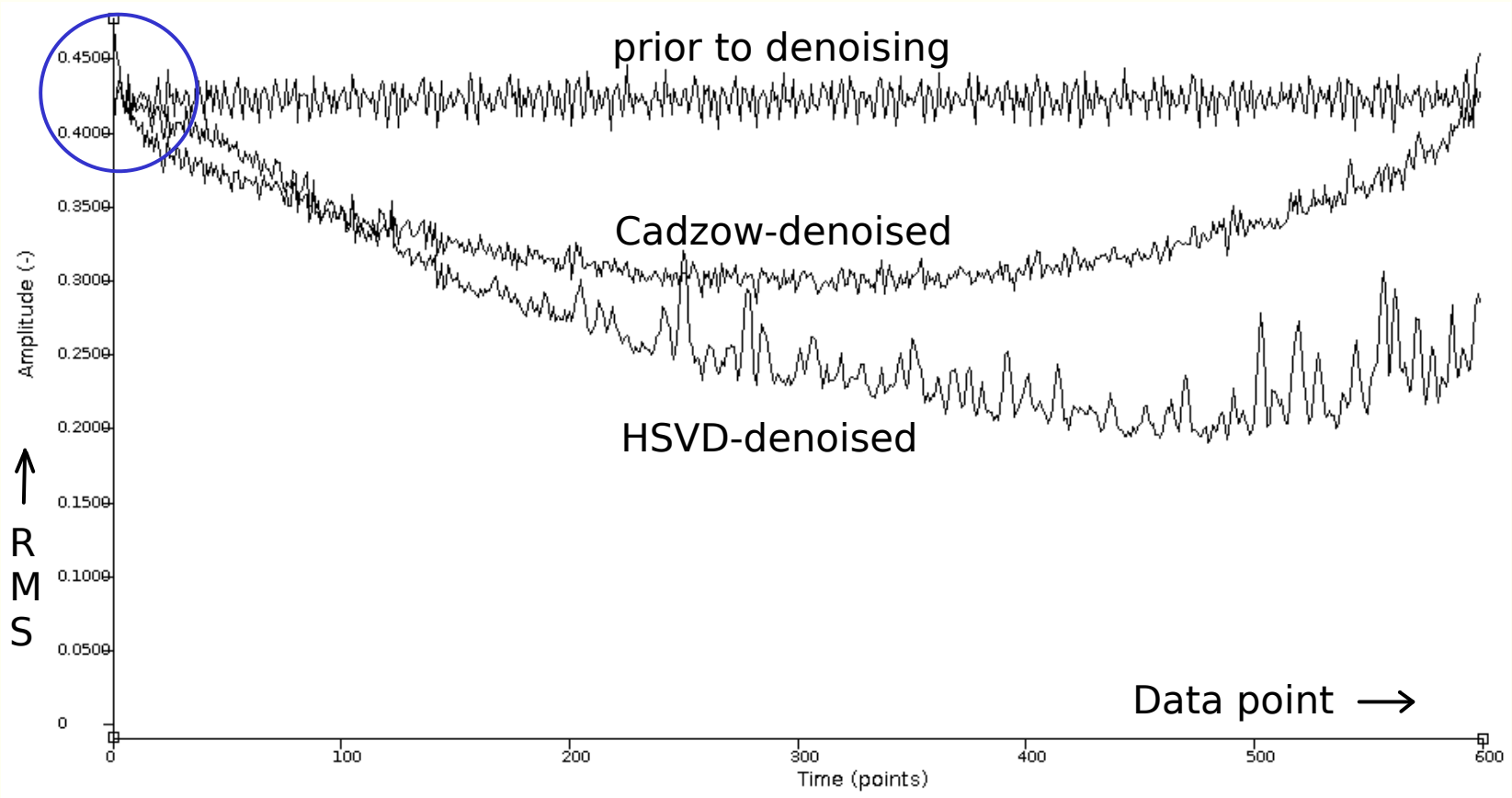
pdf of noise perturbed ⇑



Superimposed FFTs of the 20 corresponding original noise realisations. Absolute values.

DENOISING, 'SVD-truncation' III. Time domain.

$$\mathrm{RMS}\left[\left|\boldsymbol{s}_{\text{not-/post-denoised}} - \boldsymbol{s}_{\text{true\_noiseless}}\right|\right]$$



For each data point: RMS of noise in original noisy signal and in two denoised versions, using 10^3 noise realisations. MRS model function not used. RMS = root-mean-square.

DENOISING IV. Remarks

- Denoising of signals is indeed observed,
  - in both time-domain and frequency-domain.
    - Useful for, e.g., MRI (non-parametric).
  - Denoising of metabolite resonances?
  - Metabolite quantition benefits?
- Parametric metabolite quantitation with
  jMRUI, LCModel, etc.,
  already amounts to optimal denoising, because :
  - Parametric estimation errors, obtained with the un-denoised signal, reach the CRLowerB. Hence : ☞
  - Reconstruction of the signal from the estimated model parameters yields optimal denoising.
- statusquo@dvo :
  Using Monte-Carlo simulations, reduction of error bars of metabolite quantitation not found, so far.

ACKNOWLEDGEMENT

TRANSACT is made possible by the EUROPEAN UNION and its common currency, the EURO.

Delors

Euro coins

Draghi

“UNITED WE STAND, DIVIDED WE FALL”
In 26 centuries old fable : The Four Oxen and the Lion.

Two alternative definitions of 'estimation'

www.merriam-webster.com/dictionary/estimation :

1. **Guess**  **about size, amount, cost, ... , of something.**

   ☞ **Not meant here.**

2. **Use of a function or formula — 'estimator' — to derive a solution or make a prediction. Unlike guess, it has precise connotations.**

☞