Diversity of NMR Line-Shapes

[1]Reino Laatikainen, Pekka Laatikainen and Henri Martonen
[2]USP Team: Sunil Paudel, Christine Castagna, Jana Brcek and Ben Shapiro
[3]UEF:Tuulia Tynkkynen
[1]Spin Discoveries Ltd., Kuopio, Finland
[2]USP: US Pharmacopeia, USA
[3]UEF: University of Eastern Finland

ChemAdder line-shape can be composed from of the following terms:

- Lorentzian(%).
- Gaussian(%, global or proton specific).
- Asymmetry (%, global or proton specific).
- Dispersion (%, not very useful).
- Out-of-Coil (Hz), useful for benchtop and if the spectrum contains strong or broad signals.
- Virtual couplings (Hz, nuclei specific), if there are long-range couplings (like in steroids) the origin of which is unclear.
- Isotope shifts (^{13}C, Cl, Si, S) (ppm), if the H,^{13}C couplings are removed by decoupling, there remain ^{13}C isotope shifts, which may lead to a visible 1-3% shoulder at the high field (right) sides of the proton signals. Significant, for example, for glucose in biofluids.
- Fourier correction (33 terms) for observed-calculated difference, can be used to decrease RRMS and to reveal impurity signals under the target compound spectrum.
- Some essential signals, like TMS, TSP, DSS, Maleic acid, dimethyl sulfone, may have a special isotopic structure demanding a specific QM model …see QMSA Letters.

Fourier correction* of **observed-calculated difference** spectrum:

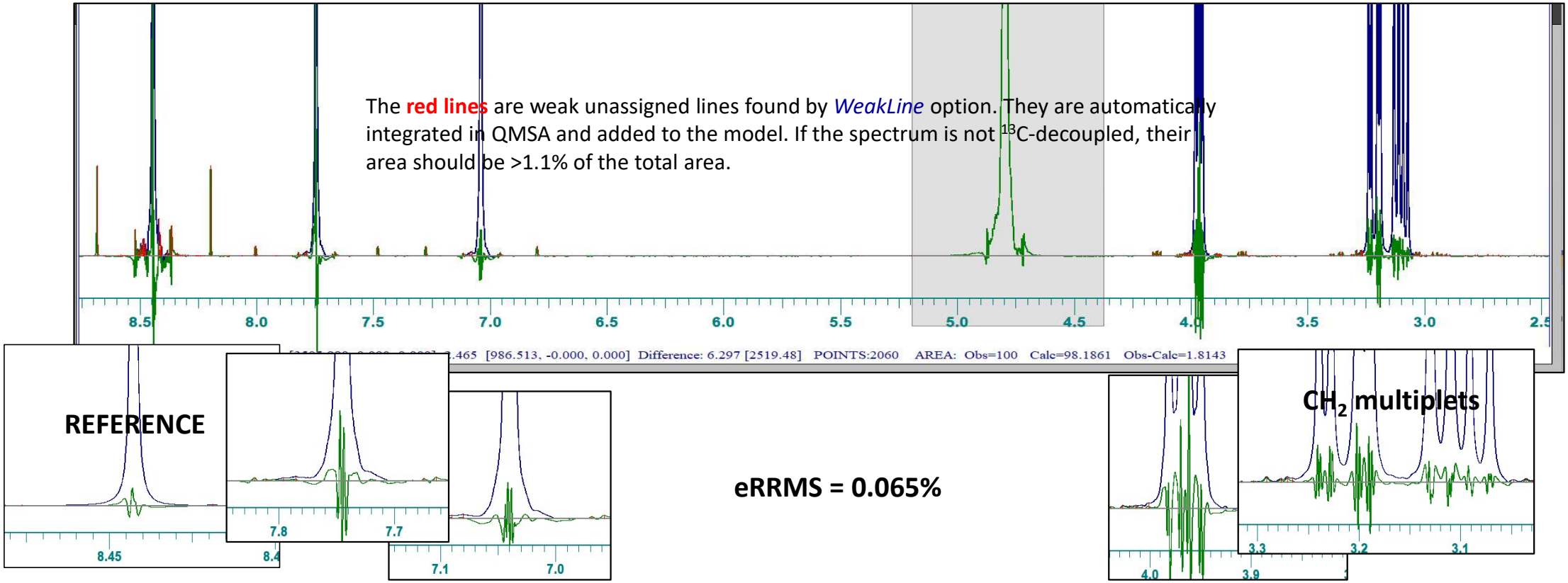
The **observed-calculated spectrum** can be fitted by n-terms (max. 33/proton) **Fourier function**, which can be then subtracted from the observed spectrum.

If the **Fourier correction** was the same for every line and the QM model perfect (= all the long-range couplings correct, the line-shape same for every line or species, etc), the subtraction should lead to zero **difference!** Unfortunately, this is seldom the case, but the subtraction typically leads to 40-70% decrease in eRRMS.

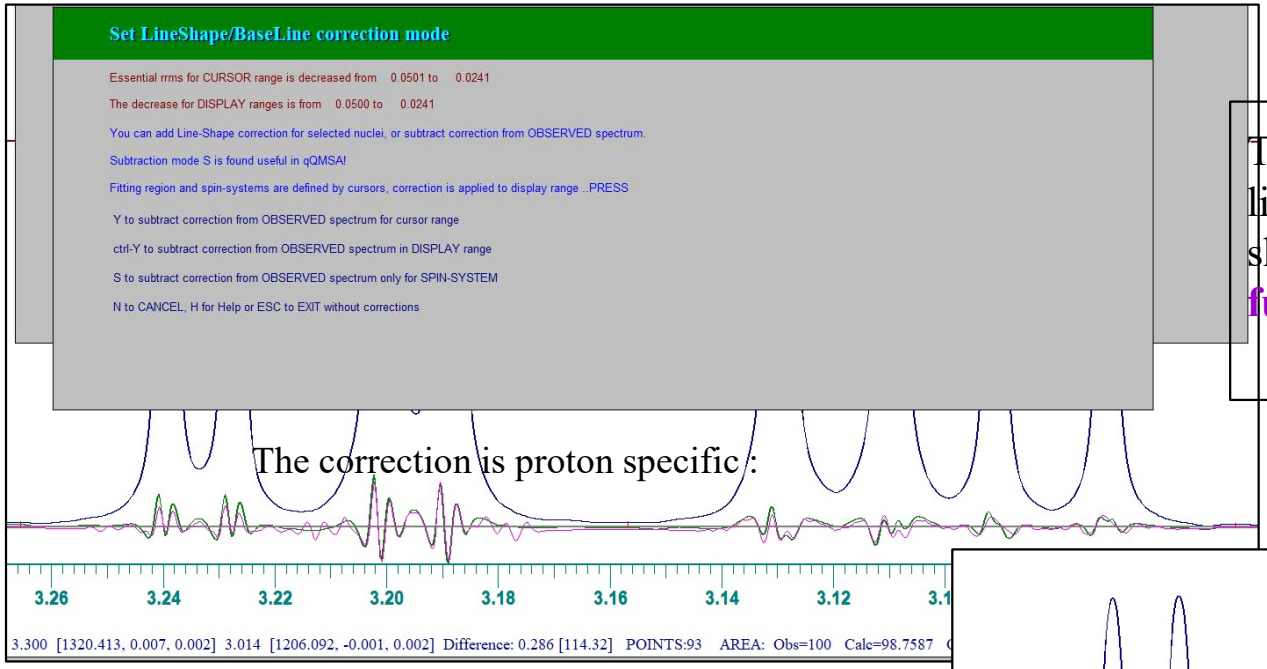
In principle, the subtraction should not remove impurity signals! However, if the correction is done for one multiplet, it may decrease the eRRMS by >90%, but at the same time it may remove the impurity signals hiding under the multiplet!!

*The ChemAdder *Fourier correction*' is more than a straightforward Fourier expansion and is under tuning.

Histidine spectrum after asymmetrical Lorentzian-Gaussian TLS-fitting:

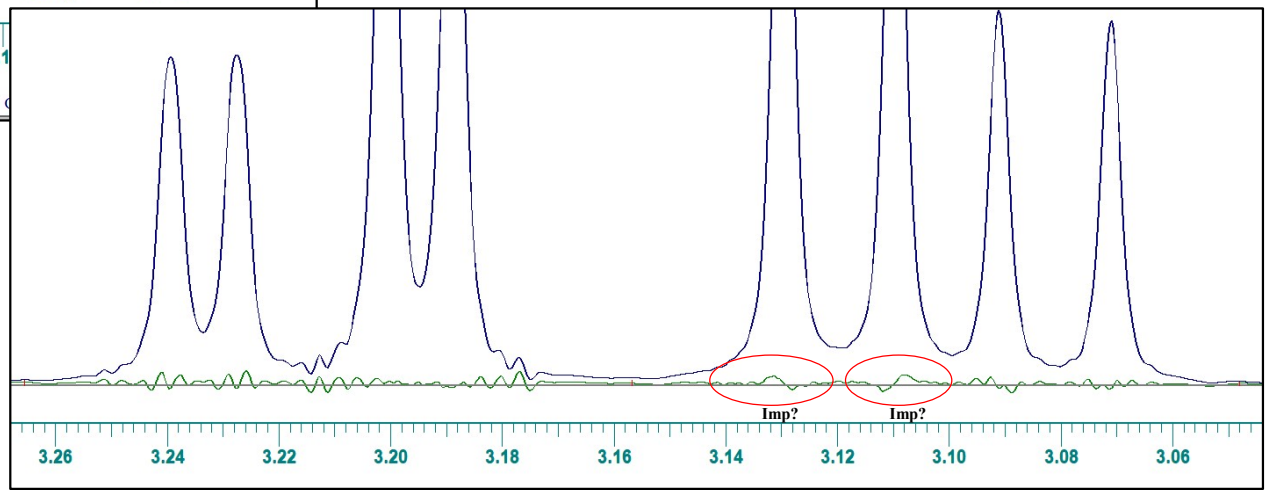


Histidine spectrum after **FOURIER correction:**



The correction is proton specific :

The CH_2 signals **observed-calculated difference** after line-shape optimization. The **Fourier correction** shows the fit of the **difference** with a 33 terms **Fourier function**:



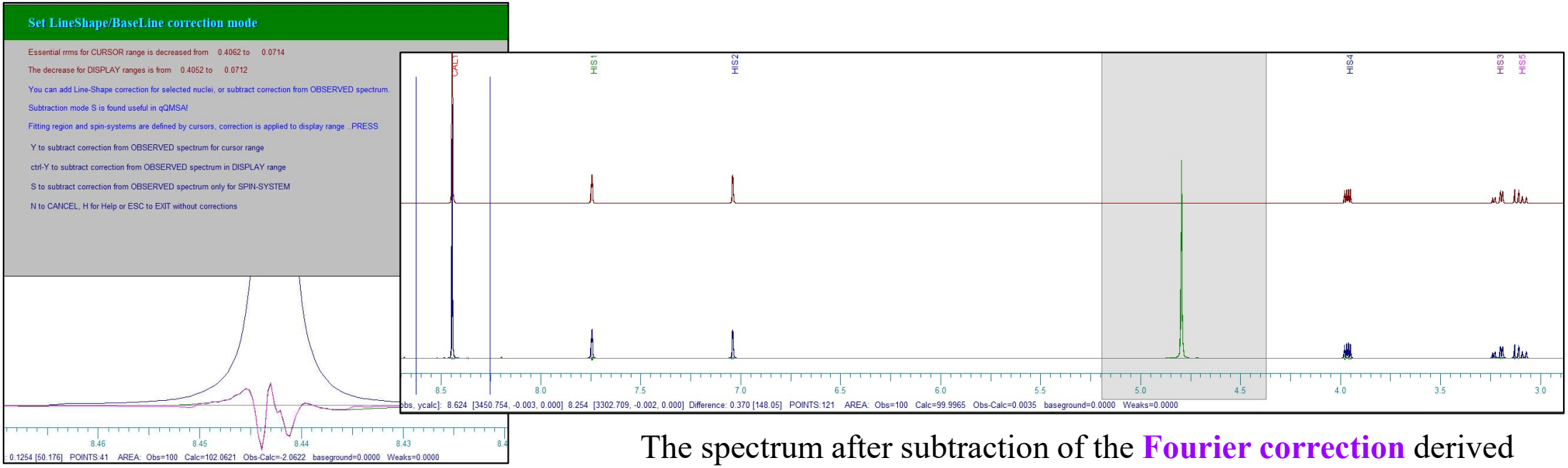
The CH_2 signals and the **difference** after subtraction of the **Fourier correction**:

eRRMS = 0.024%

Here different Fourier functions were optimized for the two protons). The correction is somewhat proton specific.

However (next page)…

..a fair decrease of RRMS is obtained also when the **correction** is derived from a well-defined signal (here the reference signal) and then applied for all the lines:



The reference **Fourier correction:**

eRRMS from 0.40 to 0.07%

The spectrum after subtraction of the **Fourier correction** derived from the reference signal:

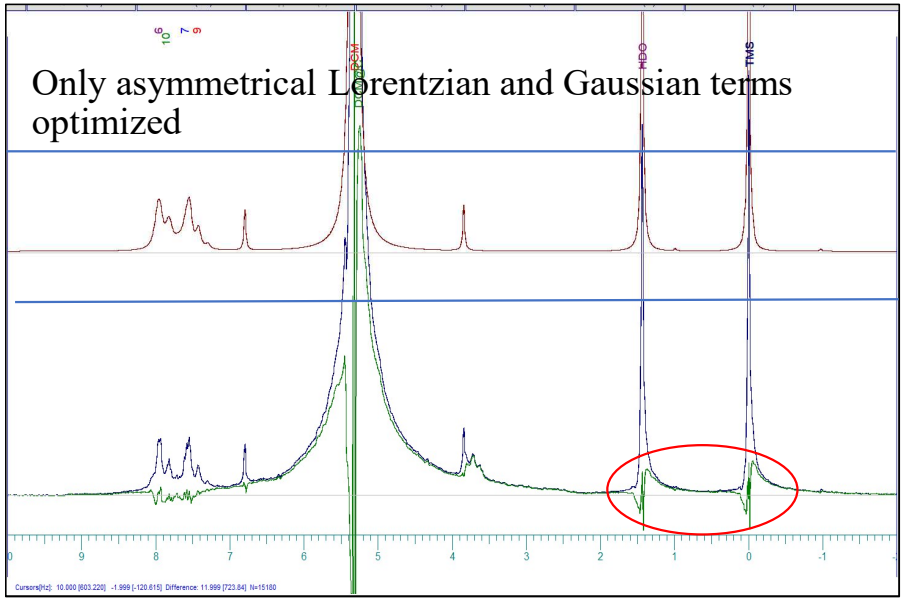
eRRMS decreased from 0.065 to 0.032%

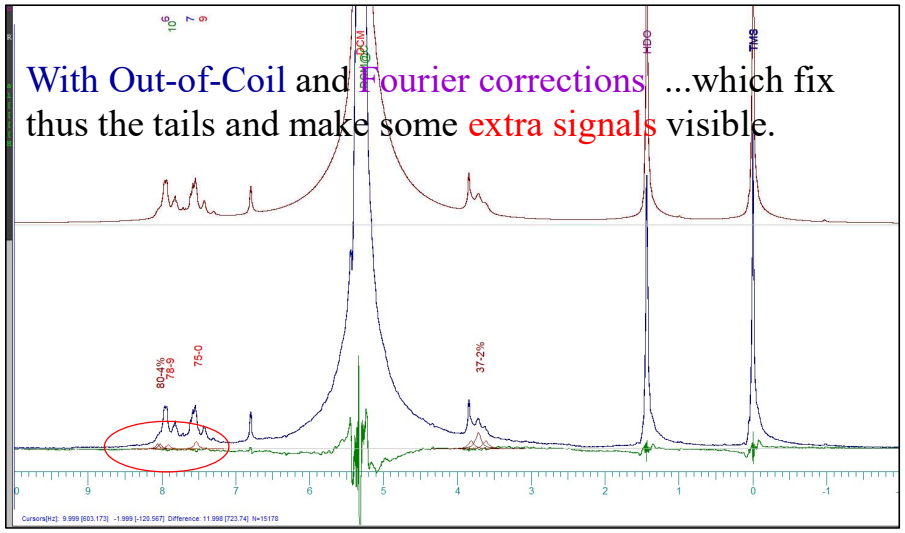
Out-of-coil correction (OoC)

The correction is actual if a spectrum contains strong asymmetrical and broad lines on the tails of which the target signals lie, and which cannot be satisfactorily described by the asymmetrical Lorentzian & Gaussian function. The feature is supposed to be especially important with benchtop spectra.

The observed-calculated difference spectrum can be fitted in ChemAdder by a 10 terms non-symmetrical function, which can be then subtracted from the observed spectrum. The correction compensates also a part of isotope shift shoulders.

From R. Laatikainen[a], S. Paudel[b], B. Shapiro[b], J. Zhang [c], J. Hein[c] and P. Laatikainen[a], *ChemAdderAnatomy of a 60 MHz Benchtop NMR Spectrum – Dissection*, QMSA Letters

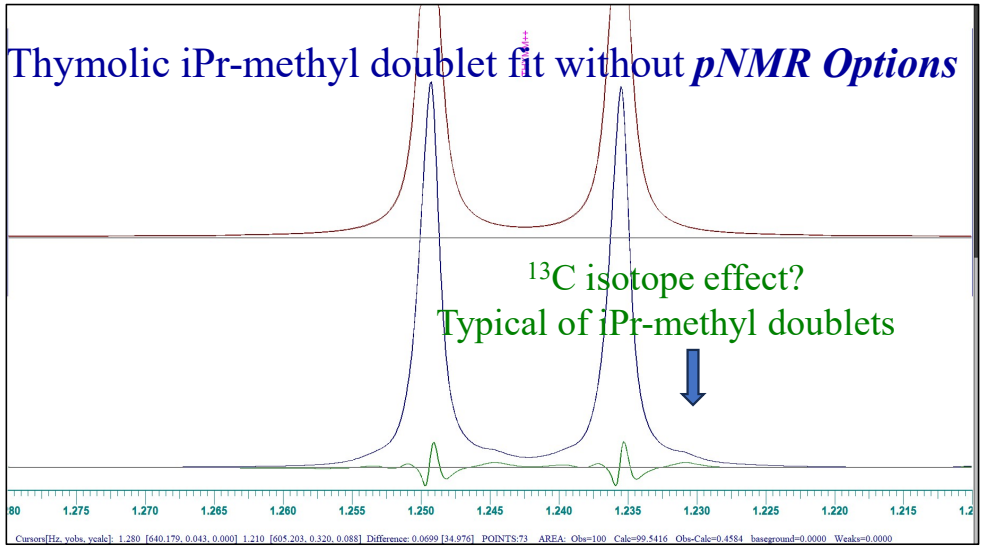




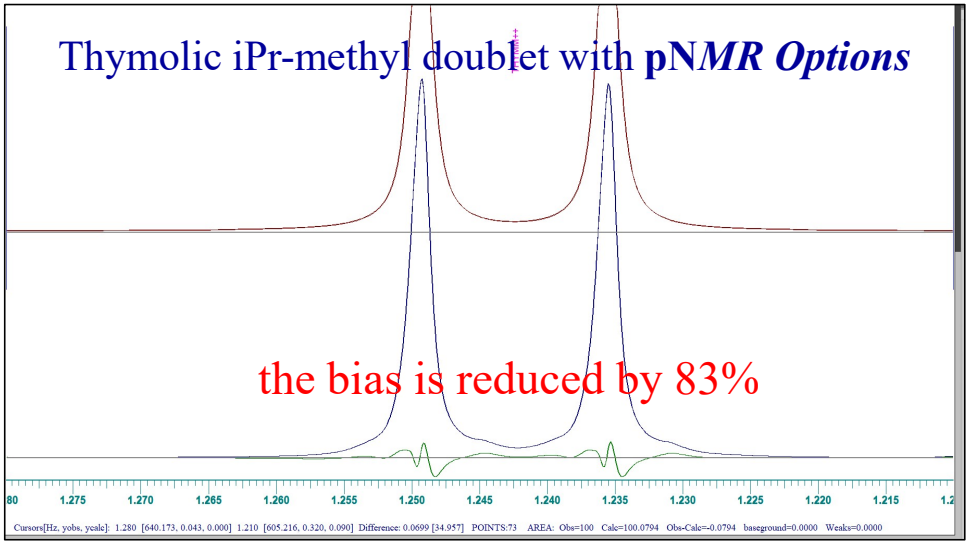
PurityNMR and IT-supported qQMSA

For example, long-range ^{13}C couplings and isotope shifts lead to structures which cannot be fitted by even the most sophisticated line-shapes. This may lead to bias of a few percent bias in PURITY%.

The ChemAdder solution is ***IT Supported qQMSA!***

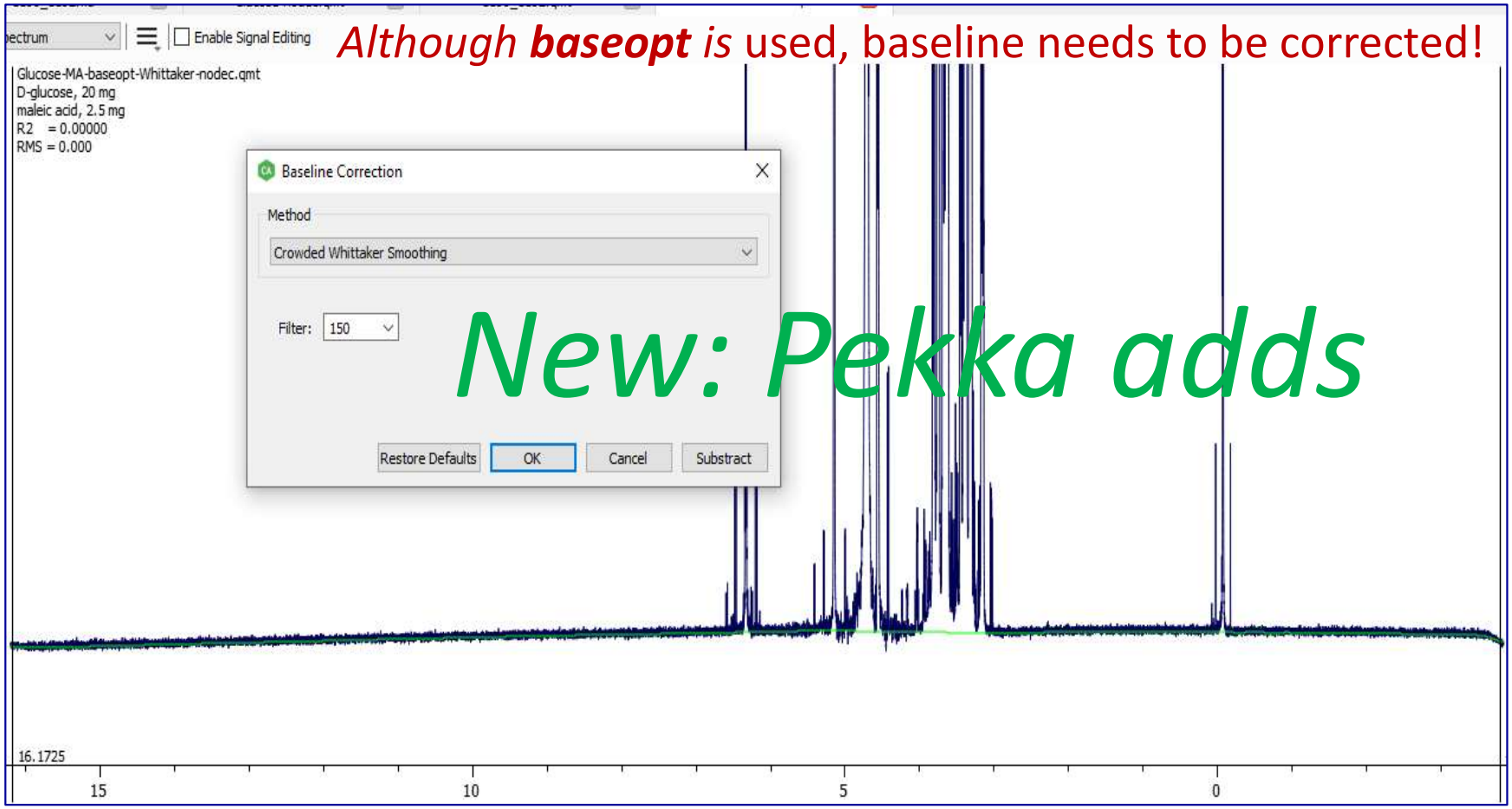


The observed-calculated area = 0.46% of the calculated area



The observed-calculated area = 0.08% of the calculated area

Whittaker baseline correction & smoothing



Isotope effects of ^{13}C, $^{29,31}Si$, $^{35,37}Cl$ and ^{34}S

- If the H,^{13}C couplings are removed by decoupling, there remain ^{13}C isotope shifts, which may lead to a visible 1-3% shoulder at the high field (right) sides of the proton signals. Significant, for example, for glucose in biofluids.
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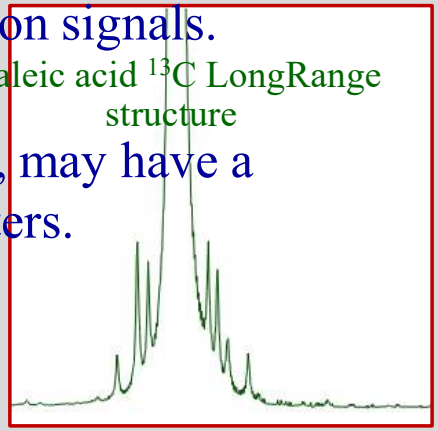

Virtual Couplings

- Virtual couplings, if there are long-range couplings (like in steroids) the origin of which is unclear.
- In ChemAdder one can define a coupling that splits all the lines of a nuclei to a regular Pascalian doublets, triplets or quartets, without defining the origin of the coupling.
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