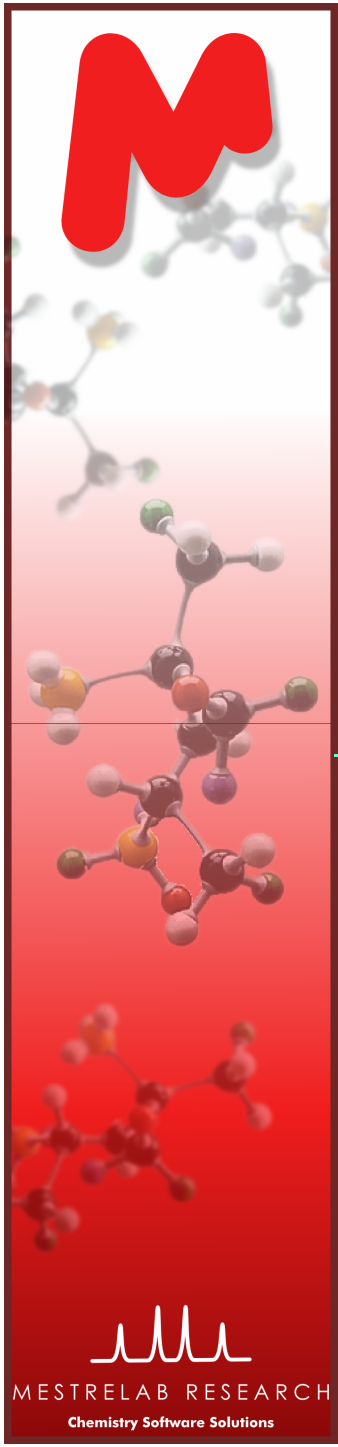

GSD & Structure Verification

Stan Sykora, Carlos Cobas, Felipe Seoane, et al

The science behind it all!

What is the current status?

The next three months

Playing 1D against 2D

Automatic elucidation

Omni-scient NMR wizard

The Sceptical Chymist

all over again

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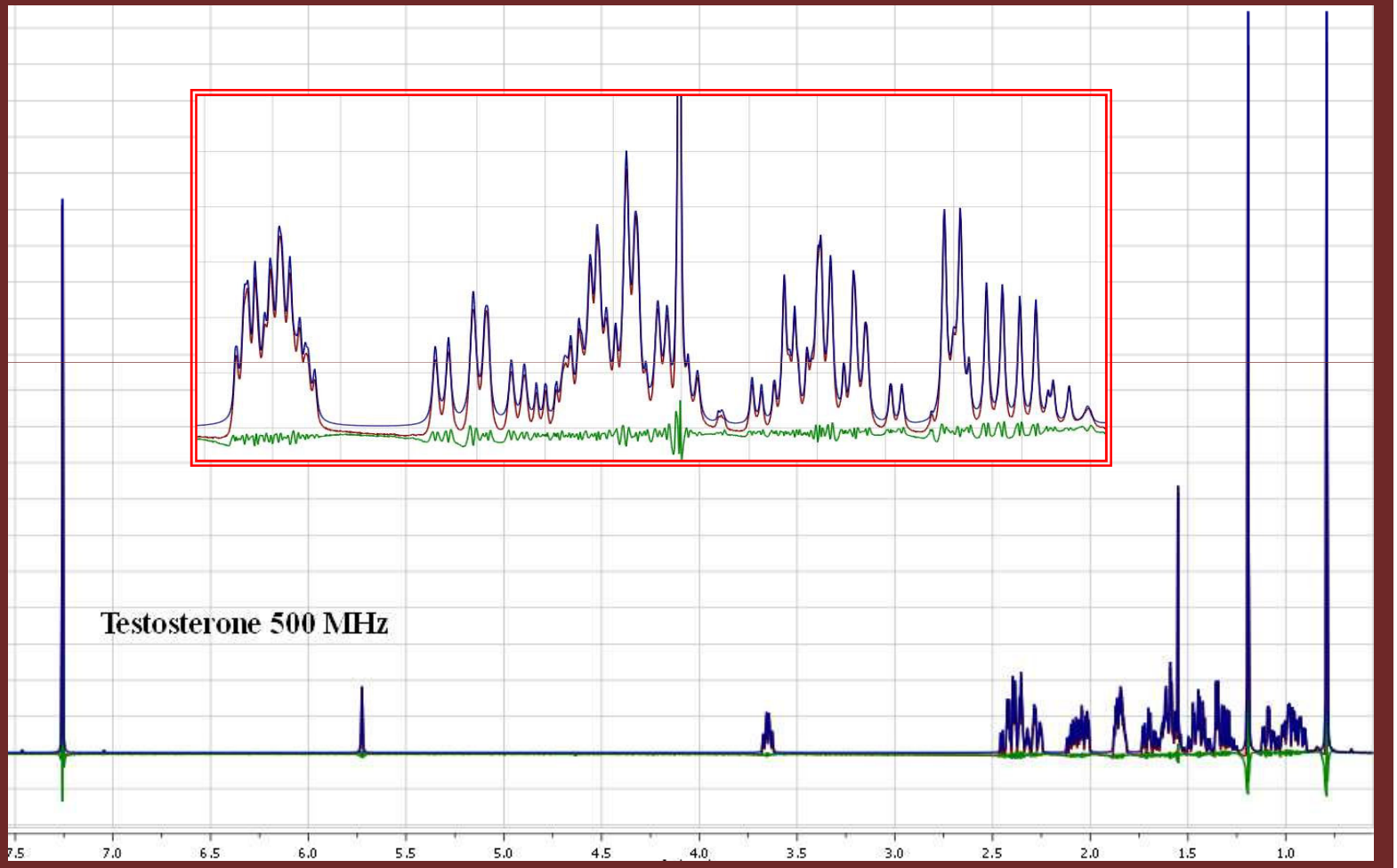
Chemistry Software Solutions

www.mestrelab.com

www.ebyte.it

GSD: Global Spectral Deconvolution

As announced at MMCE, February 2009, it is now fully operative



Idea introduced at SMASH, September 2007 (Metrelab User meeting)

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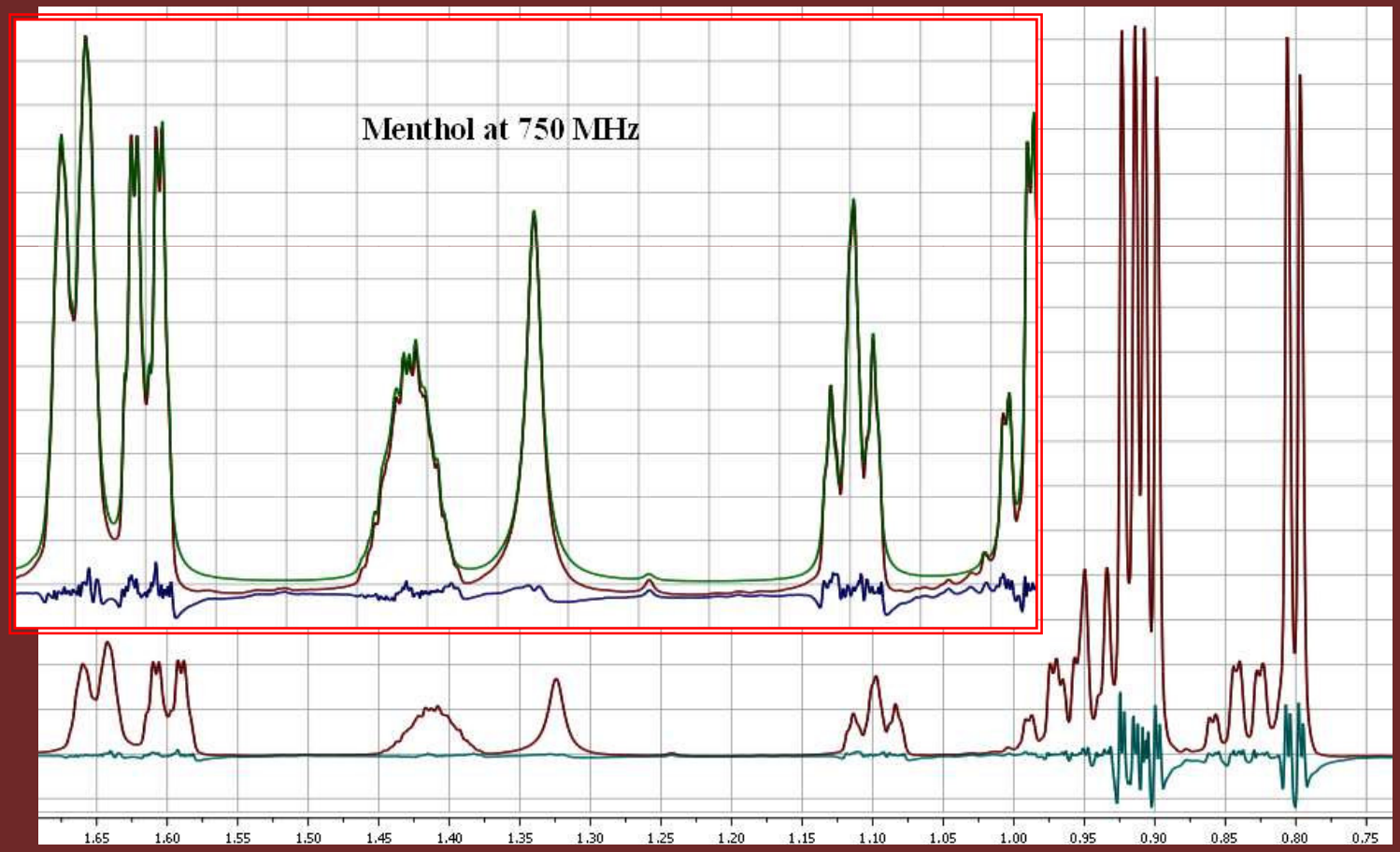
GSD definition

Automatic multiplet deconvolution **applied to the whole spectrum** without asking the User to select multiplets, specify number of lines and their approximate locations, etc …



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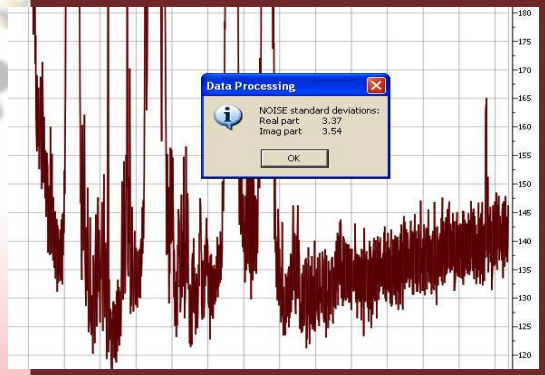
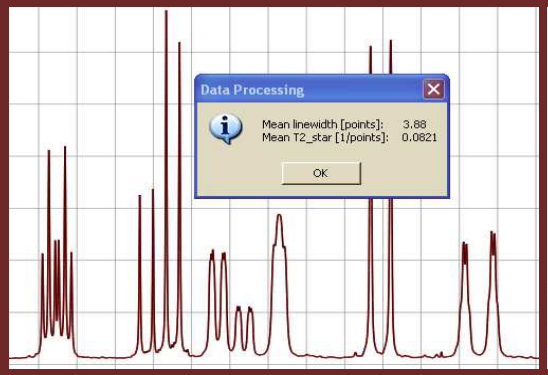
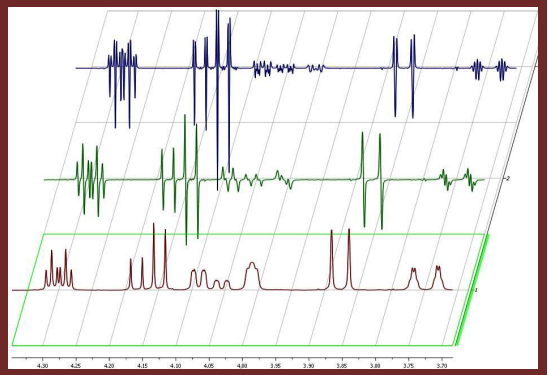
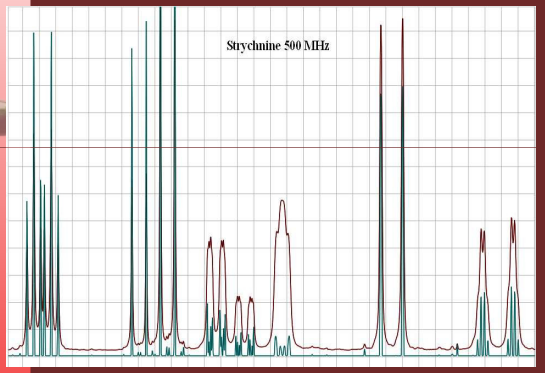
GSD algorithm

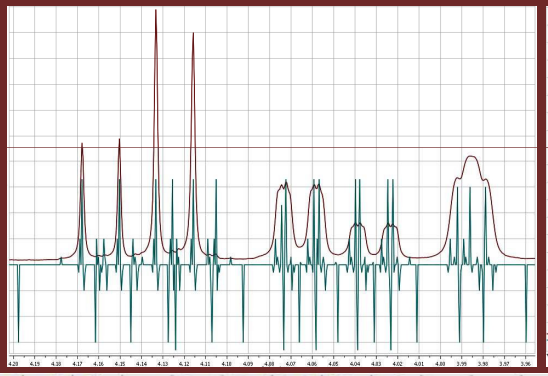
The algorithm is quite complex and has been presented elsewhere.

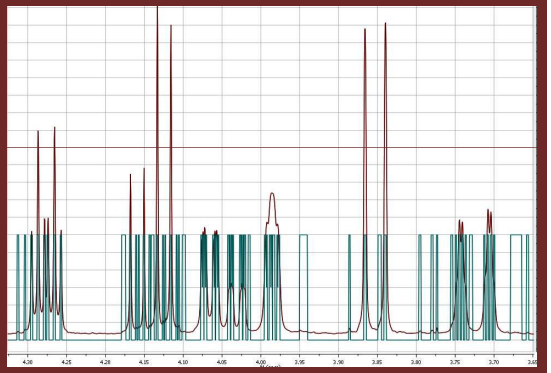


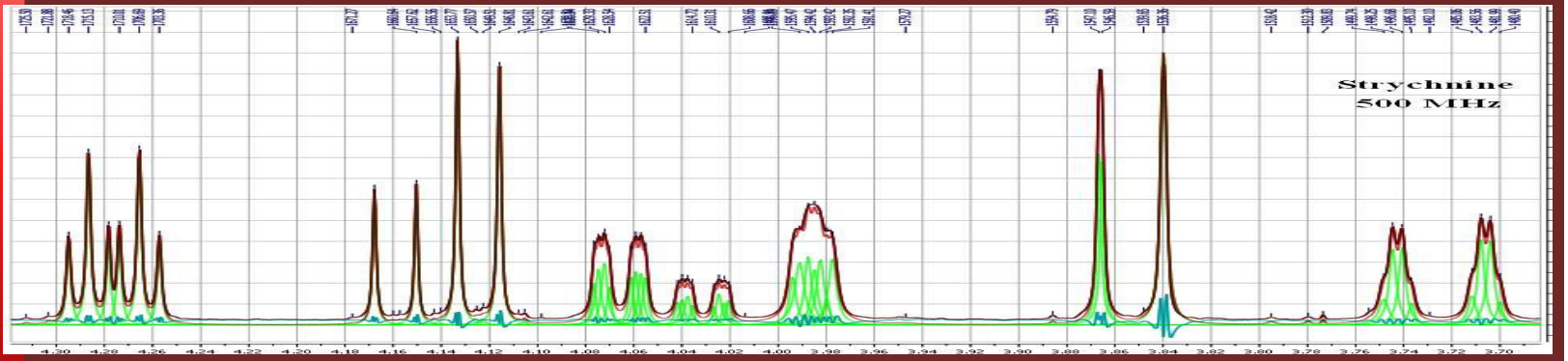












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Sorry: A full exposition would would take too long;it will be published before Xmas!

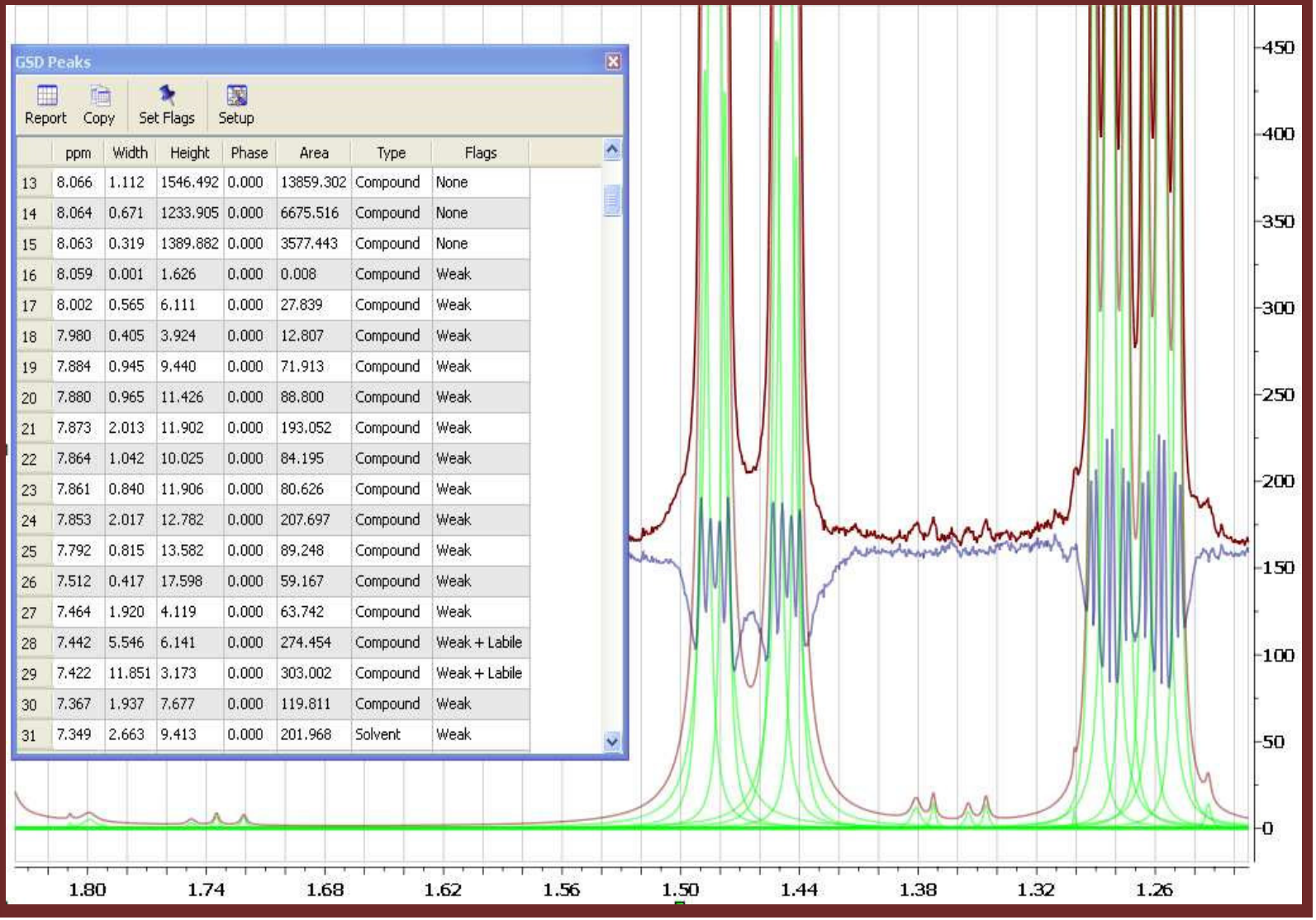
GSD primary output

The primary result is an **editable Peaks List** which is a **database** of **all objectively detectable** peaks to be used in **any** post-evaluation

GSD Peaks

Report | Copy | Set Flags | Setup

	ppm	Width	Height	Phase	Area	Type	Flags
13	8.066	1.112	1546.492	0.000	13859.302	Compound	None
14	8.064	0.671	1233.905	0.000	6675.516	Compound	None
15	8.063	0.319	1389.882	0.000	3577.443	Compound	None
16	8.059	0.001	1.626	0.000	0.008	Compound	Weak
17	8.002	0.565	6.111	0.000	27.839	Compound	Weak
18	7.980	0.405	3.924	0.000	12.807	Compound	Weak
19	7.884	0.945	9.440	0.000	71.913	Compound	Weak
20	7.880	0.965	11.426	0.000	88.800	Compound	Weak
21	7.873	2.013	11.902	0.000	193.052	Compound	Weak
22	7.864	1.042	10.025	0.000	84.195	Compound	Weak
23	7.861	0.840	11.906	0.000	80.626	Compound	Weak
24	7.853	2.017	12.782	0.000	207.697	Compound	Weak
25	7.792	0.815	13.582	0.000	89.248	Compound	Weak
26	7.512	0.417	17.598	0.000	59.167	Compound	Weak
27	7.464	1.920	4.119	0.000	63.742	Compound	Weak
28	7.442	5.546	6.141	0.000	274.454	Compound	Weak + Labile
29	7.422	11.851	3.173	0.000	303.002	Compound	Weak + Labile
30	7.367	1.937	7.677	0.000	119.811	Compound	Weak
31	7.349	2.663	9.413	0.000	201.968	Solvent	Weak



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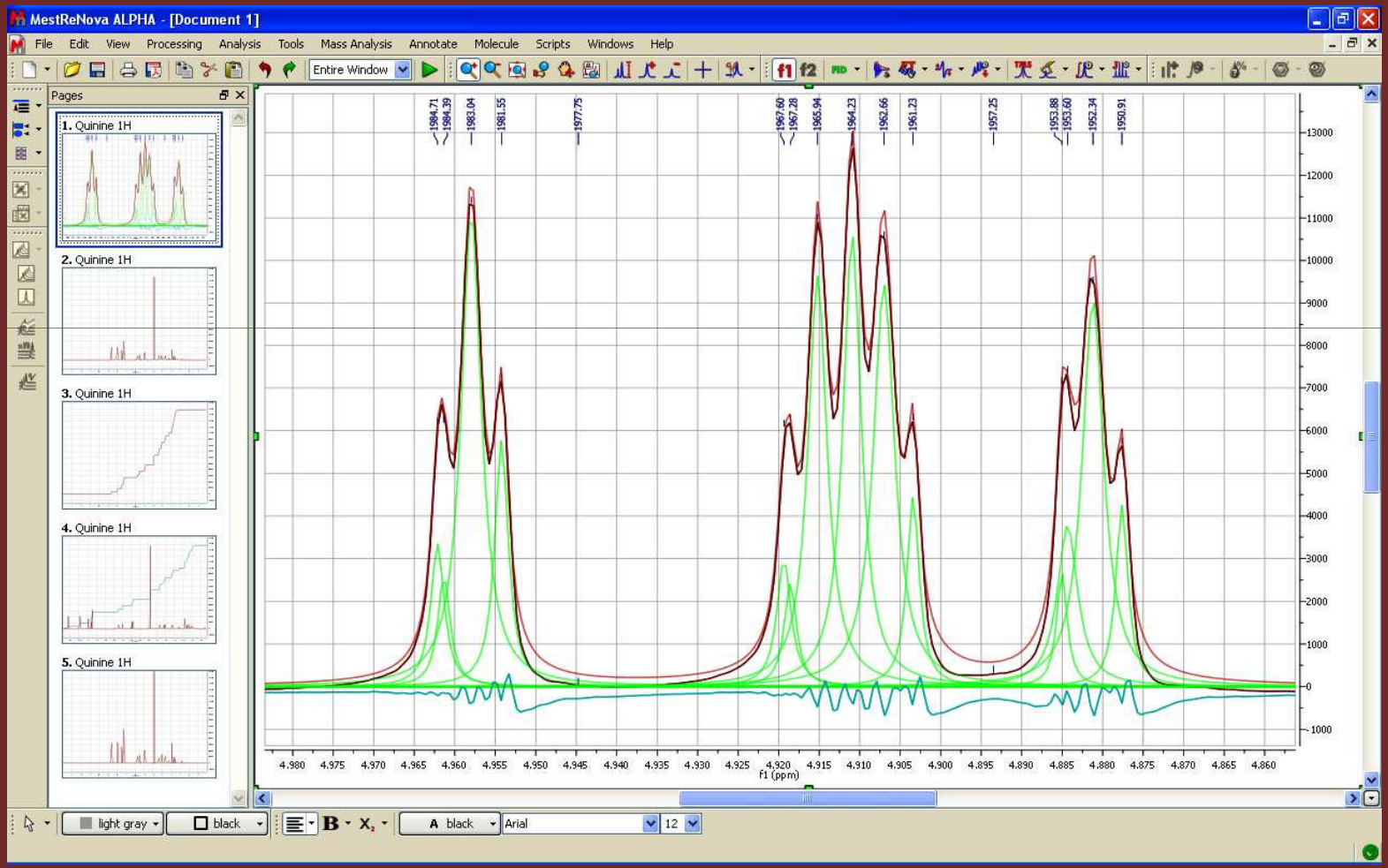
A first side-effect of GSD

Forget the obsolete, old-fashioned Multiplet Deconvolution !!!

GSD is: automatic, objective, complete and fast



The residuals have a physical meaning and can't be removed by further fitting

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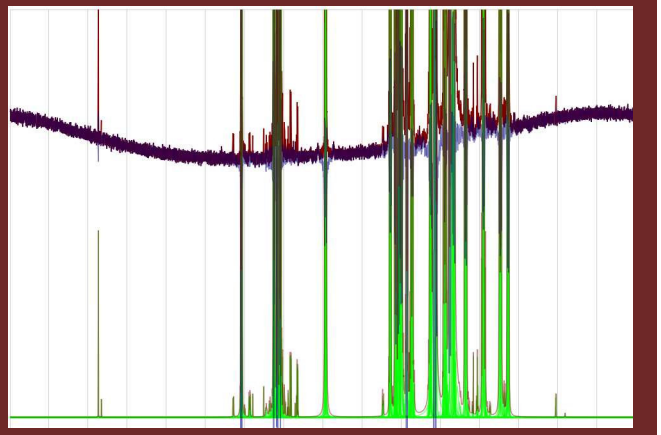
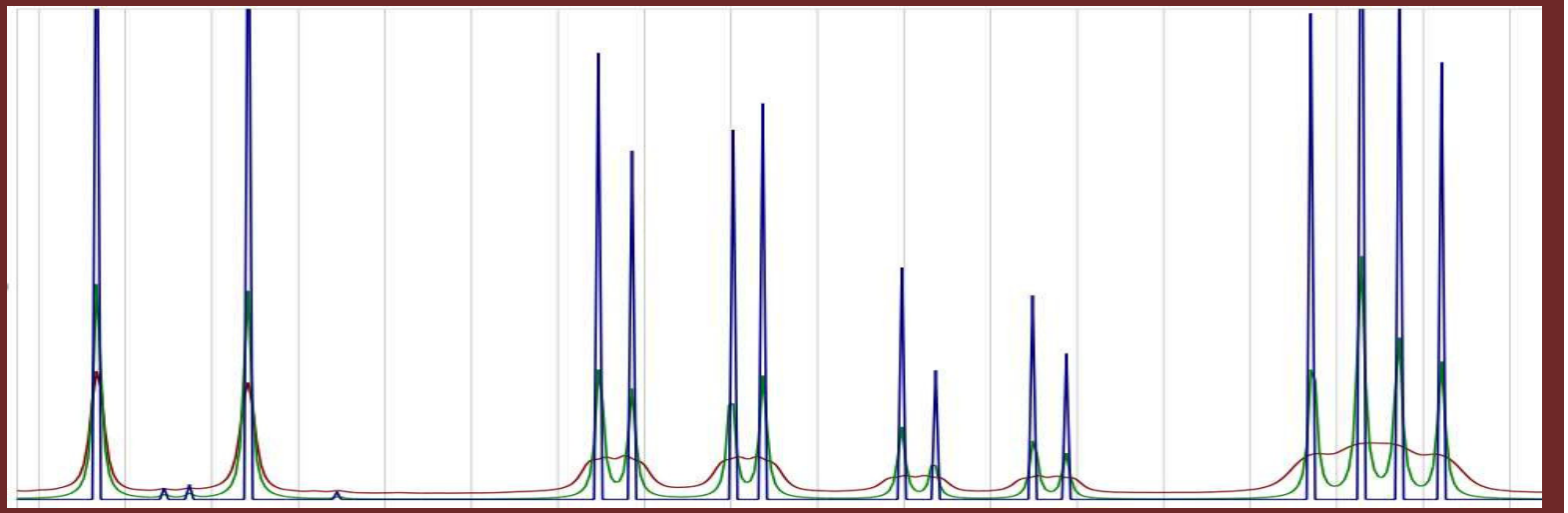
GSD: let a thousand flowers bloom!

The applications of GSD are too many to be listed and discussed here.
Actually we are ourselves still not fully aware of all of them!

1. Baseline correction
2. Linewidths regularization
3. Quantitation (better integrals)
4. Resolution enhancement
5. Peaks classification/selection
6. Etc …





Everything one might ever do with a spectrum should start with GSD

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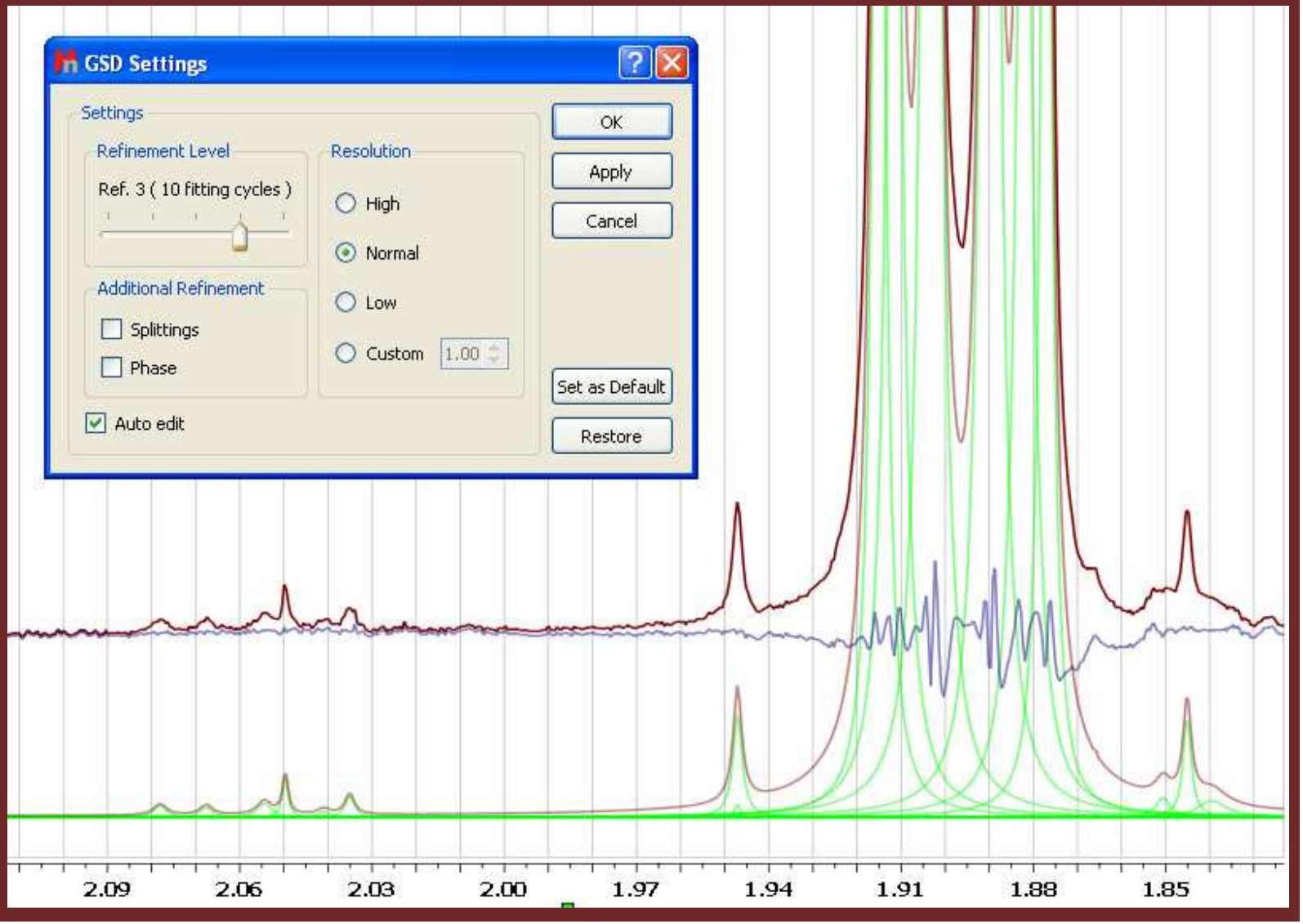
GSD in Mnova

Fully implemented, with a nice, user-friendly GUI.

For more details, please visit Metrelab stand



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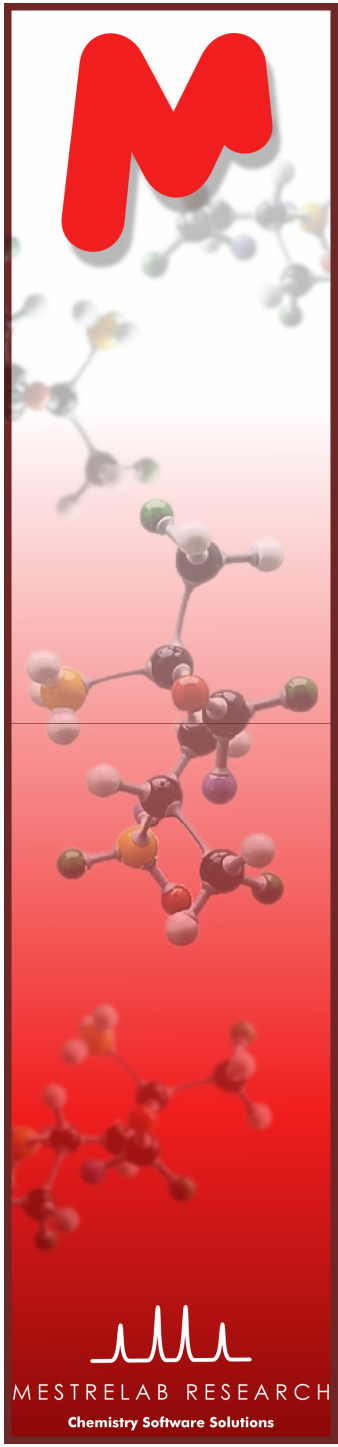


GSD blues: lineshapes and residuals

There are many very real sources of lineshape distortions

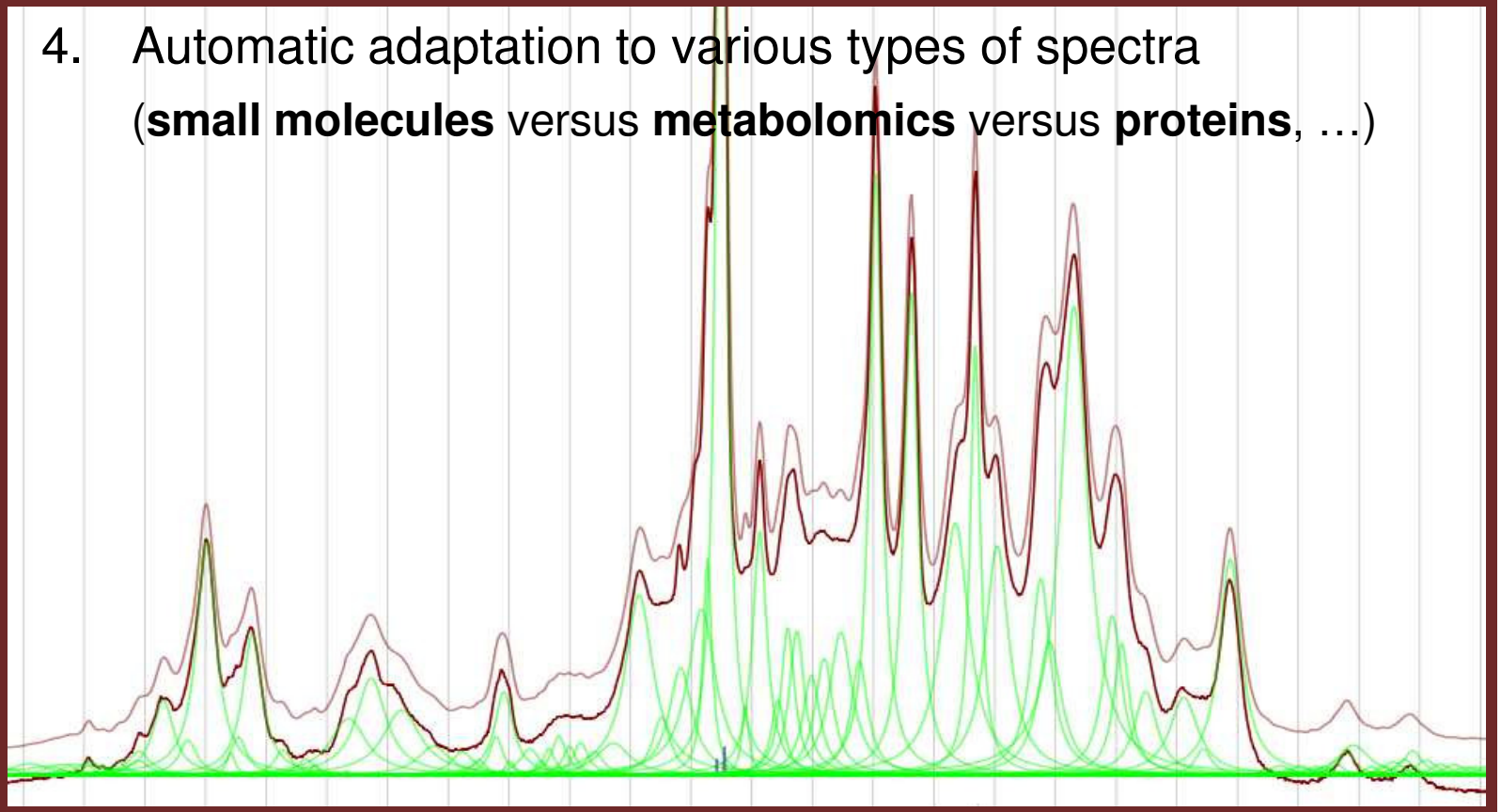
To cope with them is part of the problem

1. Magnetic field inhomogeneity (shimming)
2. Magnetic field noise
3. Sample spinning
4. Sample temperature gradients (up to 0.01 ppm/deg)
5. FID weighting before FT (Voight and other profiles)
6. Distorsions due to Discrete Fourier Transform (cyclic condition)
7. Overlap of the miriads of transitions in coupled spin systems
8. Relaxation effects (e.g., methyl lines)
9. Molecular dynamics effects (chemical exchange, limited mobility)
10. etc …

Sorry: A partial exposition of this topic took me recently 90 minutes.
It will be published before Xmas!

GSD in the works

1. Further suppression of residuals (flexible lineshape models)
2. Speed boost (particularly in the fitting step)
3. Extension to 2D spectra
4. Automatic adaptation to various types of spectra
   (**small molecules** versus **metabolomics** versus **proteins**, …)



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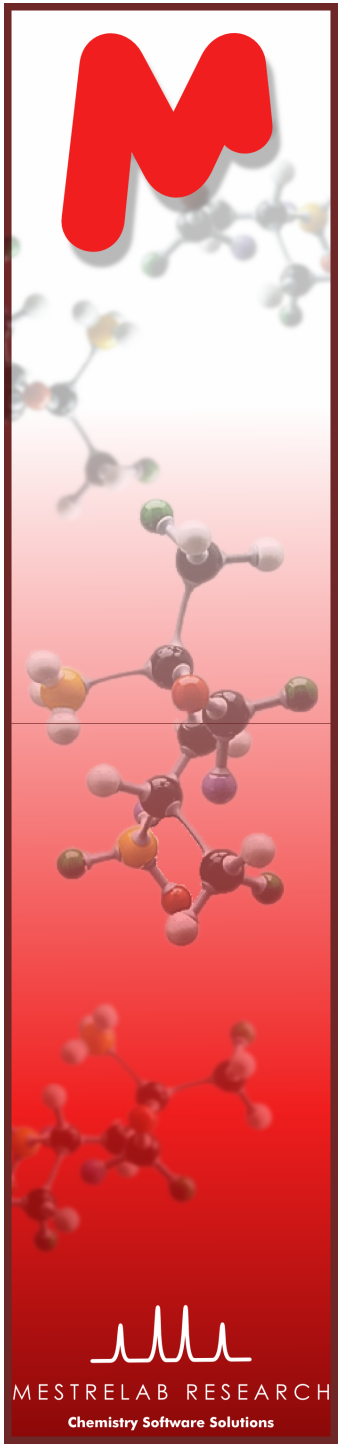


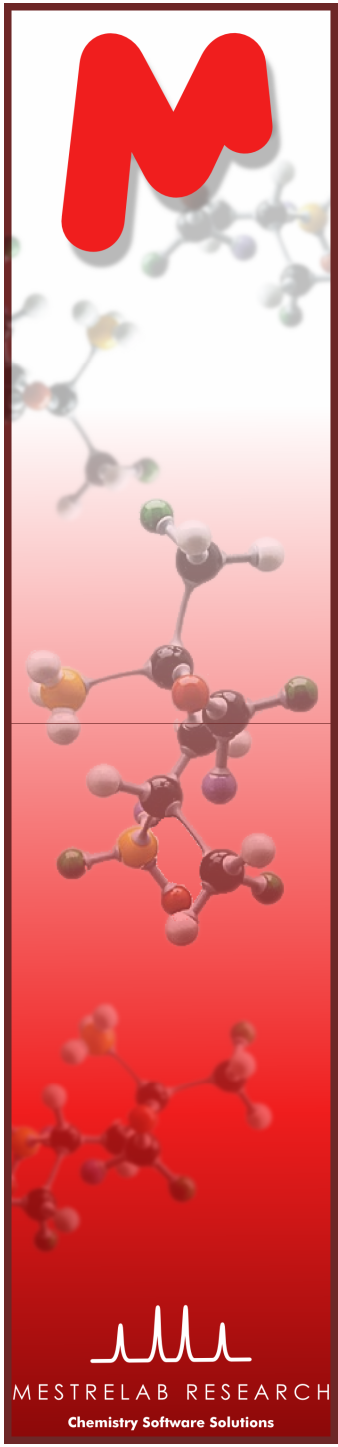
Structure Verification

This is work-in-progress, but
we are at it since several months and making very nice advances.
Official release of Verification 1.0 is planned within this year.

It is an extremely hot topic in the NMR software industry.

Here I want to give you just an idea about
the road we are following

Sorry: Some of the stuff in this category is still confidential.



Verification versus Elucidation

Molecular formula + Experimental spectrum

⇒ **VERIFICATION** ⇒

PASSED / FAILED

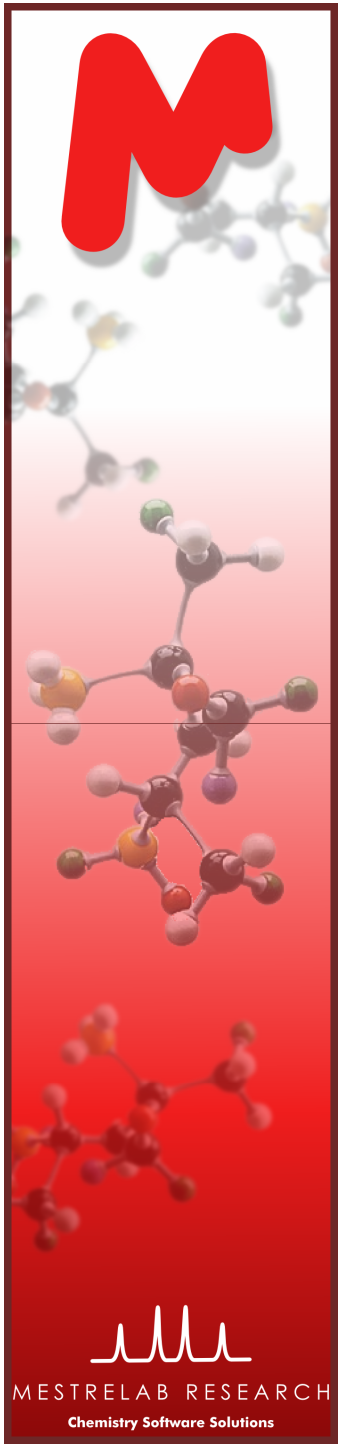
Experimental spectrum

⇒ **ELUCIDATION** ⇒

⇒ List of compatible spin systems ⇒

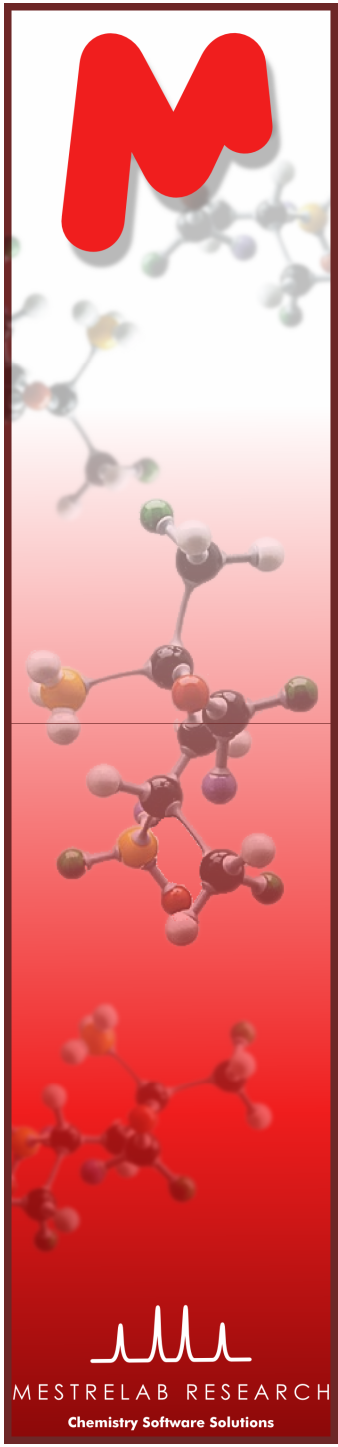
⇒ SS2MOL software ⇒

⇒ List of compatible molecules



Verification: spectrum pre-treatment

1. Generation of GSD peaks list: absolutely essential
2. Pruning of the GSD paeks list: eliminate solvent lines, reference line, 13C satellites, impurities, etc.
   This can be either manual or automatic
3. Detection and handling of possible labile proton peaks

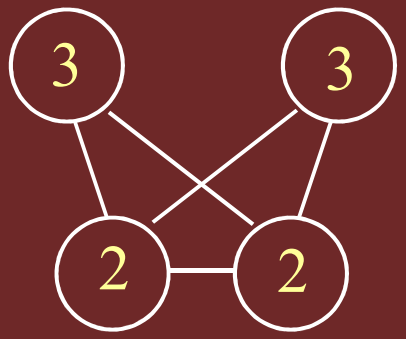


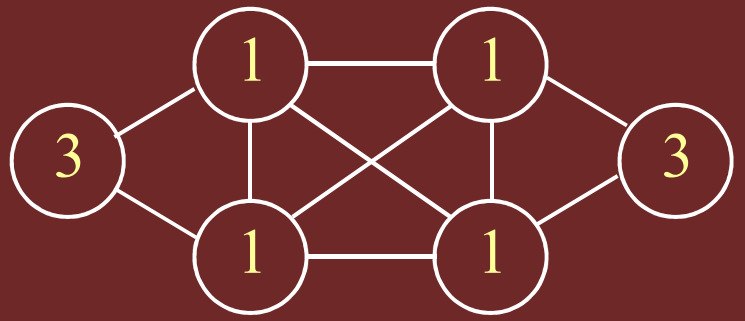
Verification: mol pre-treatment

1. Conversion of mol script to a spin system graph
2. Prediction of the spin system parameters (shifts+J's)

Step 1 is NOT trivial. Example:

CH_3-CH_2-CH_2-CH_3





WRONG

2 δ's, 3 J's

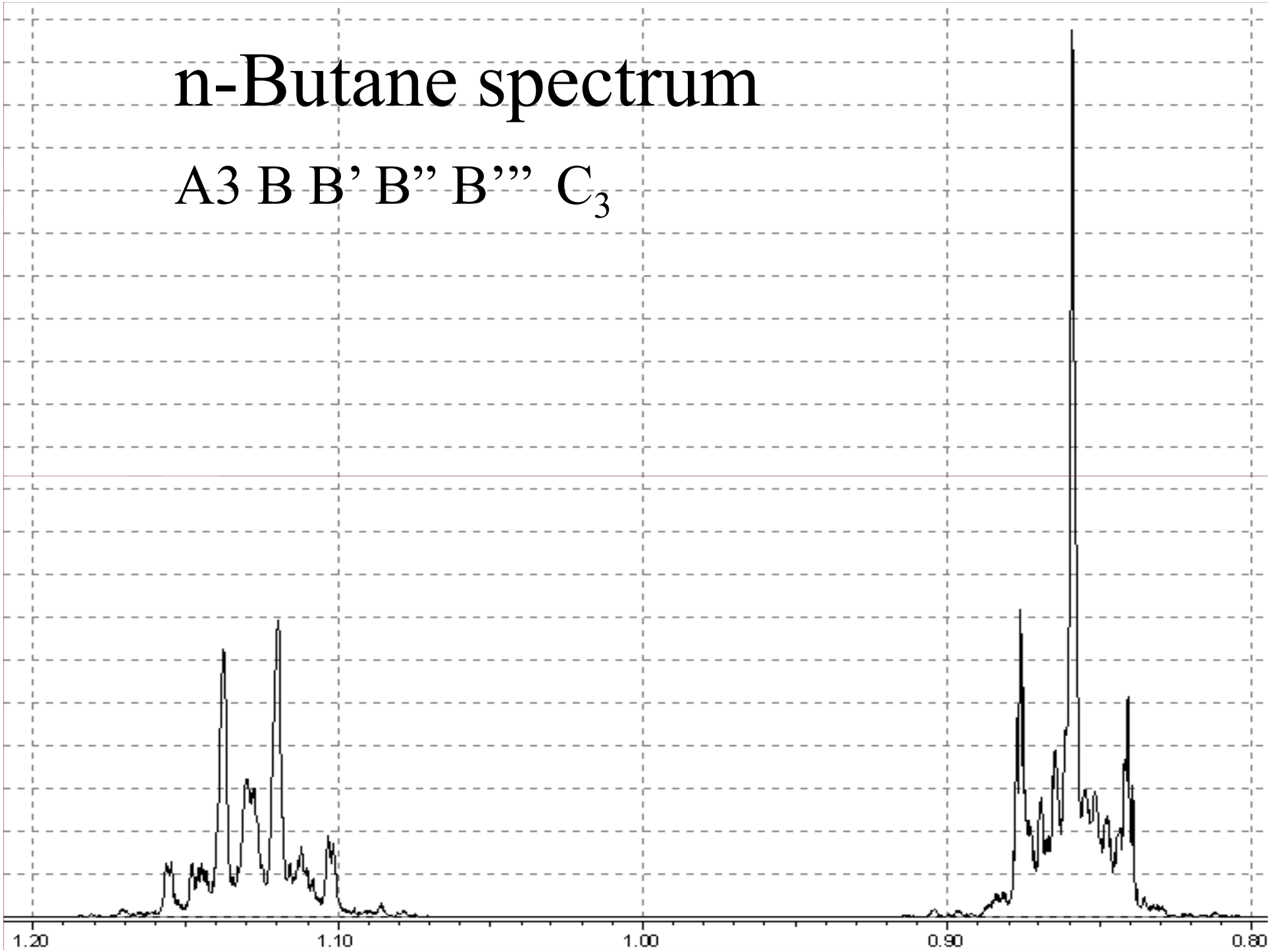
← fittable →

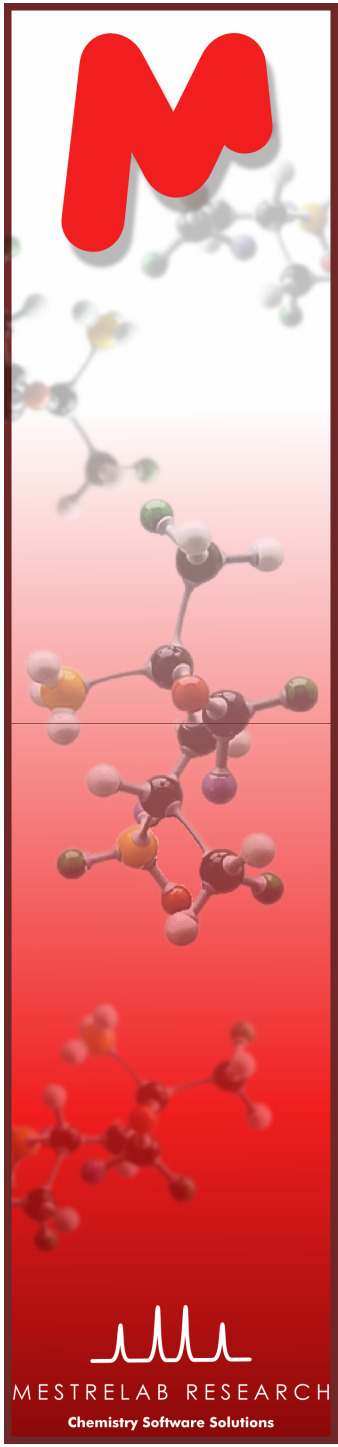
CORRECT

2 δ's, 4 J's

n-Butane spectrum

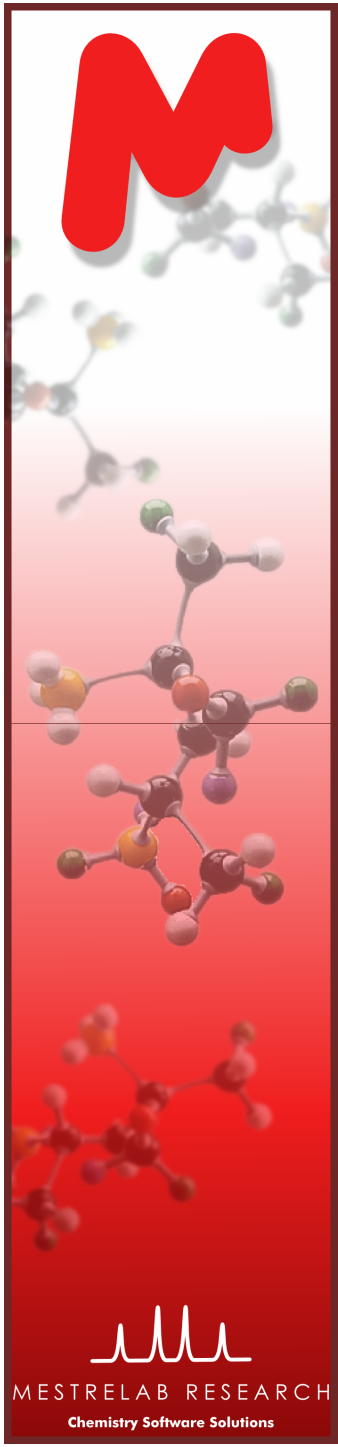
A3 B B’ B” B”” C_3





Verification: distinct modalities

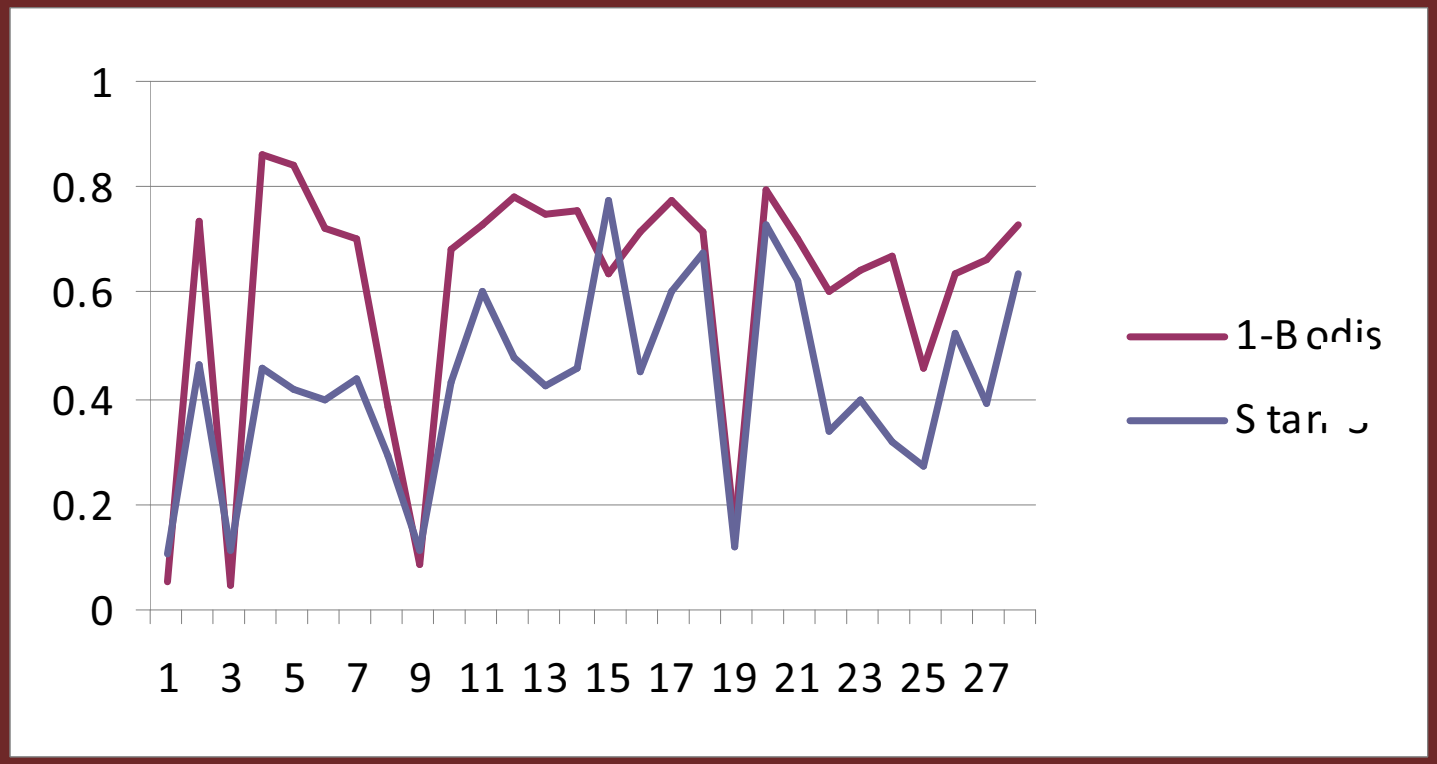
1. Simple: 1 Mol against 1 spectrum
2. M Mols against a 1 spectrum
3. 1 Mol against N spectra
4. 1 spectrum against a database



Verification: subsequent steps

1. Generation of a simulated spectrum (where needed)
2. Application of spectra comparison metrics (SCM):
   BRP (Bodis,Ross,Pretch) and Stan's (so far confidential)
3. SCM's applied to distinct regions
4. Automatic definition of coupling multiplets
5. SCM's applied to distinct multiplets
6. Number-of-Nuclides tests on multiplet subsets
7. Etc …

Verification: BRP metric versus Stan's



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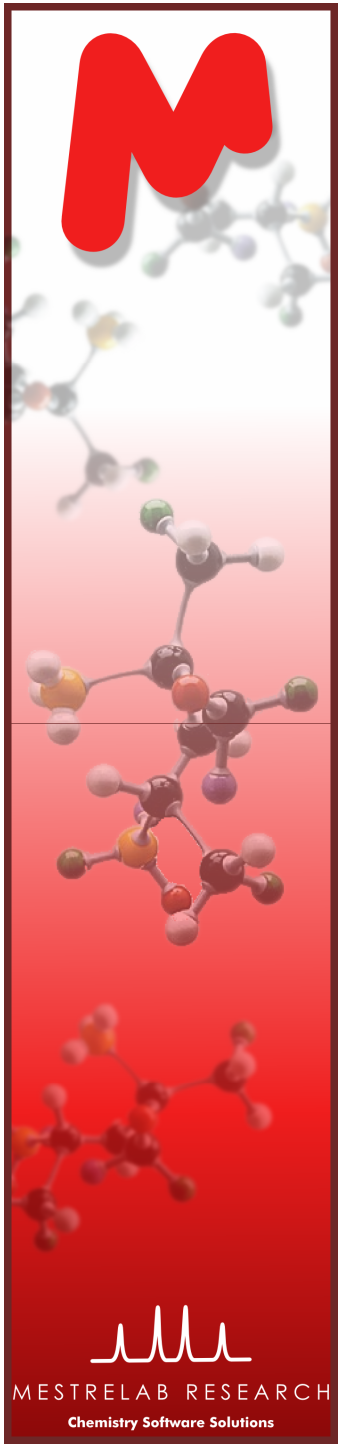


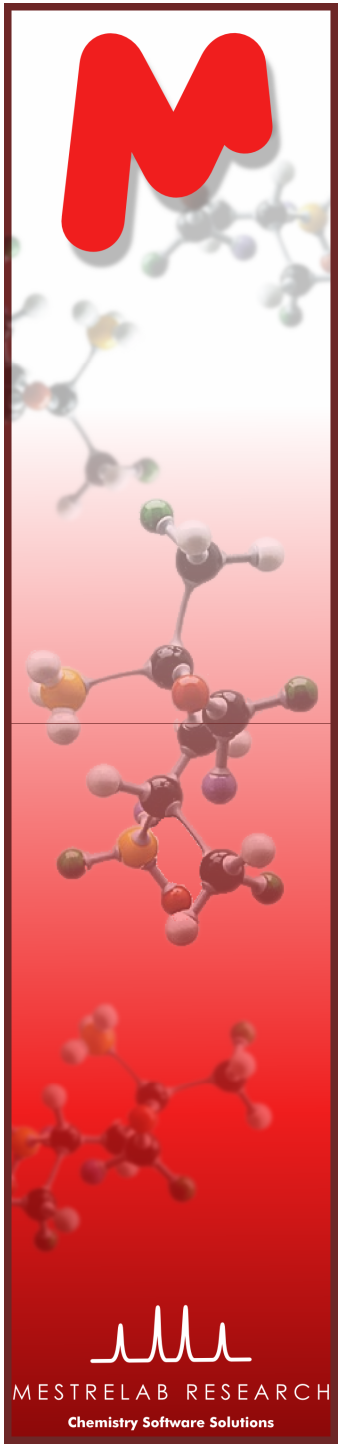
Verification: the Scoring System

A scoring system combines results of many different tests, each of which is by itself not decisive.

The single tests may have different significance which, in addition, may correlate with the principle outcome

Each test generate a pair [probability, significance]

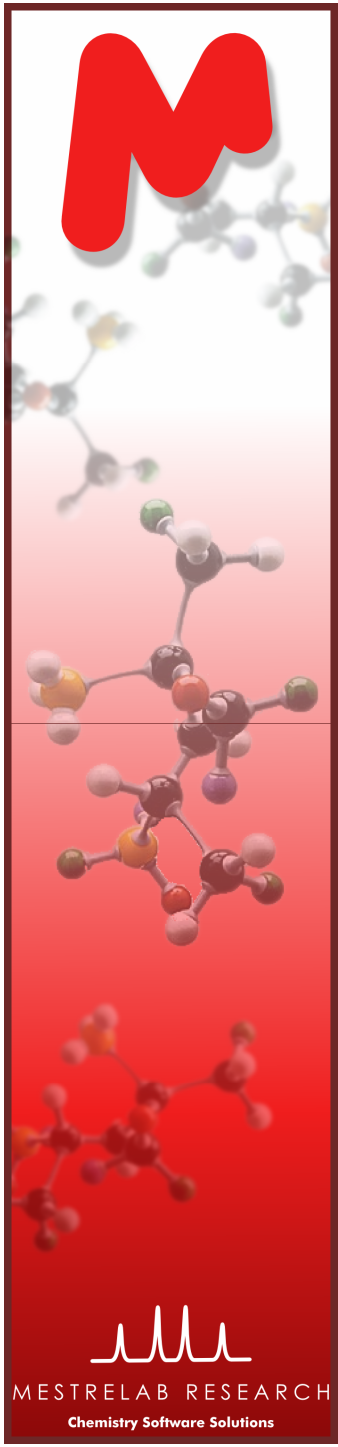
A scoring system is statistical and software construct applicable well beyond the boundaries of NMR



Verification and Fitting

Just a few words

This is work in progress but I would already need min. 3h to present it well



Thanks for your patience

and visit us at the Mestrelab stand