Non Uniform Sampling

What is Non-Uniform Sampling?

Non-Uniform Sampling (NUS)

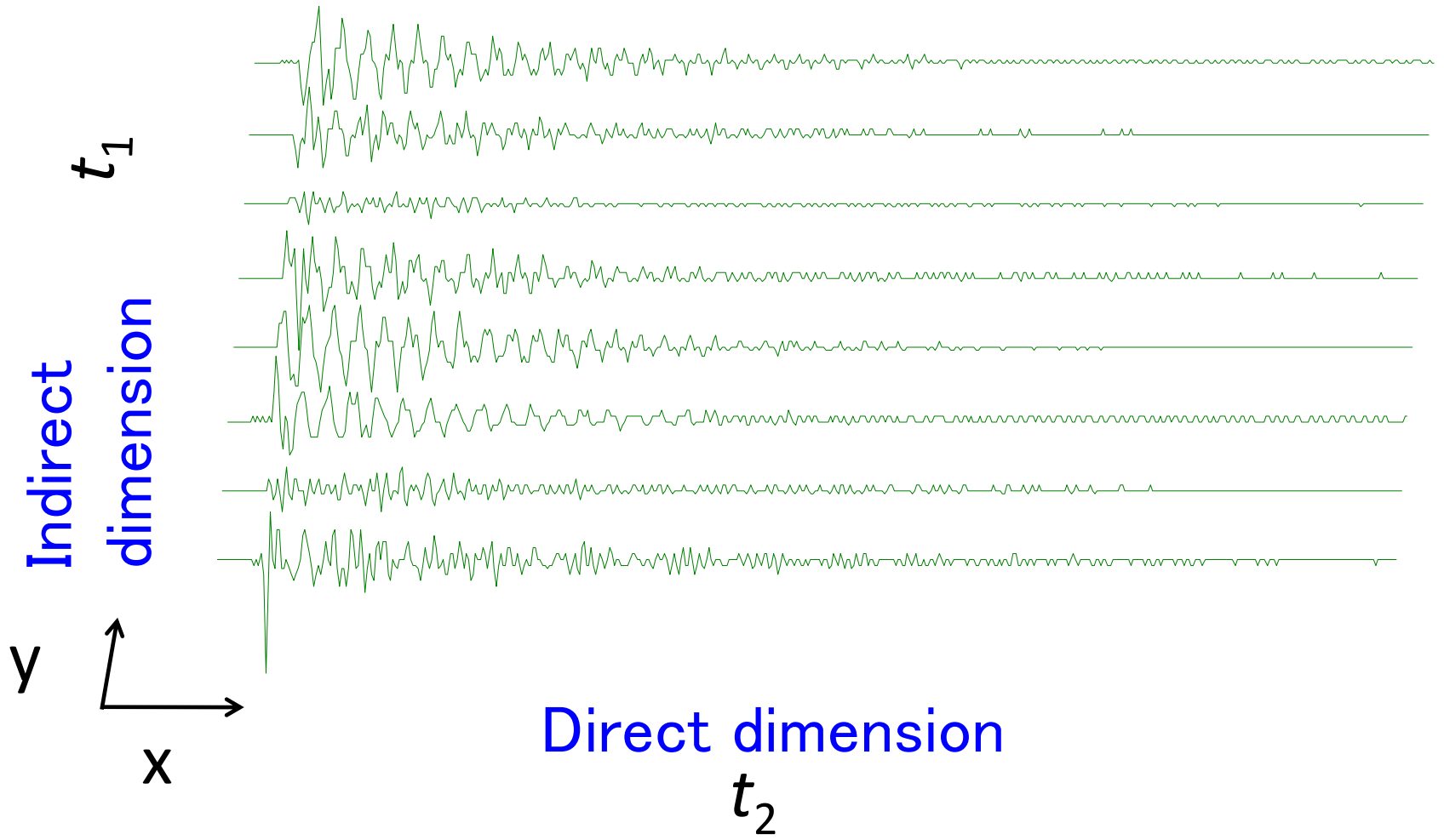
is a sampling technique which samples points in indirect dimension(s) of multidimensional experiment ***non-uniformly*** (= sparsely, randomly)

Multidimensional correlation experiments can be made shorter

Caution!

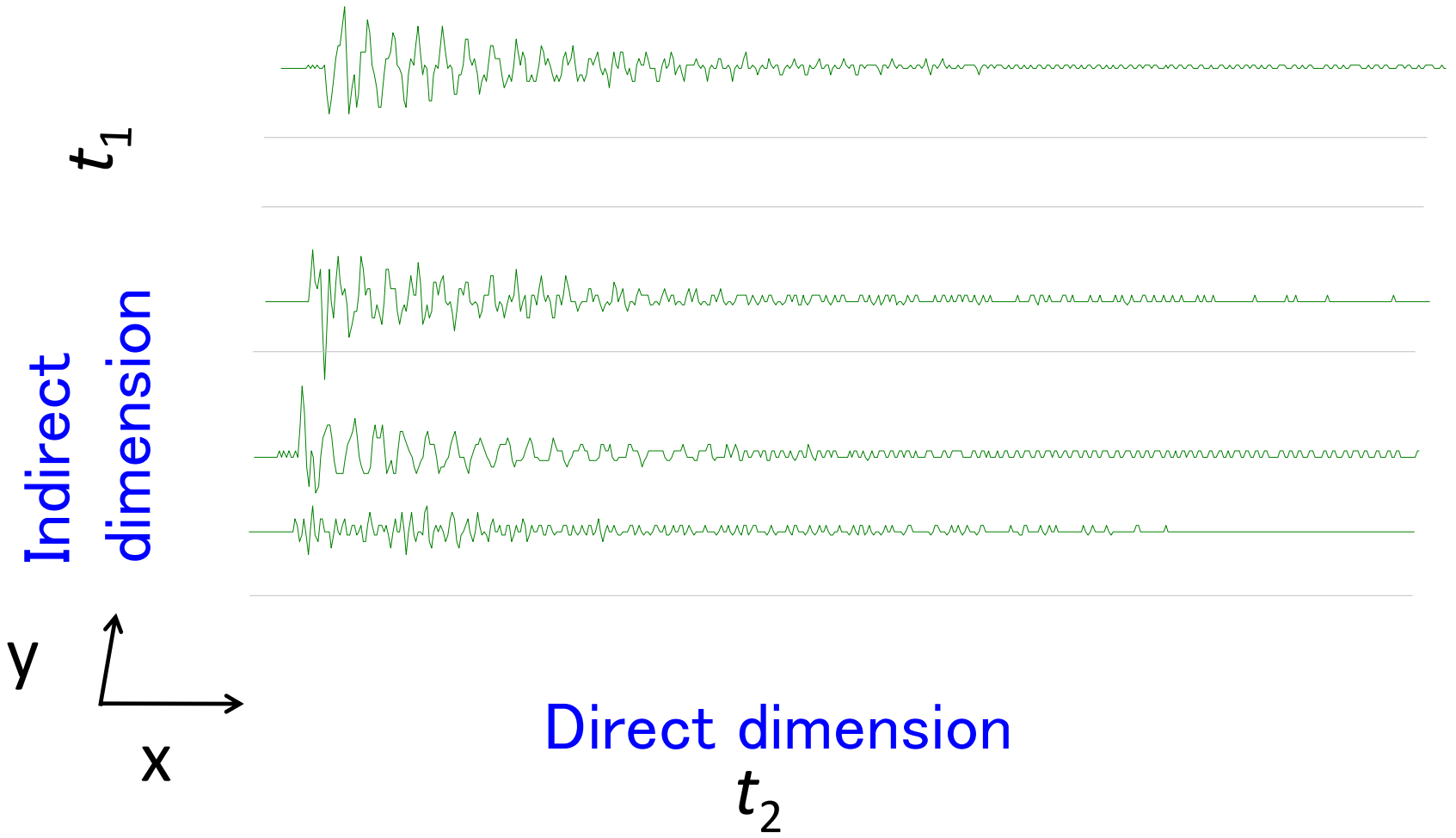
NUS is not bulletproof

Uniform Sampling



FIDs acquired with uniform increments of t_1

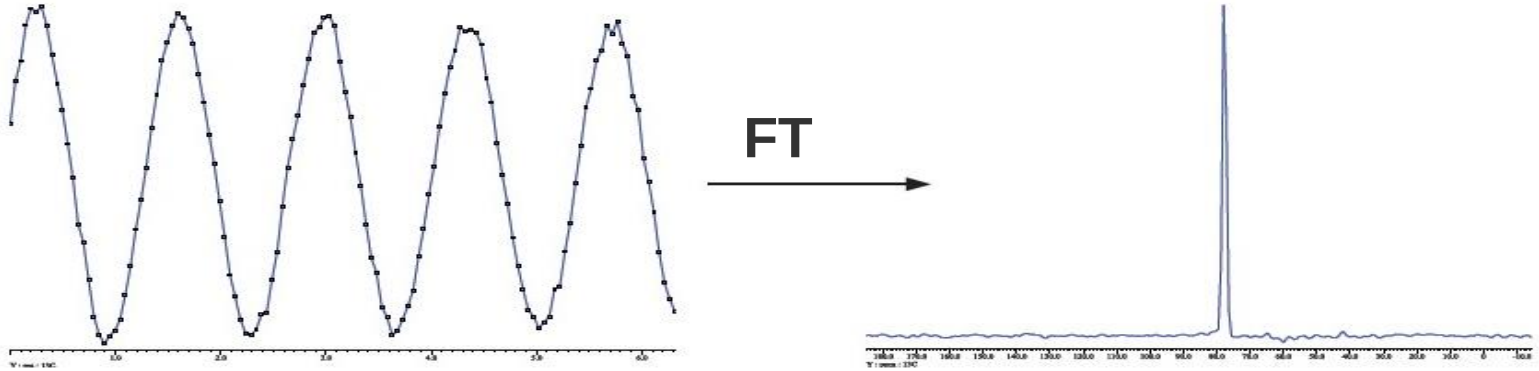
Non-Uniform Sampling



FIDs acquired with non-uniform increments of t_1

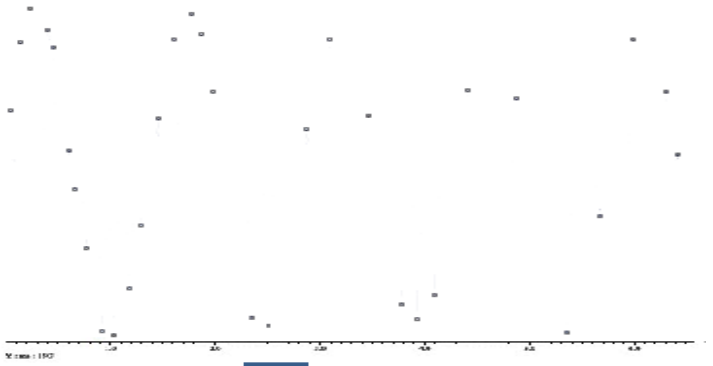
Dealing with non-uniform sampling (indirect dimension)

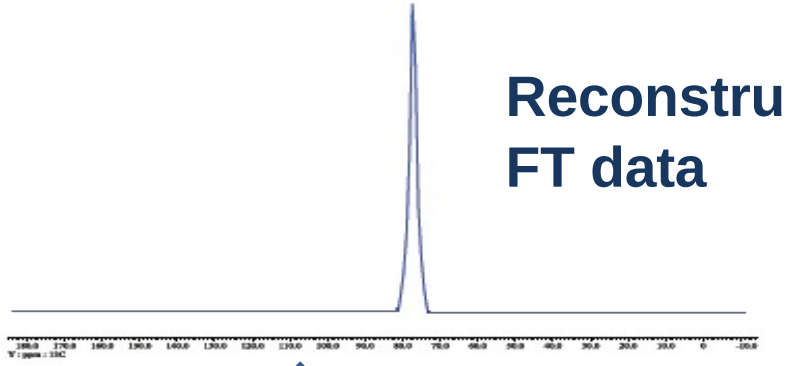
Uniform sampling



Iterative Soft Thresholding

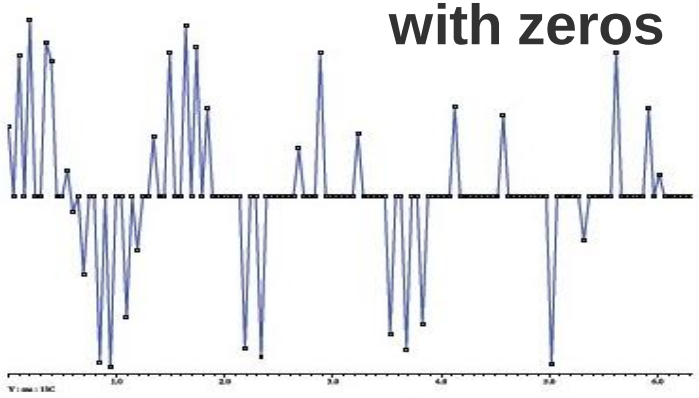
Raw data



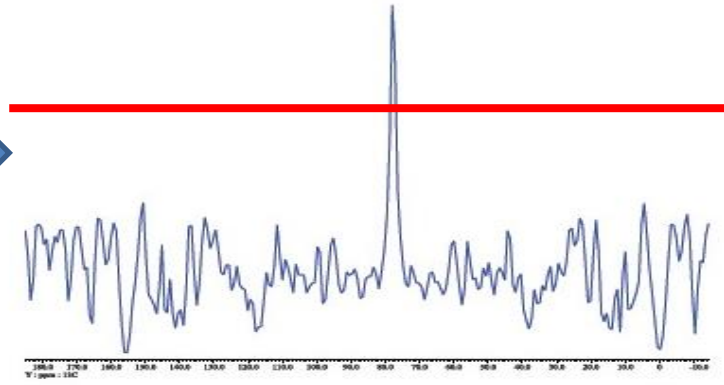


Reconstructed FT data

Replace original gaps with zeros

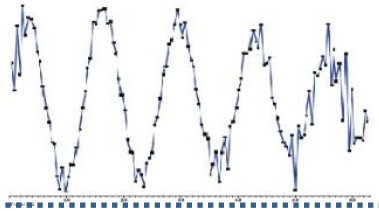


FT



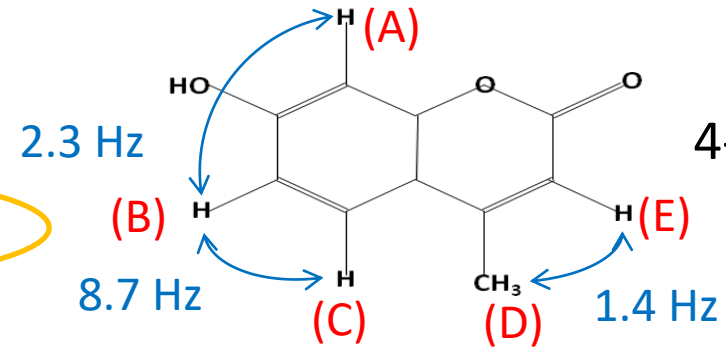
Extract top part and add to final spectrum

Extract bottom part and do inverse FT



Replace original gaps with zeros

Effect of NUS on COSY



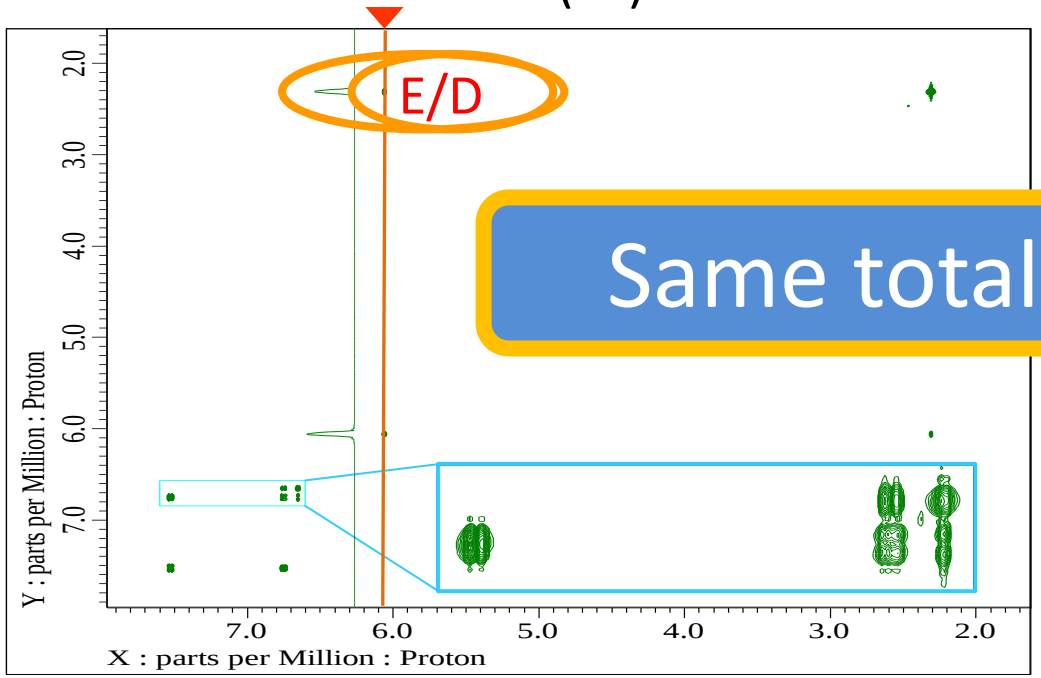
4-methylumbelliferone

256 sampled points

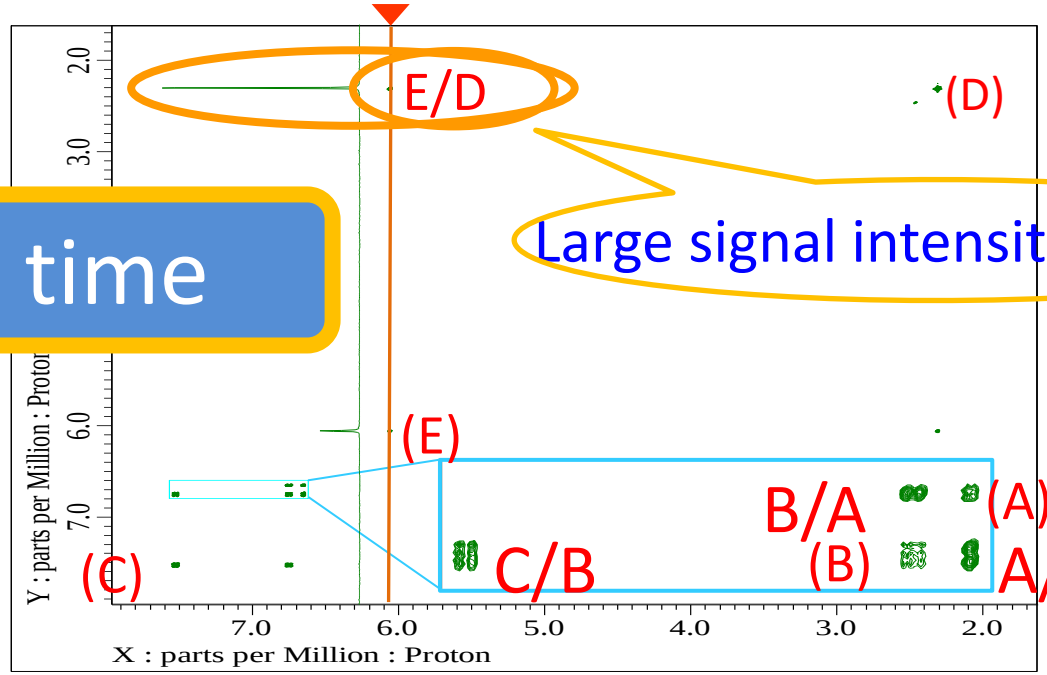
Uniform (y_points = 256)
+ zero fill (257→1024)
+ 2D Fourier transform (FT)

256 sampled points

NUS (y_points = 1024, NUS% = 25%)
+ Compressed sensing (CS)



Same total time



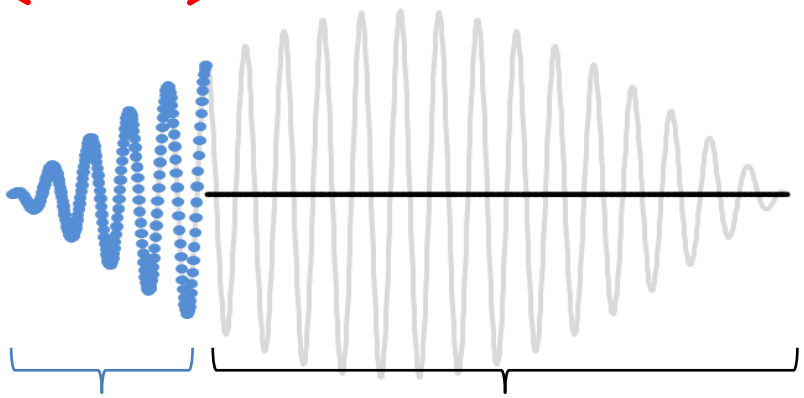
Large signal intensity

COSY signal

Interferogram (t_1 FID) is an echo signal

Uniform sampling + zerofilling

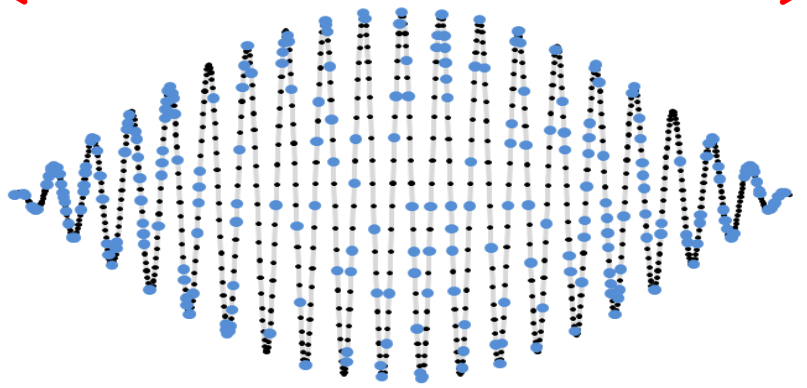
Sampling time



Sampled points　　Zerofilled points

NUS + CS

Sampling time



Non-uniformly sampled points

Reconstructed points

Same number of sampled points

NUS allows us to sample the signal in t_1-domain for longer

NUS is efficient in COSY, DQF-COSY, E. COSY, etc.

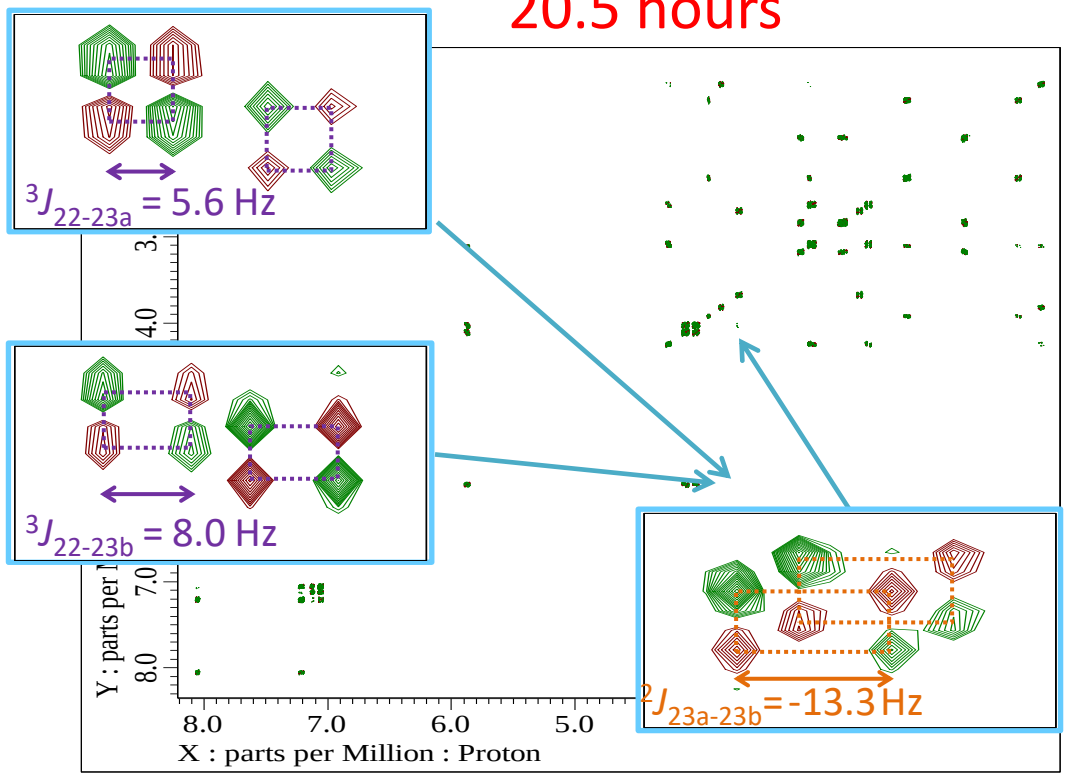
Example of E. COSY (determination of relative sign of J)

E. COSY requires 24 scans for phase cycling => very long

Even if your sample is concentrated

Even if you have a high-sensitivity NMR probe

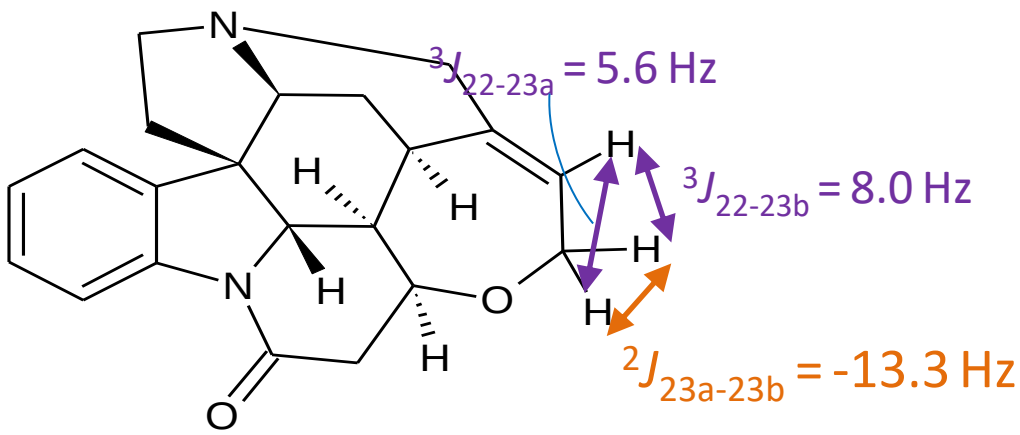
20.5 hours



Uniform sampling + 2D FT

512 sampled y_points

100 mM strychnine



In order to measure ^{1}H-^{1}H coupling constants, high resolution is required

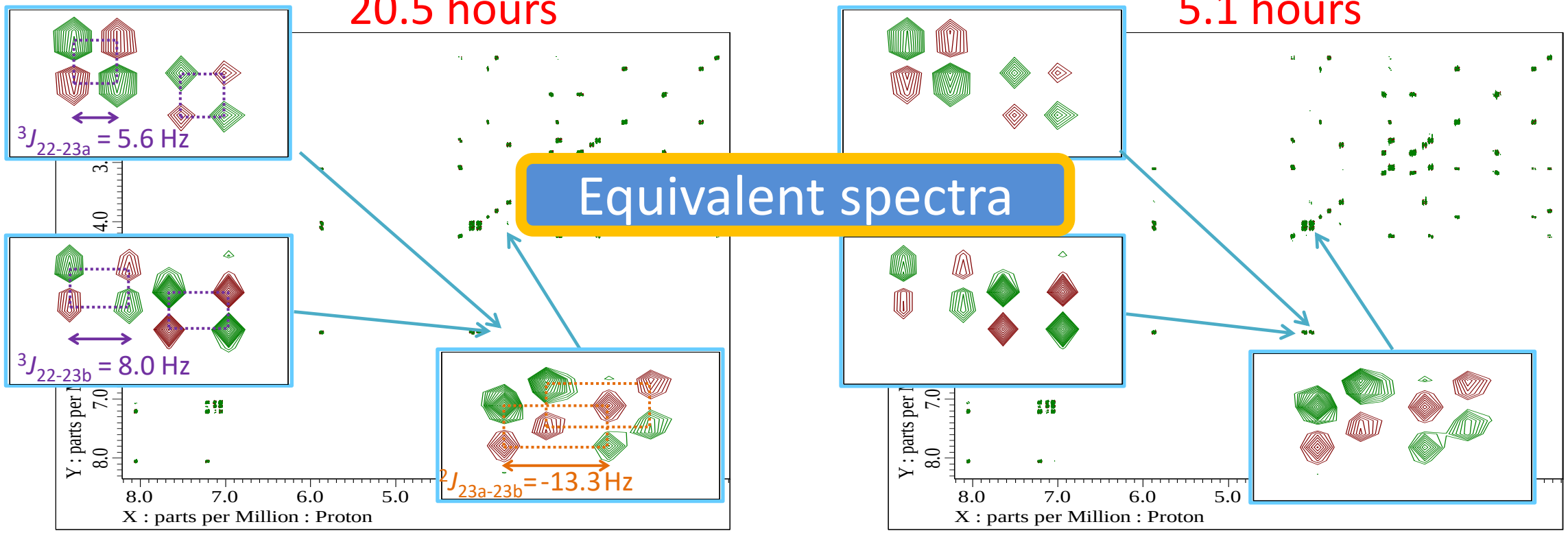
Example of E. COSY

E. COSY requires 24 scans for phase cycling => very long

Even if your sample is concentrated

Even if you have a high-sensitivity NMR probe

Shortened to ¼!



Uniform sampling + 2D FT

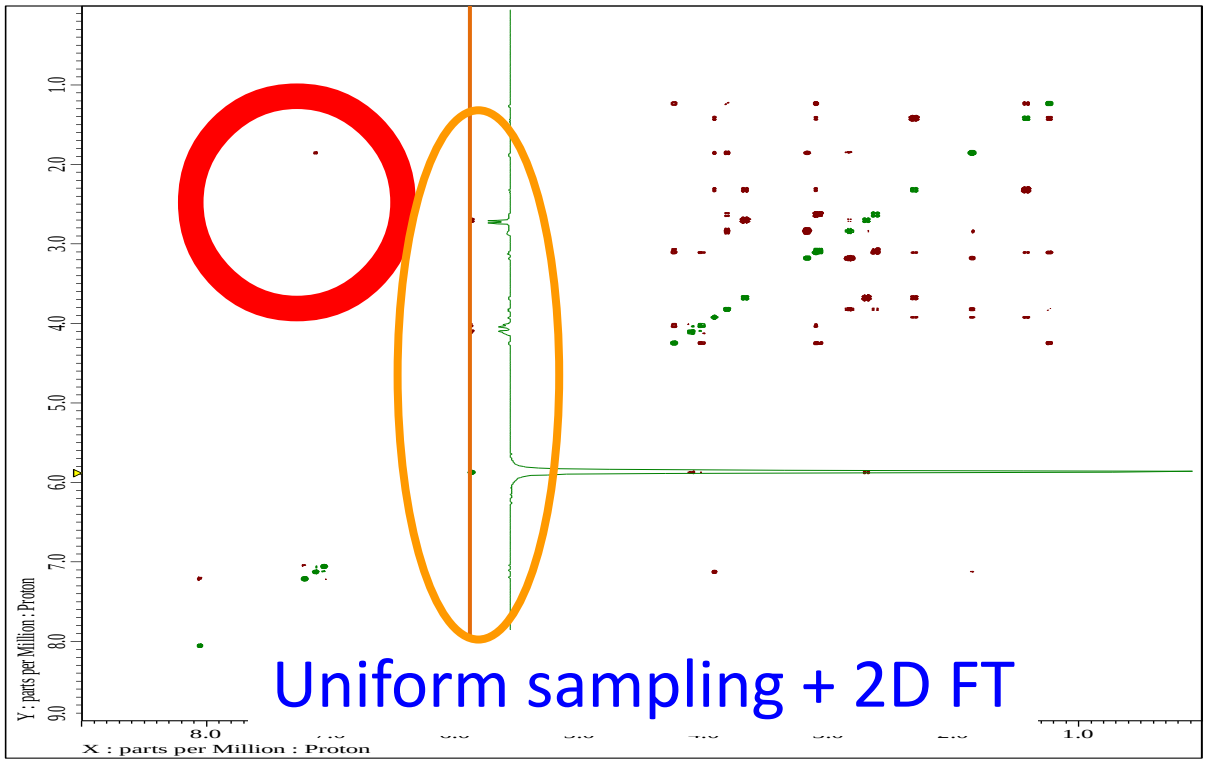
512 sampled y_points

25%-NUS + CS

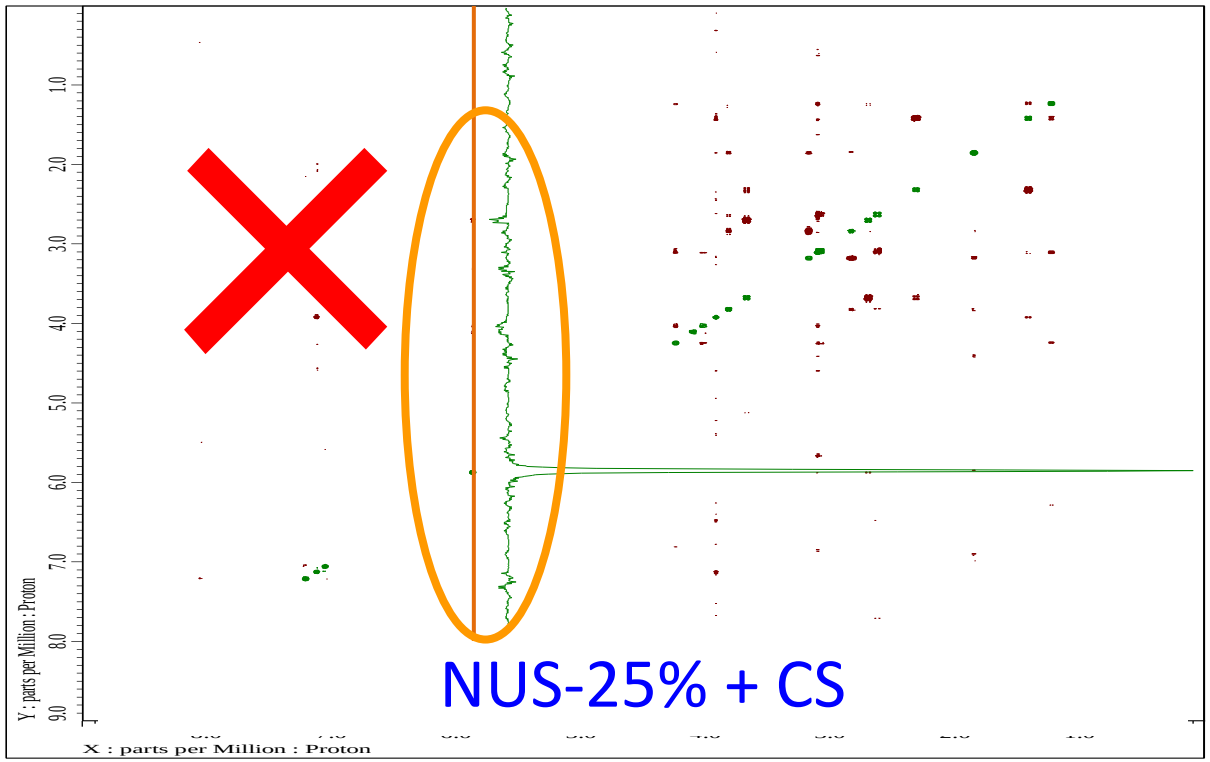
128 sampled y_points

NOESY

^{1}H-^{1}H NOESY 200 mM strychnine



Uniform sampling + 2D FT

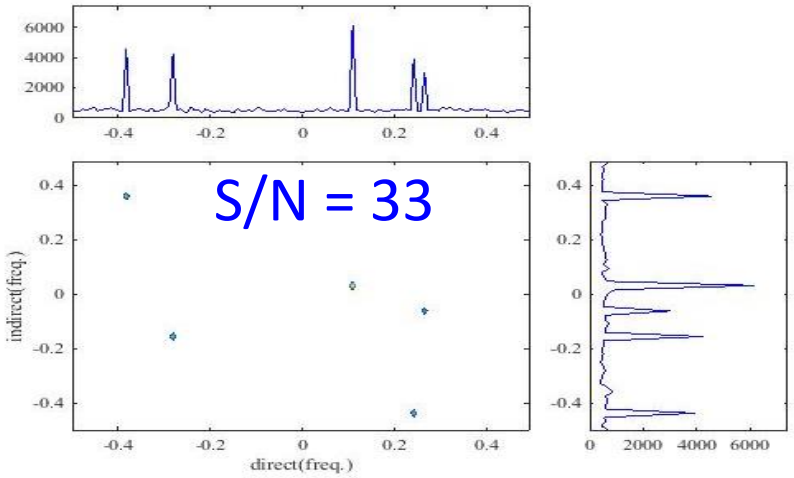


NUS-25% + CS

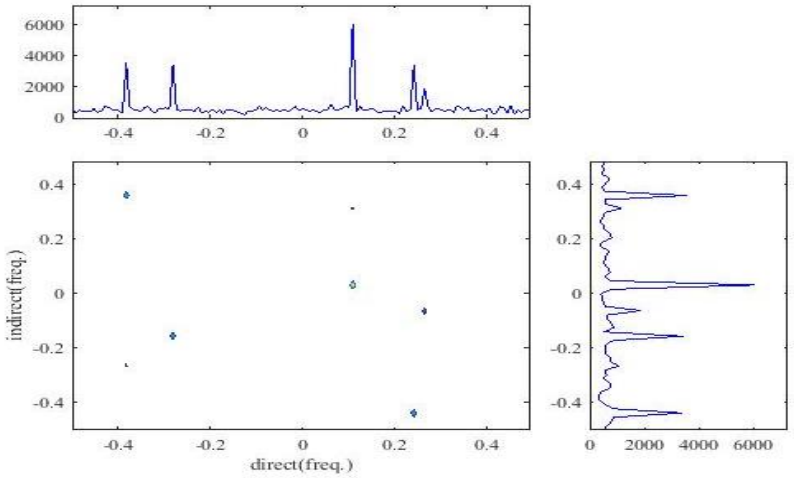
Incomplete reconstruction of low-intensity cross-peaks in the presence of large diagonal peaks

Influence of noise

full S/N = 33



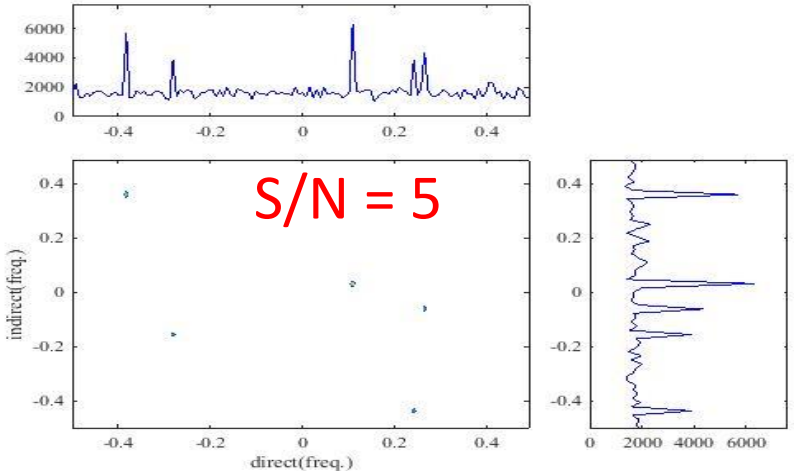
NUS (25%)



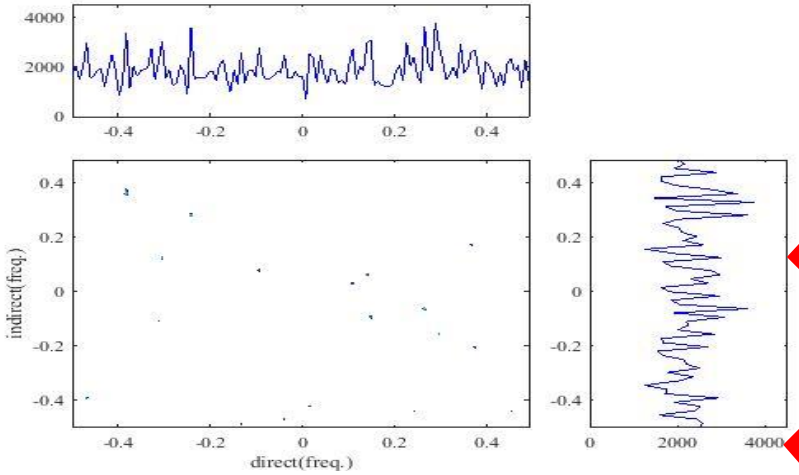
2D FT: High S/N

CS: High S/N

full S/N = 5



NUS (25%)

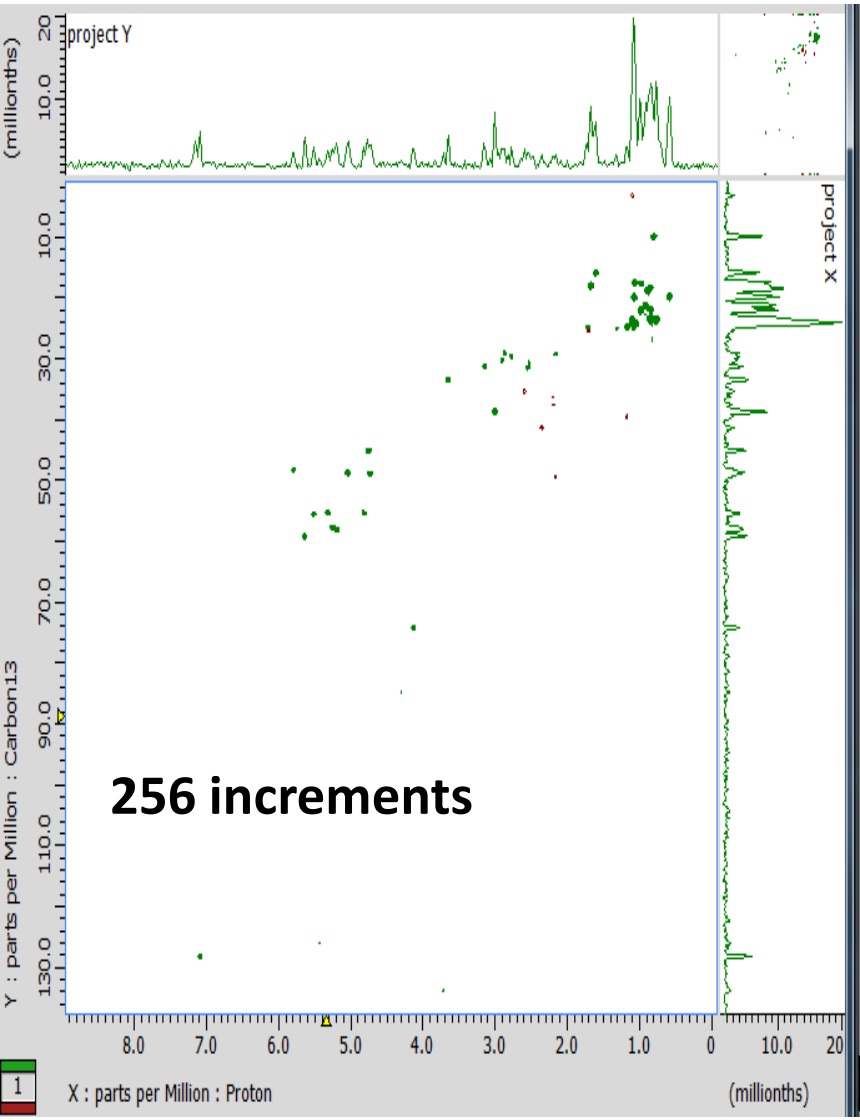


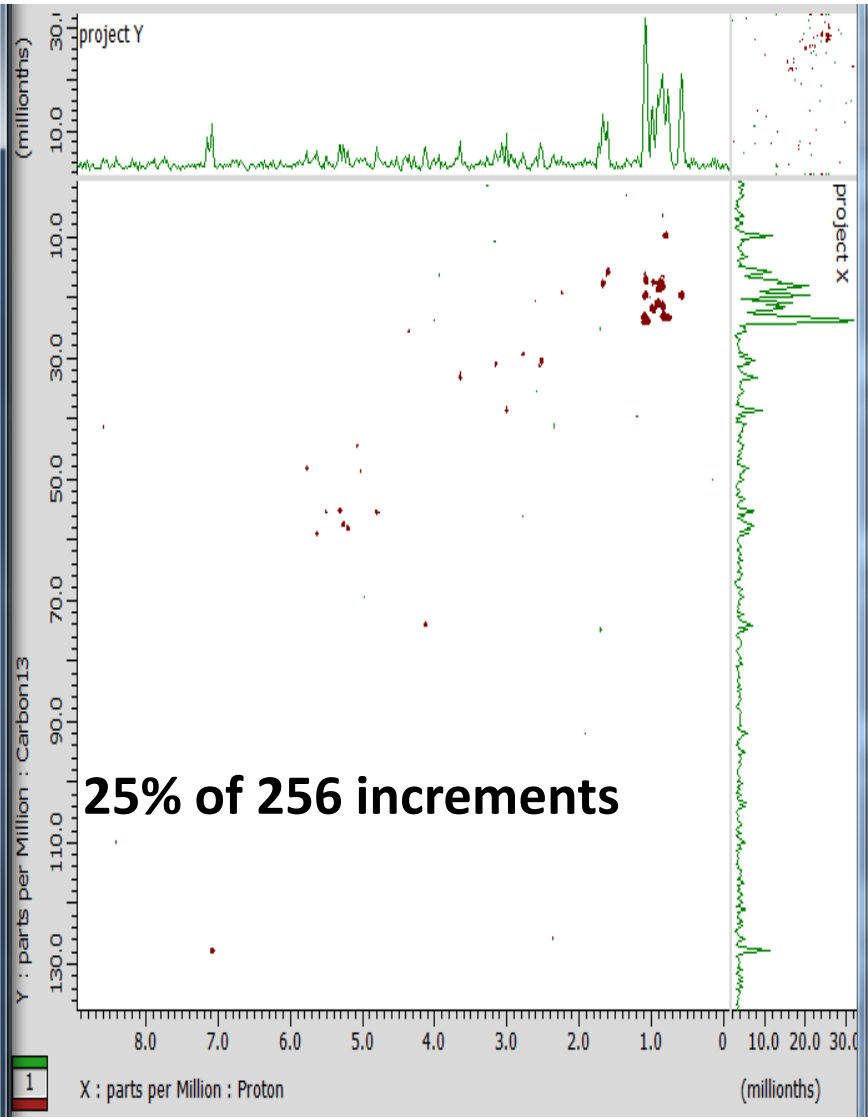
2D FT: Low S/N

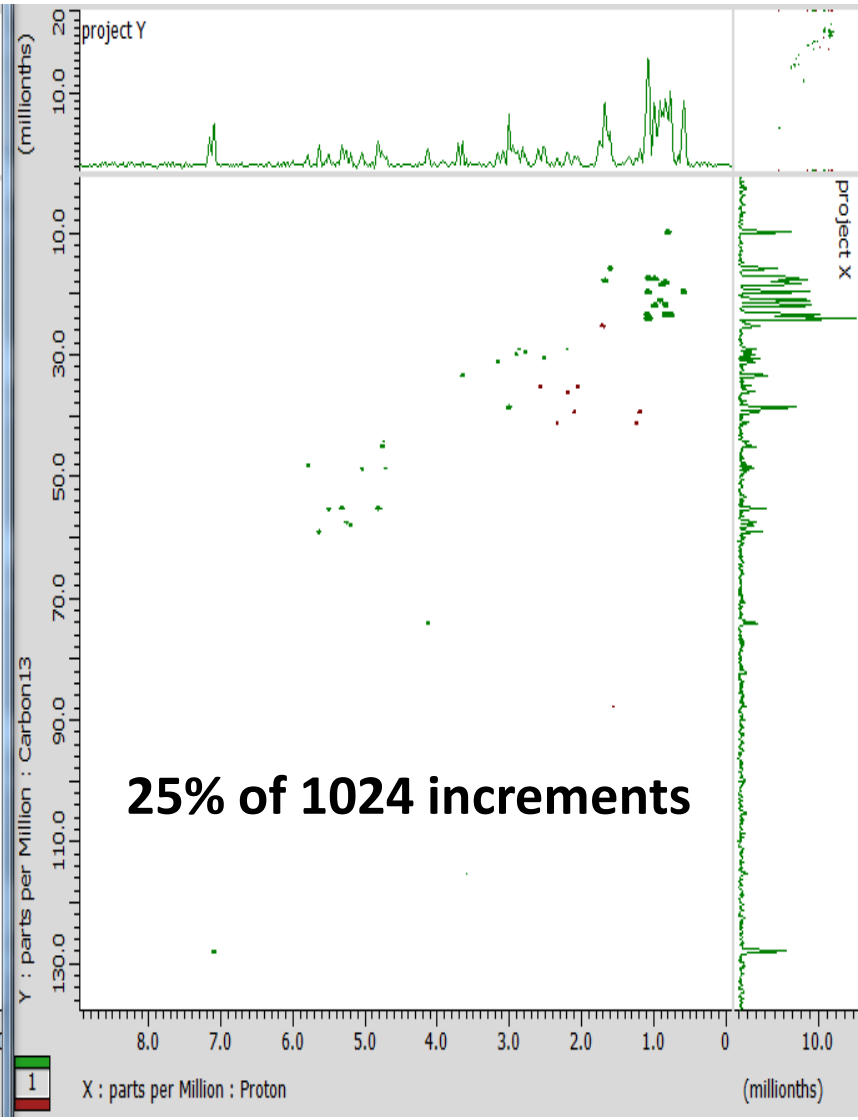
CS: Low S/N

NUS data reconstruction is difficult if S/N is low

HSQC of cyclosporine







Reduced the receiver gain to look for trouble

So what is the best sampling scheme?

There is no universal solution (just like there is no best pulse flip angle and relaxation delay for pulse acquire experiments)

*Optimal resolution would require sampling up to ~3T_2, and the S/N reaches a maximum at ~1.2T_2.**

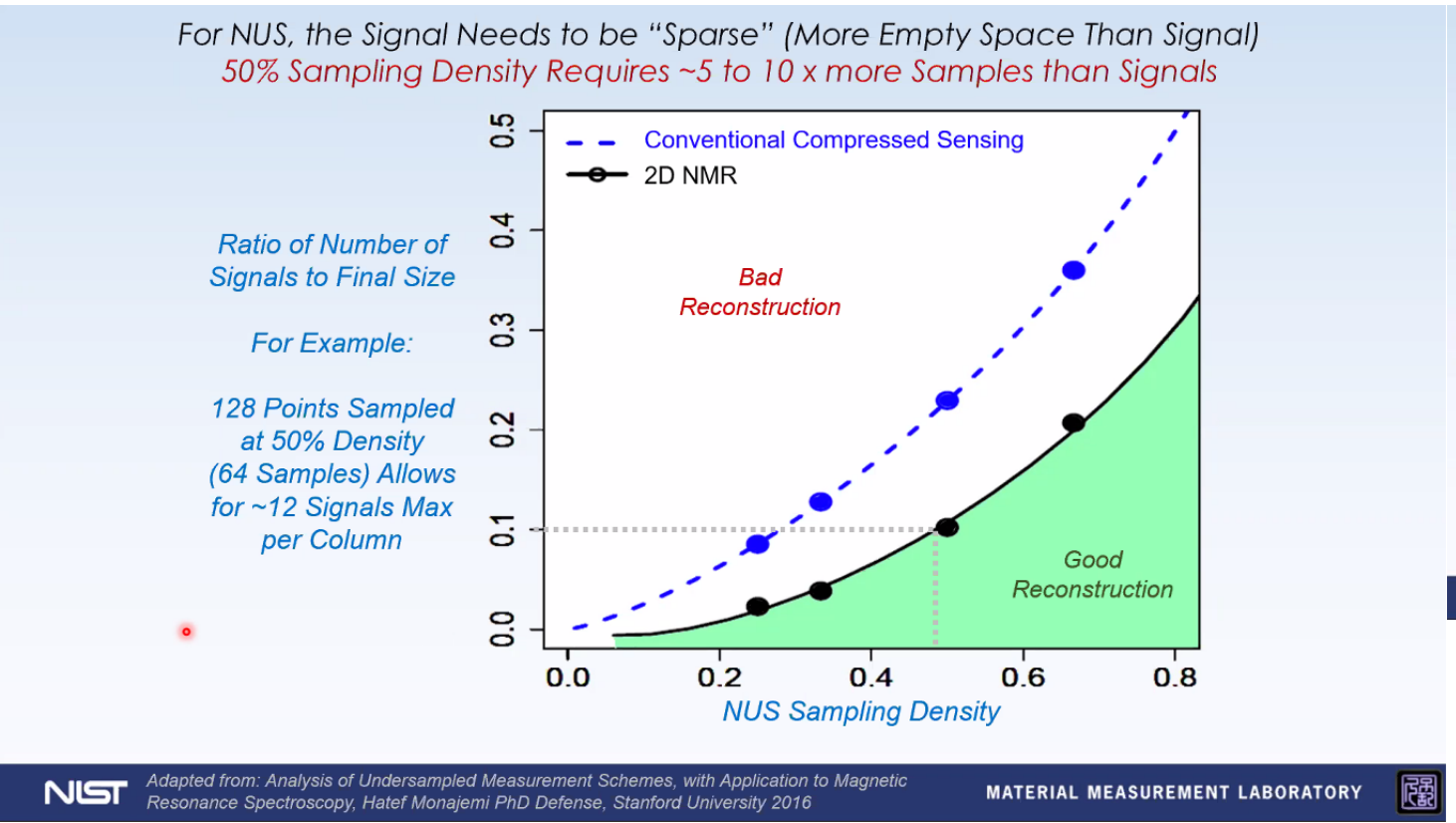
** Rovnyak, et al. J Biomol NMR **30,** 1–10 (2004) https://doi.org/10.1023/B:JNMR.0000042946.04002.19*

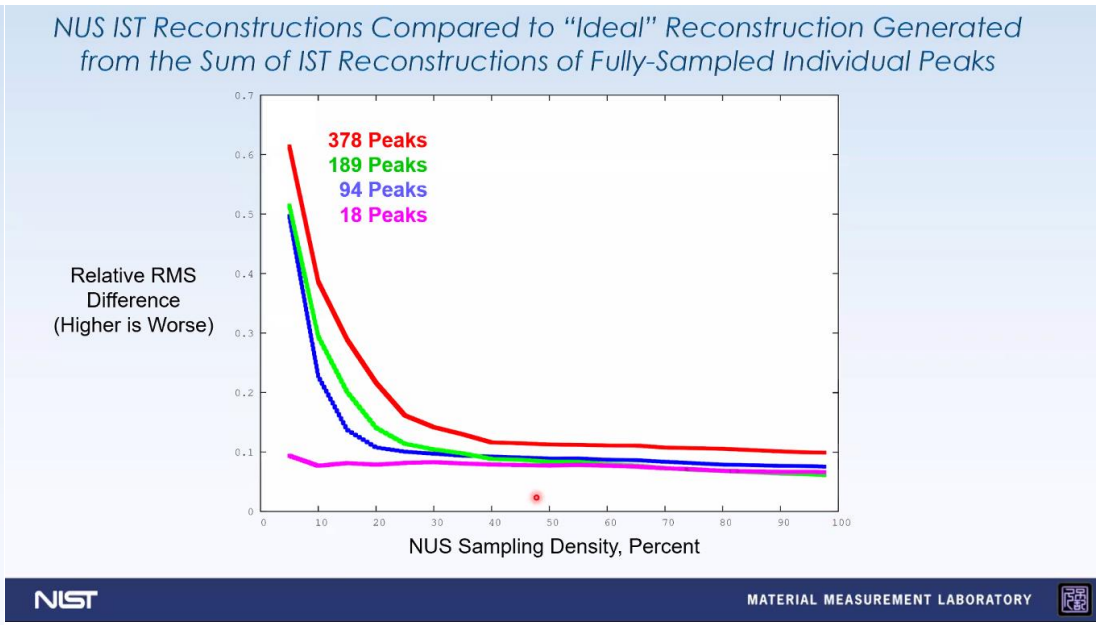
Note:
Large number of increments facilitates observation of small coupling constants correlations, which typically are caused by long range correlations. This is generally desired in HMBC, but not always in COSY.

And how many datapoints are the minimum?

Between 10 and 30 sampling points as many peaks in any column (not peaks but significant peaks, i.e, x tallest peaks),eg, 10 correlations for a proton in an HMBC, then 100-300 sampled points

[25% of 256 y_points allows detecting reliably ~2 signals per chemical shift in direct dimension]



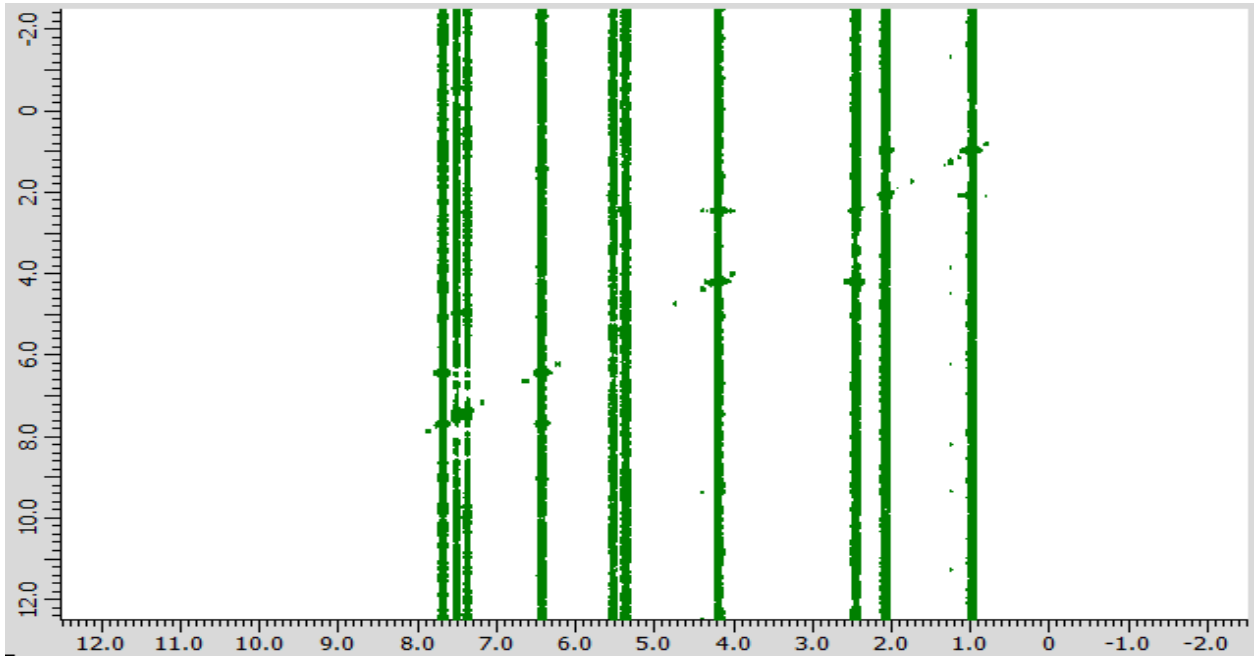


https://www.youtube.com/watch?v=hK82D-4FIyg

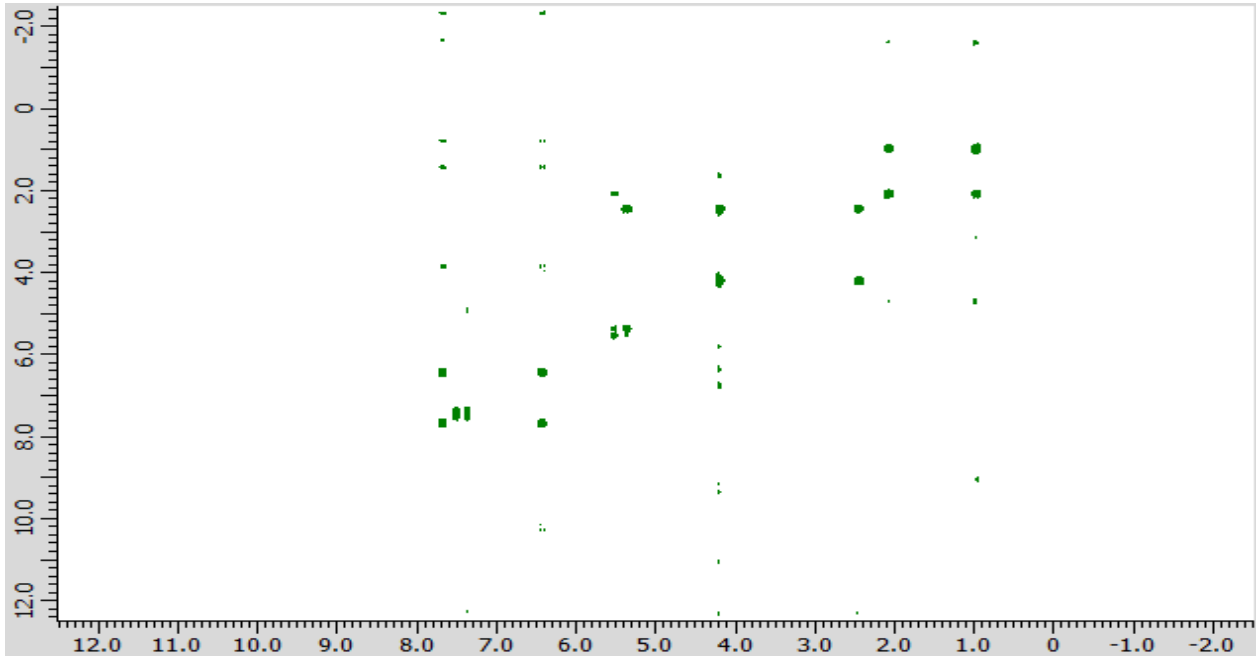
Try other algorithms

COSY 64 increments inflated to 256

- **IST reconstruction**



- **HMS IST reconstruction**



Note that if the experiment was acquired with 256 increments out of 1024, the noise from reconstruction would not be so intense. Sampling density alone does not define how tough is the reconstruction.

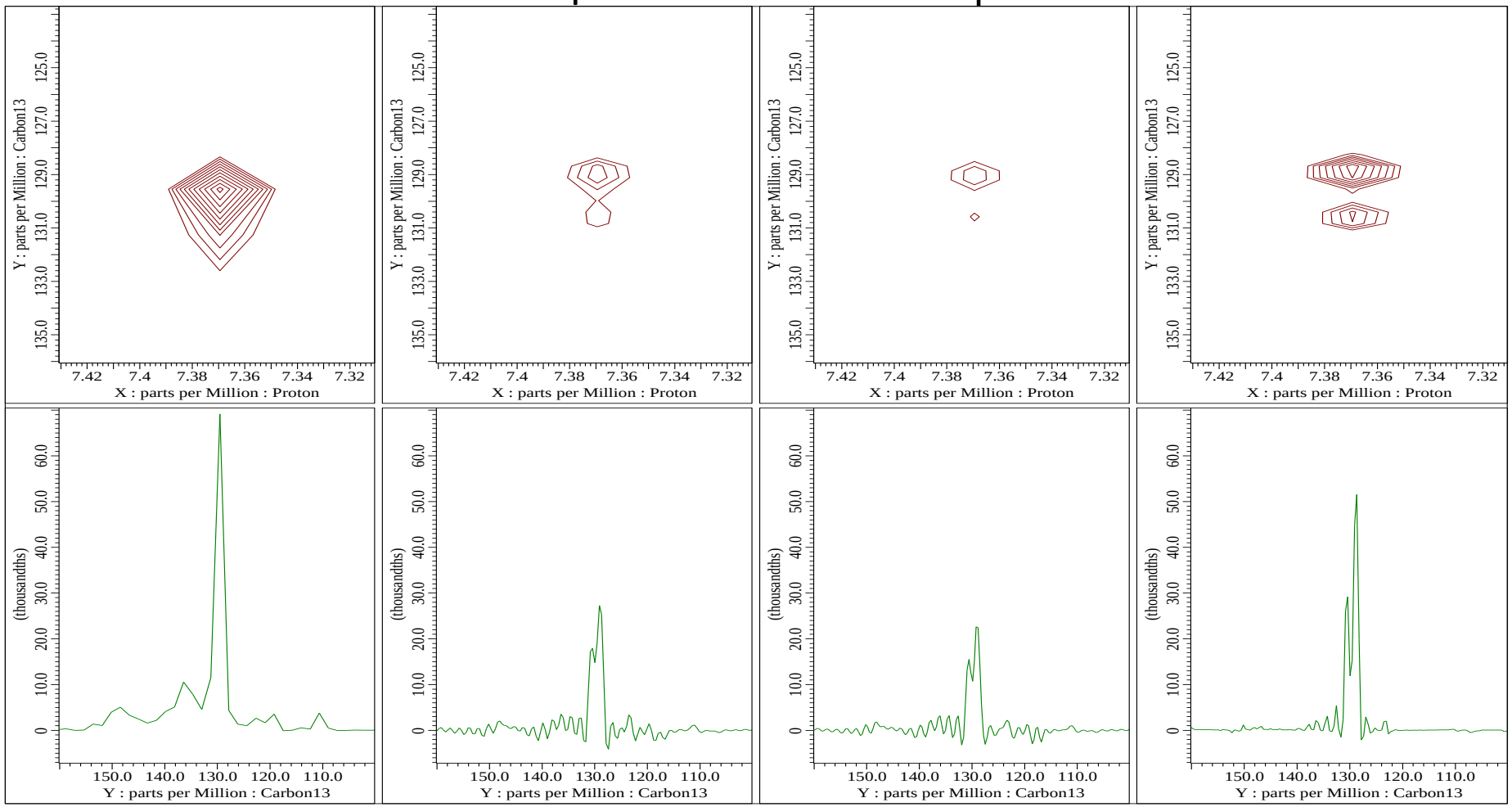
Influence of additional zero filling

A)
No Zero Filling
IST

B)
IST
ZF to 512 points

C)
IST
LP to 512 points

D)
ZF to 512 points
IST



2 peaks 1.5ppm apart

Zoomed region of a me-HSQC (25% of 128 incr.)

^{13}C Projection