

# Non Uniform Sampling

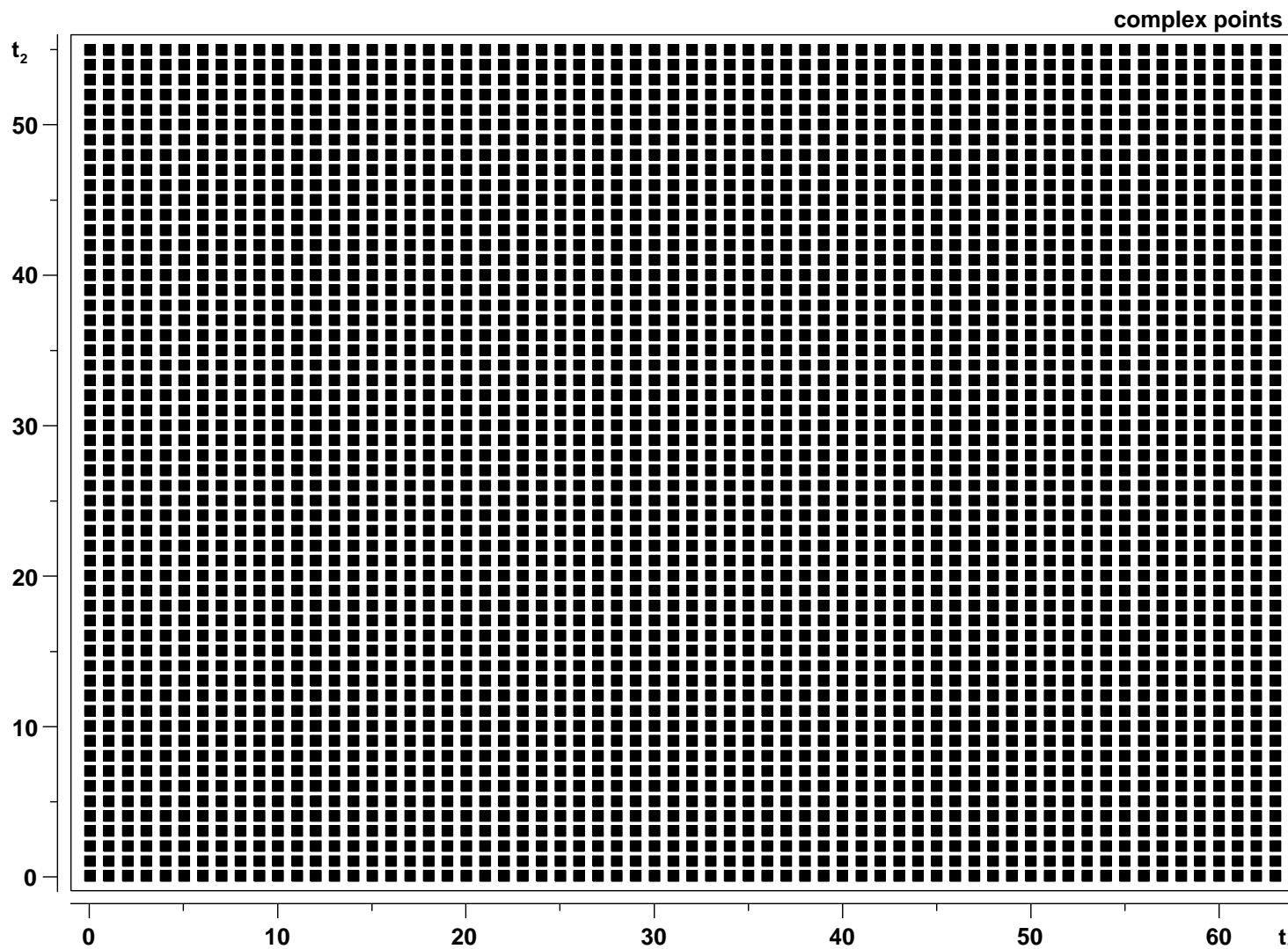
Eric Johnson

Symposium on Frontiers in Biomolecular NMR  
Vanderbilt University  
May 4, 2012

# Introduction



3D ( $t_1 t_2$  plane)

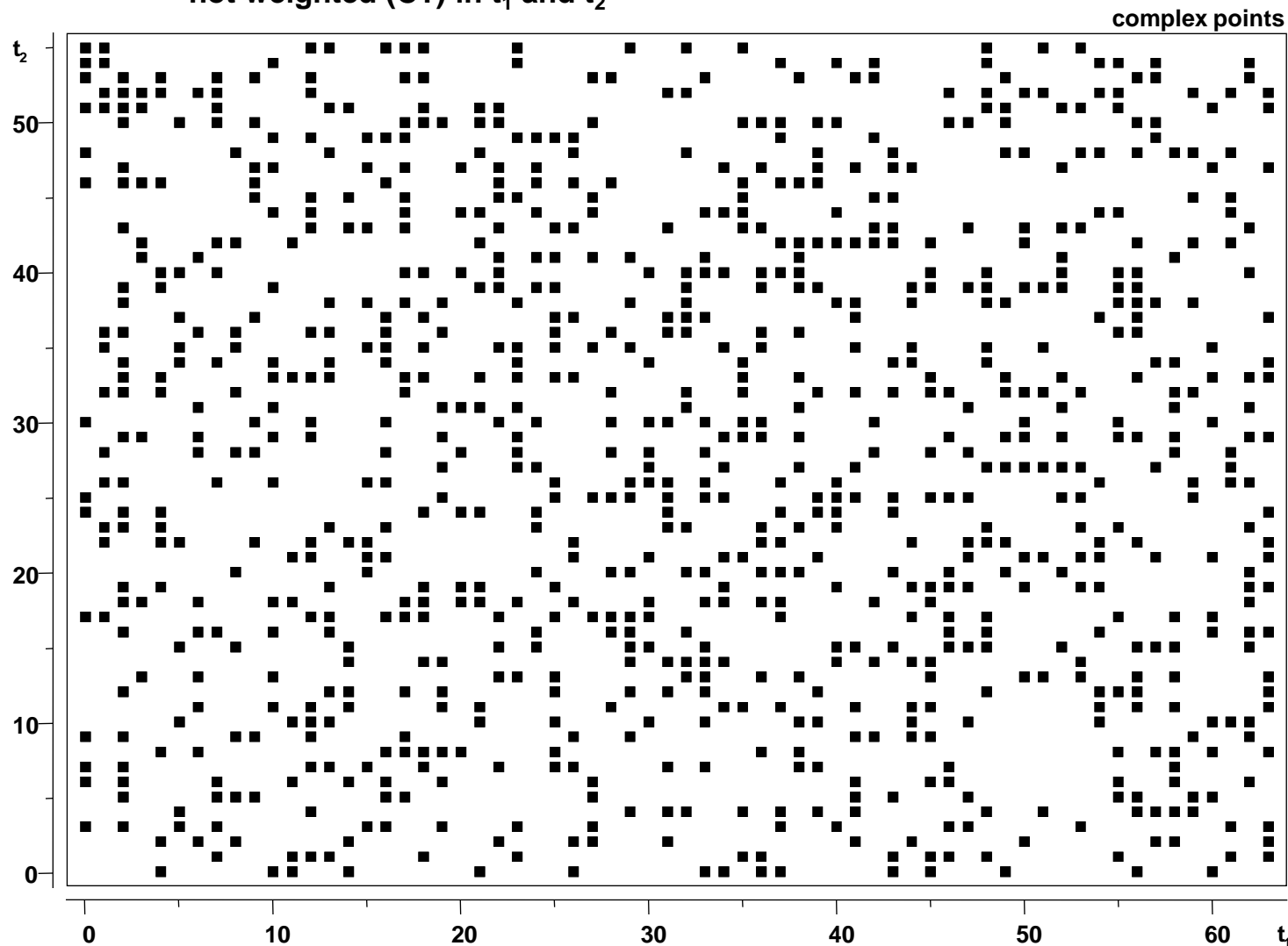


# Introduction



3D ( $t_1 t_2$  plane) - 25% sparse (nussampler)

not weighted (CT) in  $t_1$  and  $t_2$

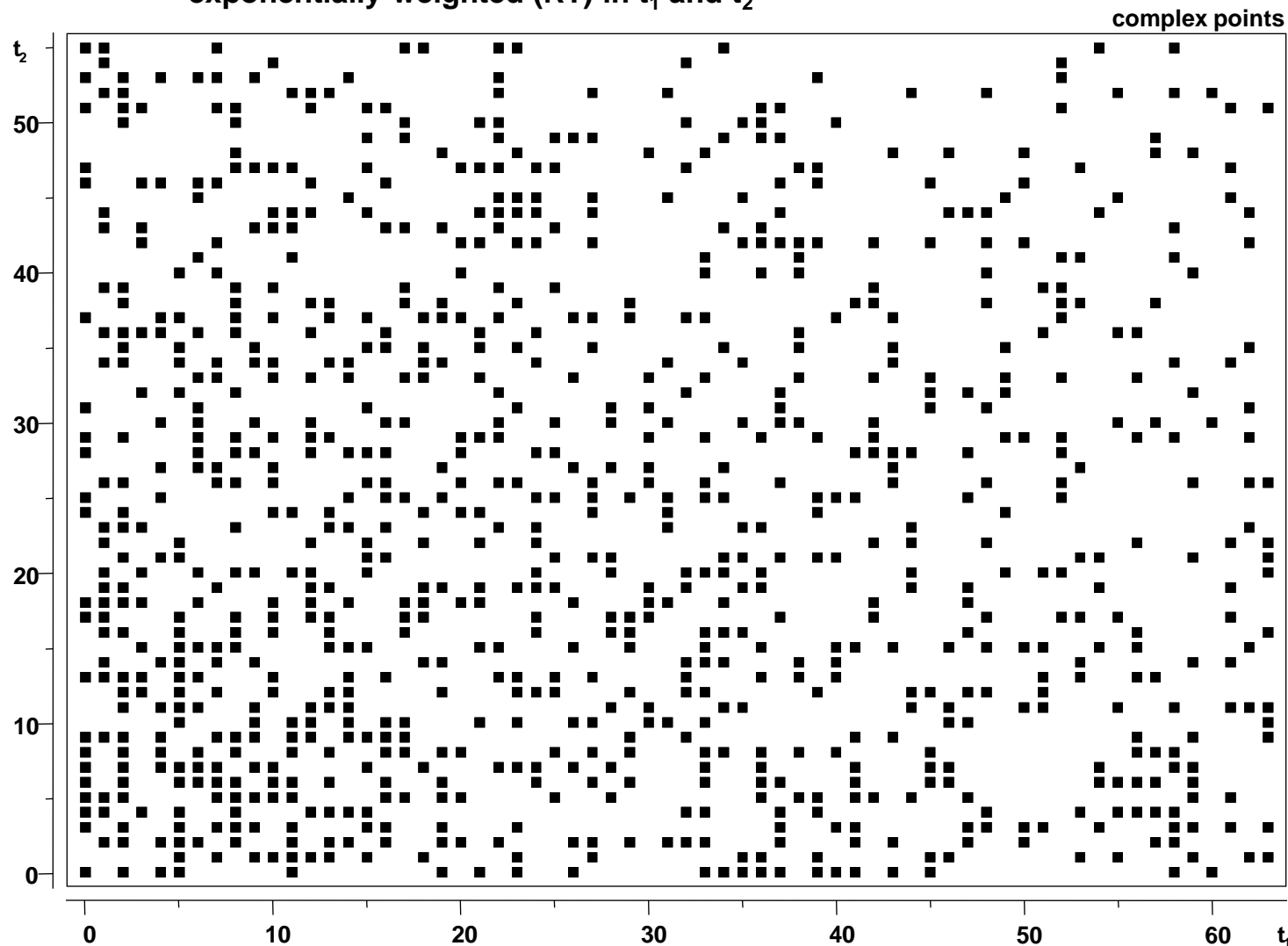


# Introduction



3D ( $t_1 t_2$  plane) - 25% sparse (nussampler)

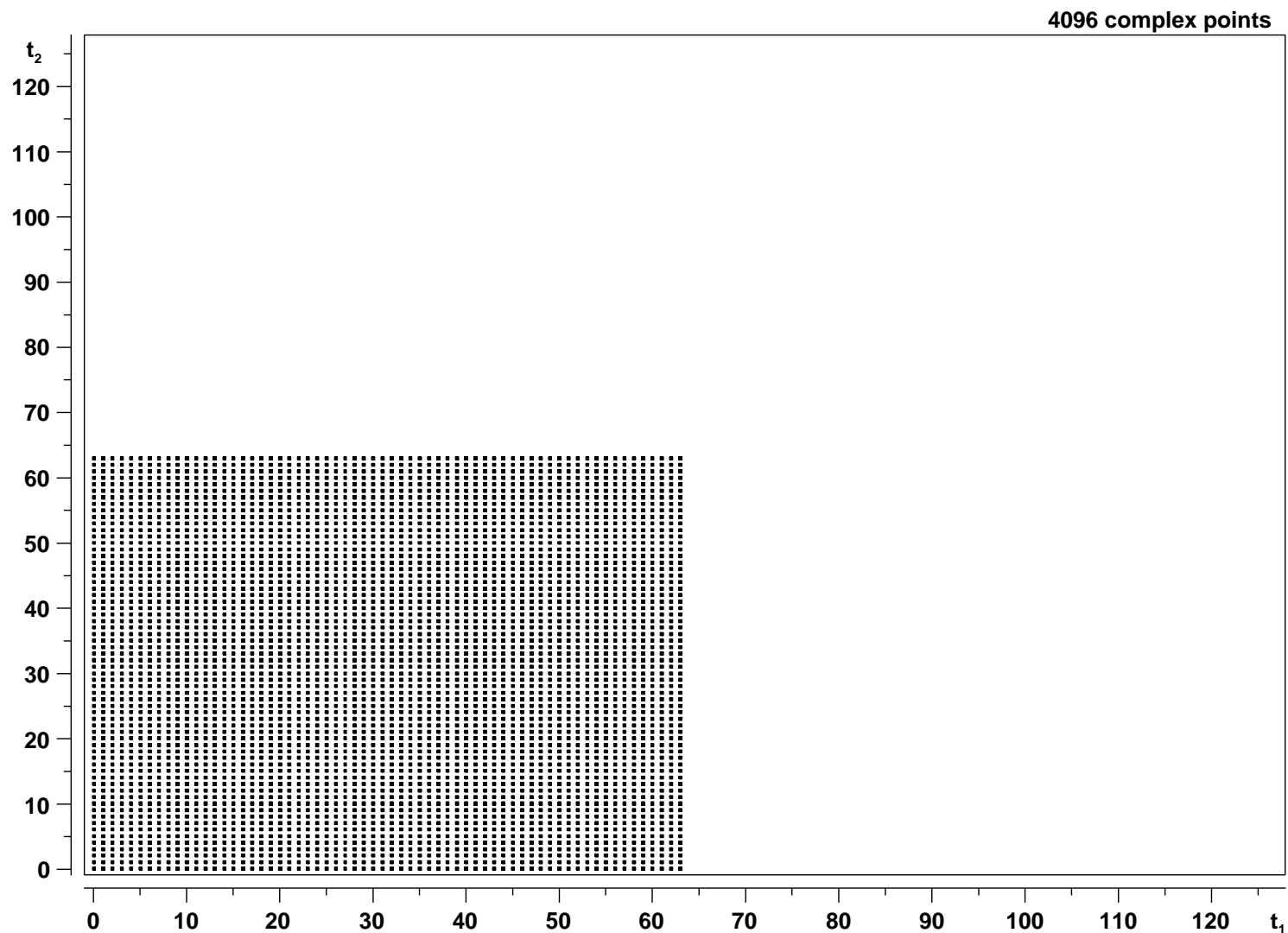
exponentially weighted (RT) in  $t_1$  and  $t_2$



# Introduction



## 3D ( $t_1 t_2$ plane)

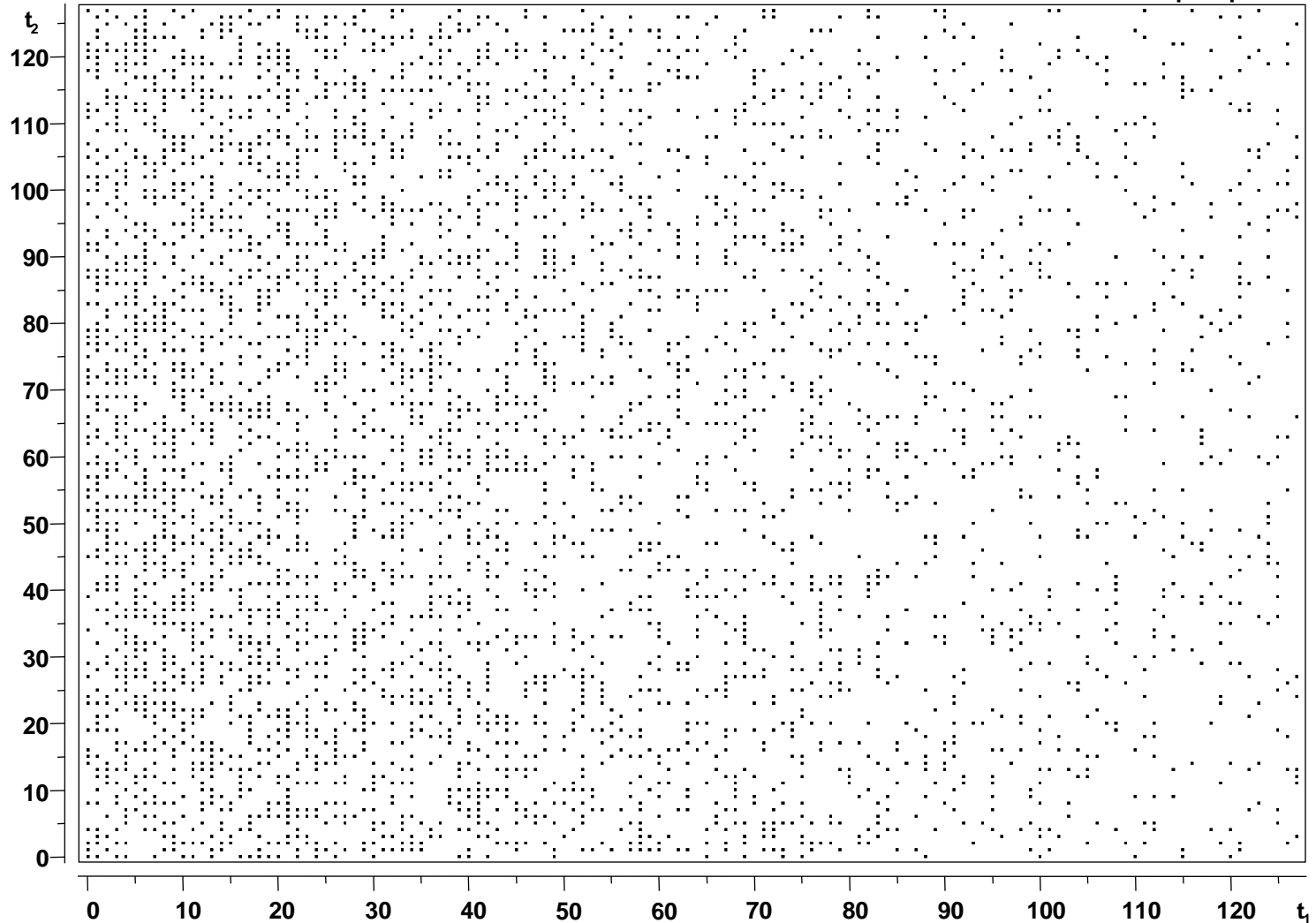


# Introduction



3D ( $t_1, t_2$  plane) - 25% sparse (nussampl)  
exponentially weighted (RT) in  $t_1$

4096 complex points



## Multi Dimensional Decomposition (MDD)

**MDD-NMR**

**Orekhov et al.**

## Maximum Entropy (MaxEnt)

**Rowland Toolkit**

**Hoch et al.**

**Forward Maximum Entropy**

**Wagner et al.**

**Azara (CCPN)**

**Laue et al.**

## Multidimensional Fourier Transformation (MFT)

**MFT**

**Kozminski et al.**

# Modifications to pulse sequences



## mc (TopSpin 2.1)

d11 do:f3 mc #0 to 2  
F1PH(rd10 & rd29 & rd30 & rp5 & ip4, id0)  
F2PH(ip5, id10 & id29 & dd30)

## new mc (TopSpin 3.0 +)

d11 do:f3 mc #0 to 2  
F1PH(caliph(ph4, +90), caldel(d0, +in0))  
F2PH(caliph(ph5, +90), caldel(d10, +in10) & caldel(d29, +in29) & caldel(d30, -in30))

+ both mc versions supported



# Acquisition parameters (TS3.0)



Spectrum ProcPars **AcquPars** Title PulseProg Peaks Integrals Sample Structure Plot Fid

Probe: 5 mm TXI 13C Z-grad

Experiment

Width

Receiver

Nucleus

Durations

Power

Program

Probe

Lists

Wobble

Lock

Automation

Miscellaneous

User

Experiment

PULPROG hsqcedetgppsp.3 Current pulse program

AQ\_mod DQD Acquisition mode

FnMODE Echo-Antiecho Acquisition mode for 2D, 3D etc.

FnTYPE **non-uniform\_sampling** nD acquisition mode for 3D etc.

TD 1024 Size of fid

DS 32

NS 16

TD0 1

Spectrum ProcPars **AcquPars** Title PulseProg Peaks Integrals Sample Structure Plot Fid

NUS

NUS (Non Uniform Sampling) parameters

CEXP	yn	RMDD/MDD flag
CT_SP	nn	Constant time
NCOMP	0	Number of components
AMOUNT [%]	50	Amount of sparse sampling
Jsp [Hz]	Edit...	J-coupling
SRSIZE [ppm]	0.15	Sub region size
T2	Edit...	T2 relaxation
acqmode		Acquisition mode
aqORD	0	Acquisition order
f180	nn	Delayed sampling flag
nholes	0	Number of holes
phase	Edit...	Phase
seed	54321	Random generator seed

# Acquisition parameters (TS3.1)



Spectrum ProcPars **AcquPars** Title PulseProg Peaks Integrals Sample Structure Plot Fid

Probe: not defined

Experiment	VCLIST		...	E	Variable counter list
Width	VDLIST		...	E	Variable delay list
Receiver	VPLIST		...	E	Variable pulse list
Nucleus	PHLIST		...	E	Variable phase list
Durations	VTLIST		...	E	Variable temperature list
Power	NUSLIST	automatic			Name of loopcounter list for NUS (Non Uniform Sampling)
Program	<b>NUS (Non Uniform Sampling) parameters</b>				
Probe	NusAMOUNT [%]	25			Amount of sparse sampling
Lists	NusPOINTS	32			Number of hypercomplex points in indirect dimension
NUS	NusJSP [Hz]	0	0		J-coupling
Wobble	NusT2 [sec]	1	1		T2 relaxation
Lock	NusSEED	54321			Random generator seed
Automation					
Miscellaneous					
User					
Routing					

Calculate

# Processing parameters (TS3.1)



Spectrum ProcPars AcquPars Title PulseProg Peaks Integrals Sample Structure Plot Fid

S 12. M

Reference  
Window  
Phase  
Baseline  
Fourier  
NUS  
Peak  
Automation  
Miscellaneous  
User

^ NUS (Non Uniform Sampling) parameters

Mdd_mod	mdd		MDD mode
MddCEXP	FALSE	FALSE	RMDD/MDD flag
MddCT_SP	FALSE	FALSE	Constant time
MddF180	FALSE	FALSE	Delayed sampling flag
MddNCOMP	0		Number of components
MddPHASE	0	0	Phase
MddSRSIZE [ppm]	0		Sub region size

# Improvements in TS3.1



## TS3.0

- NUS processing was only supported under Linux

## TS3.1

- NUS processing on Linux, Windows and Macintosh
- First data point is always same point as traditional sampling  
(you can use "rser 1" to check the 1<sup>st</sup> fid)
- Now includes two processing methods
  1. MDD (multi-dimensional decomposition)
  2. CS (compressed sensing)

- Only indirect dimension(s) is non-uniformly sampled
- Missing points are calculated with RMDD/MDD
- NUS dataset is then processed with FFT
  
- For 2D NUS datasets:  
    "xfb"
  
- For nD NUS datasets:  
    "ftnd"

# Multi dimensional transforms



ftnd has the following options

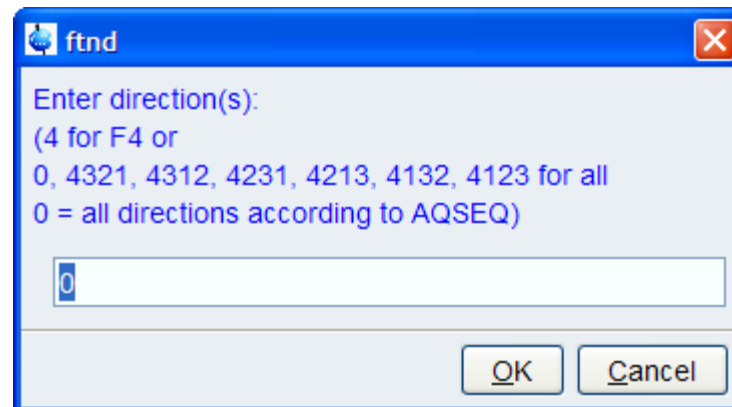
Dimension:

ftnd 0 = transform in order of acqu

ftnd 4321 or any sequence starting in 4...

fntd 4, 3, 2, 1 = transform only this dimension

Or just type "ftnd":



# Multi dimensional transforms

ftnd has the following options:

dlp: **d**elayed **l**inear **p**rediction

ftnd 0:

1. Processing in F3 (WM - FT)
2. Processing in F2 (LP - WM - FT)
3. Processing in F1 (LP - WM - FT)

ftnd 0 dlp:

1. Processing in F3 (WM - FT)
2. Processing in F2 (FT)
3. Processing in F1 (LP - WM - FT)
4. Processing in F2 (IFT)
5. Processing in F2 (LP - WM - FT)

dlp: linear prediction is performed only after FT is done in all other dimensions

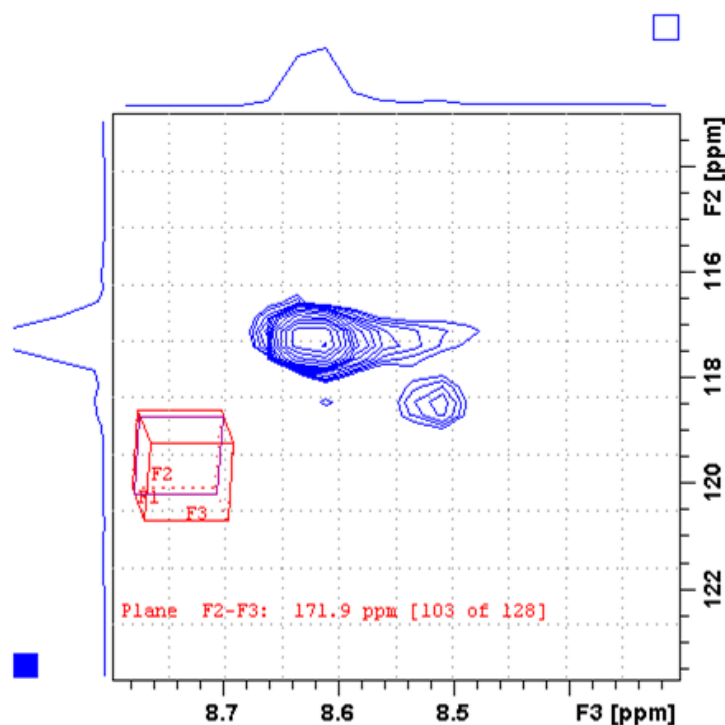
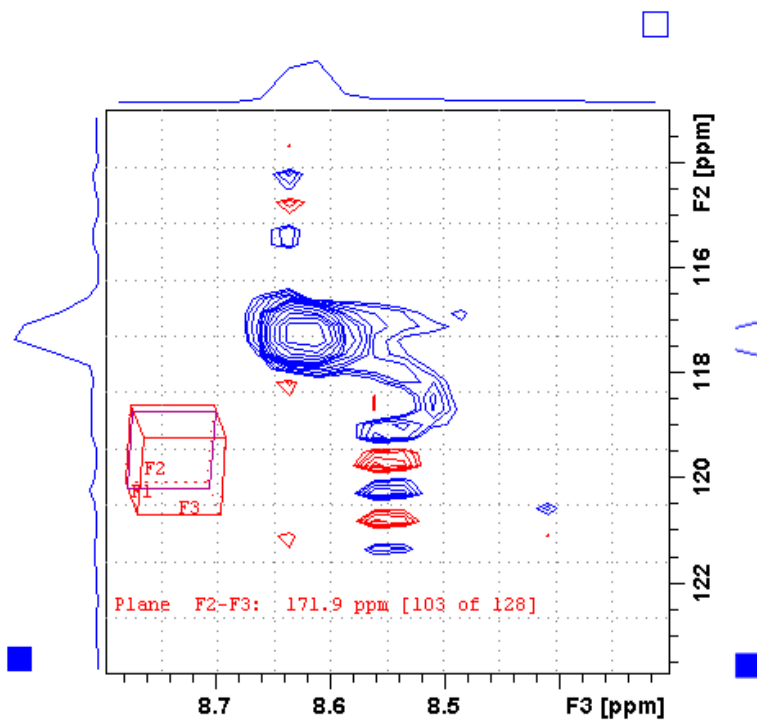
# Multi dimensional transforms



dlp: **d**elayed **l**inear **p**rediction

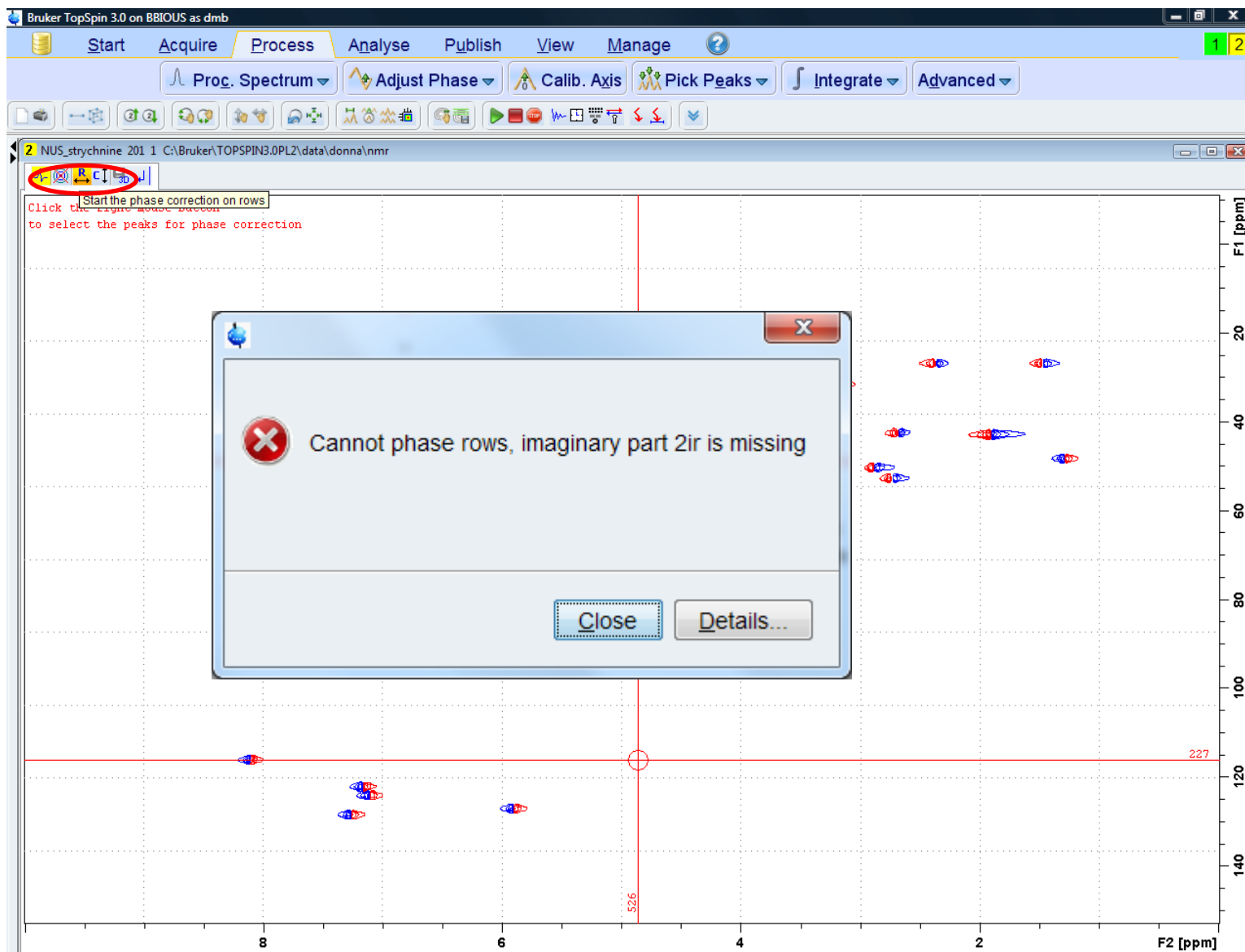
without

with

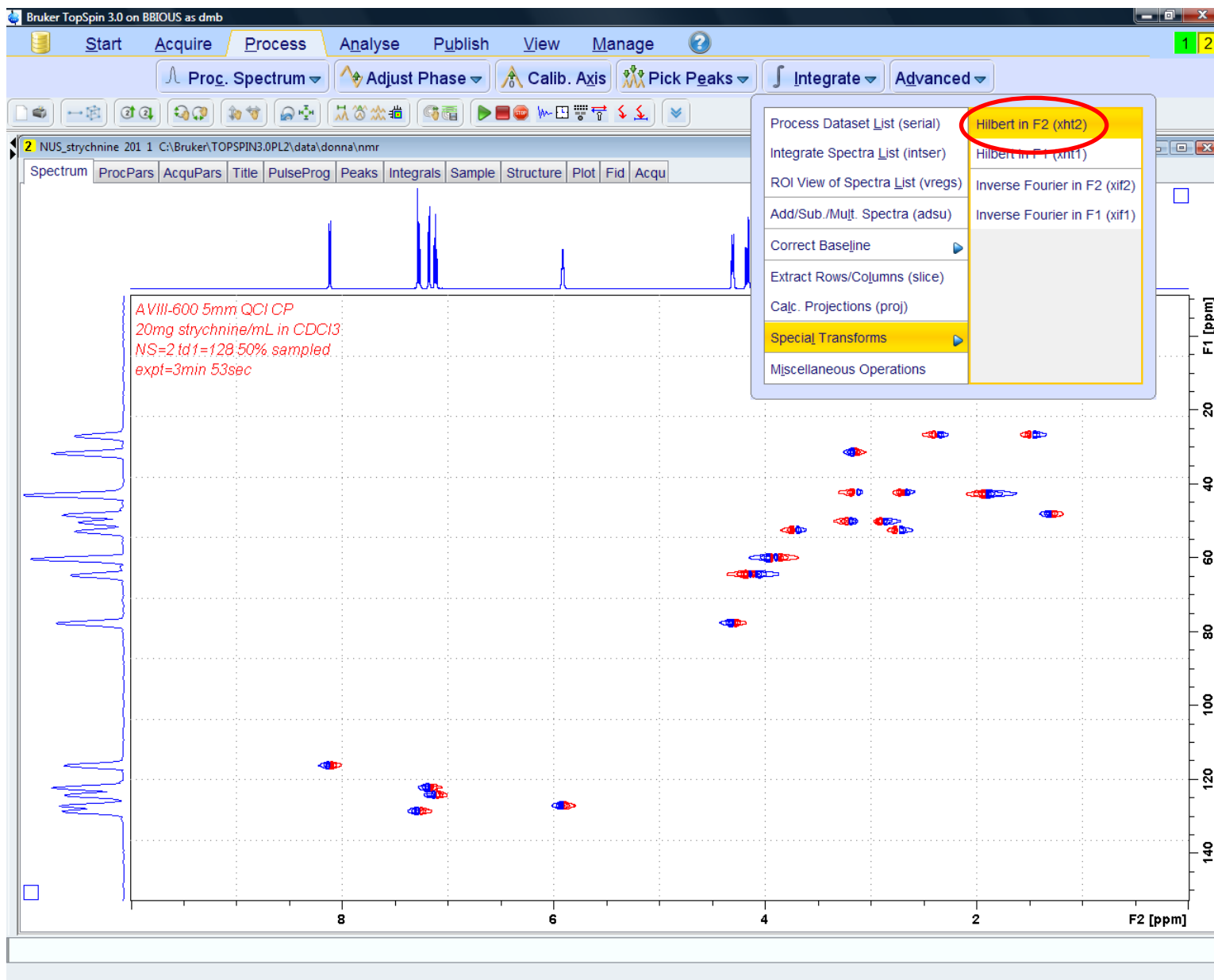




# Phasing – Hilbert transform



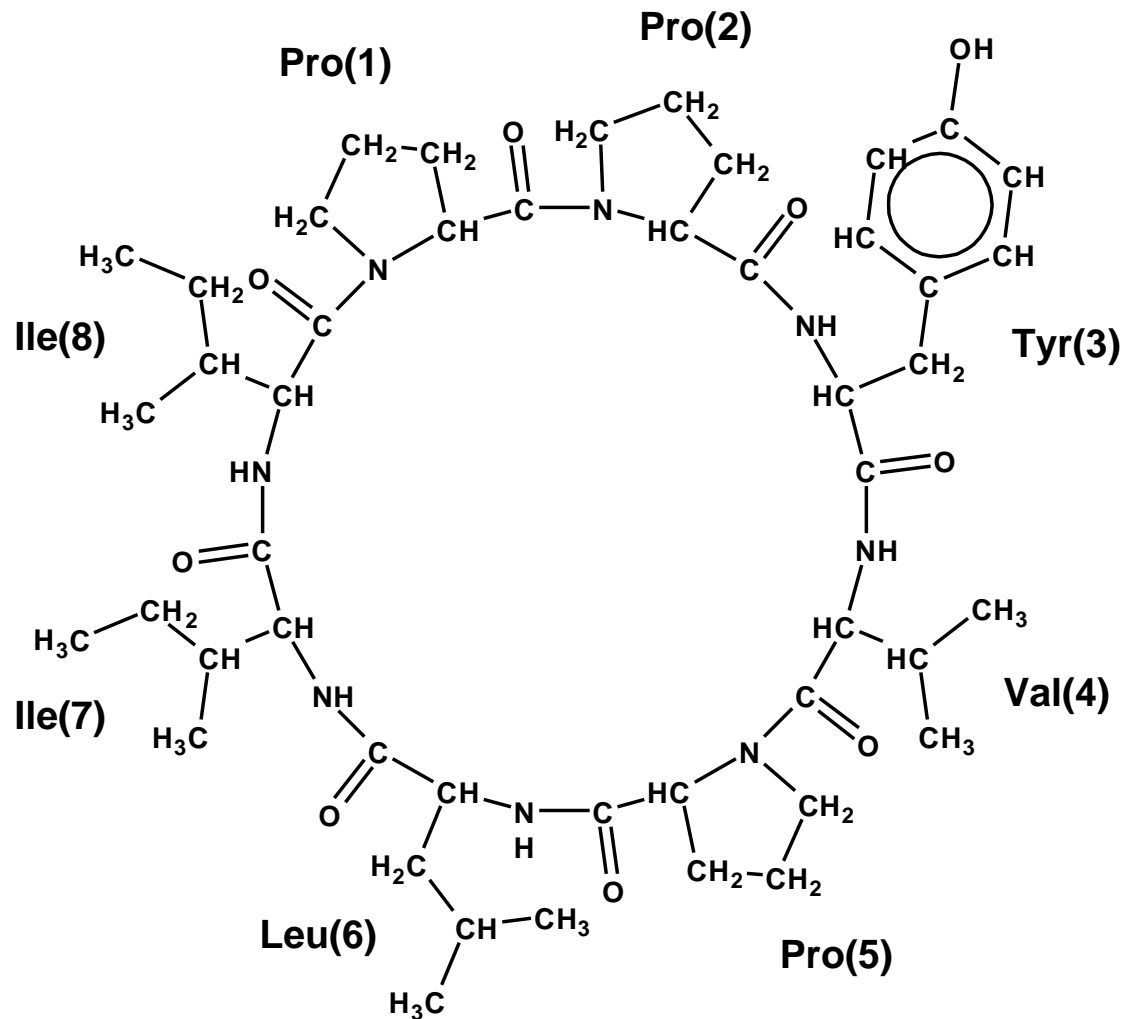
# Phasing – Hilbert transform



# Applications



## Hymenistatin



number of cross peaks  
(estimated maximum):

HSQC ( $^{13}\text{C}$ )	48
HMBC ( $^{13}\text{C}$ )	199
COSY	187
TOCSY	339

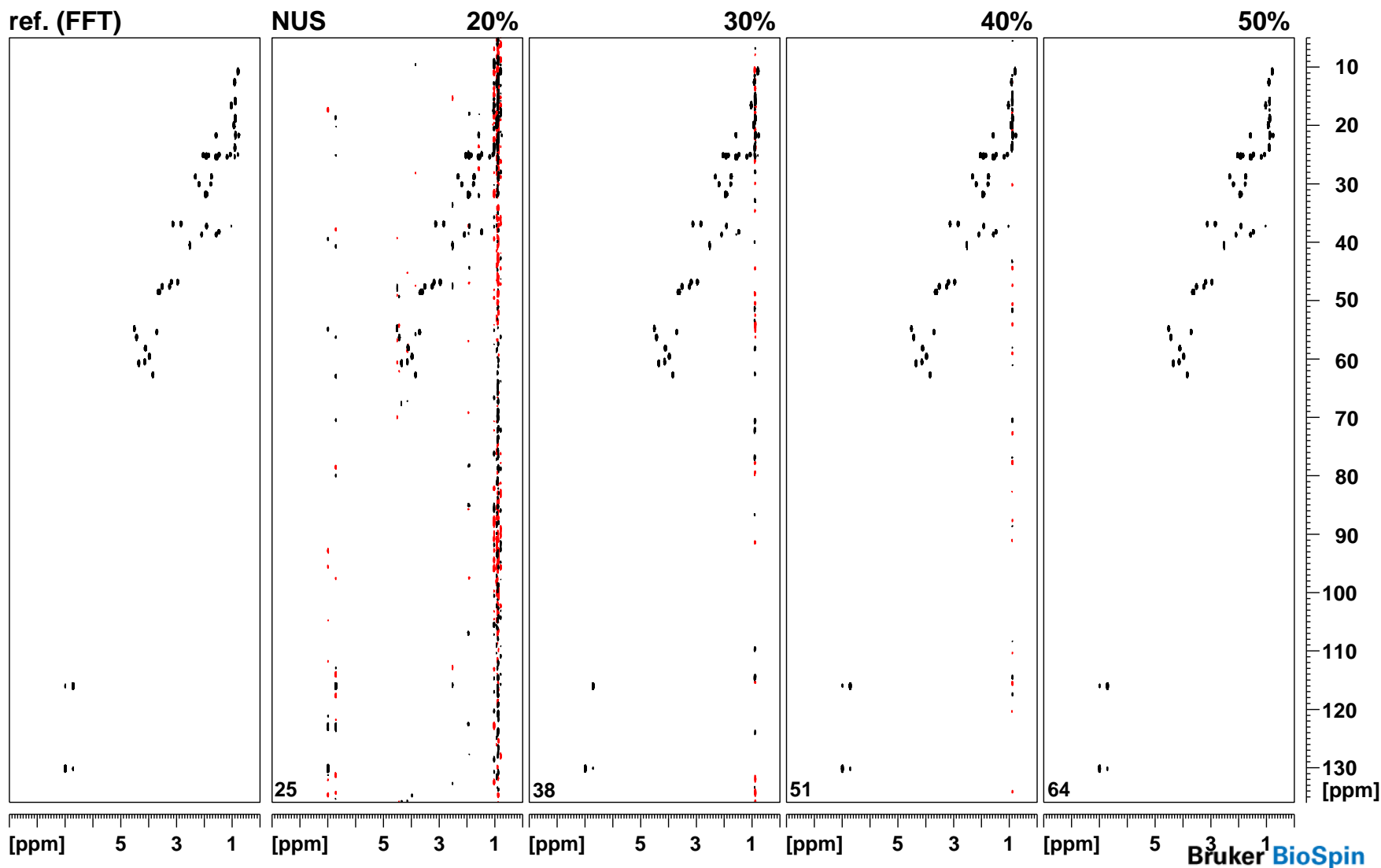
R.K. Konat, D.F. Mierke, H.Kessler, B. Kutscher, M. Bernd  
& R. Voegeli, *Helv. Chim. Acta* **76**, 1649 (1993)

Bruker BioSpin

# Applications



HSQC: td = 256



# Applications

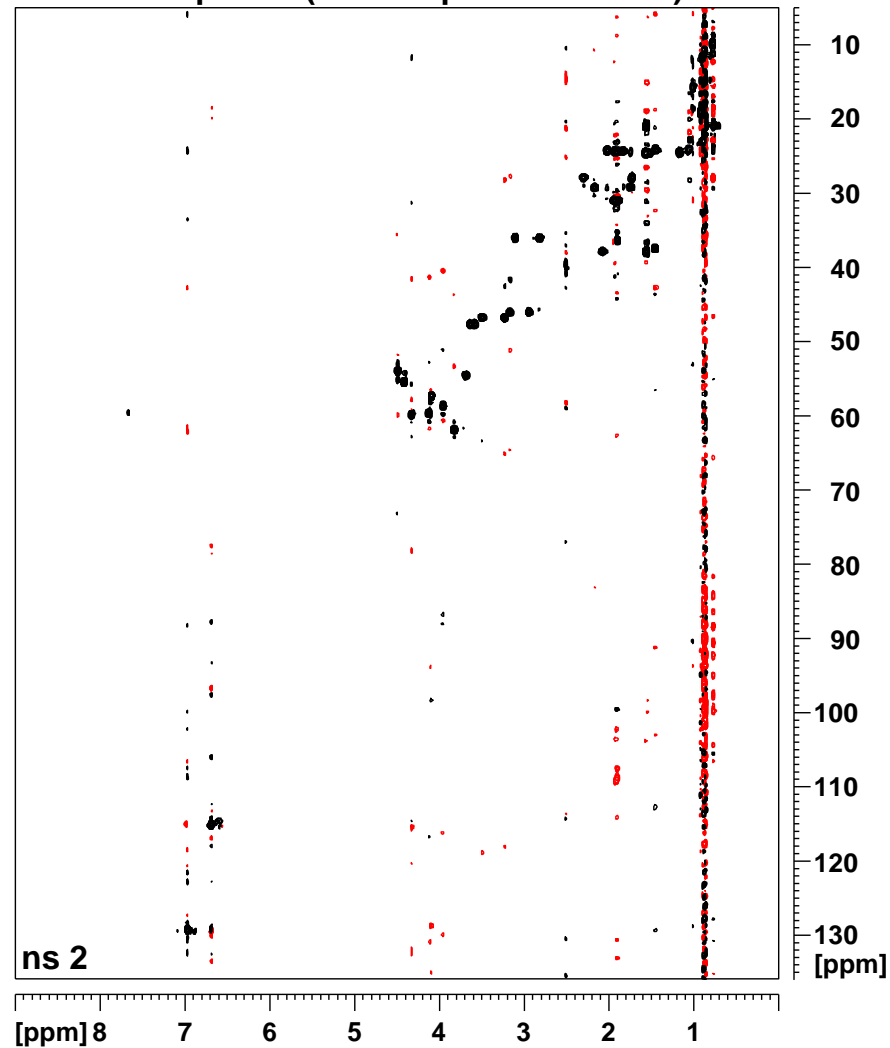
## HSQC



ref. 256 points (FFT)



25% of 256 points (nussampler/MDD-NMR)

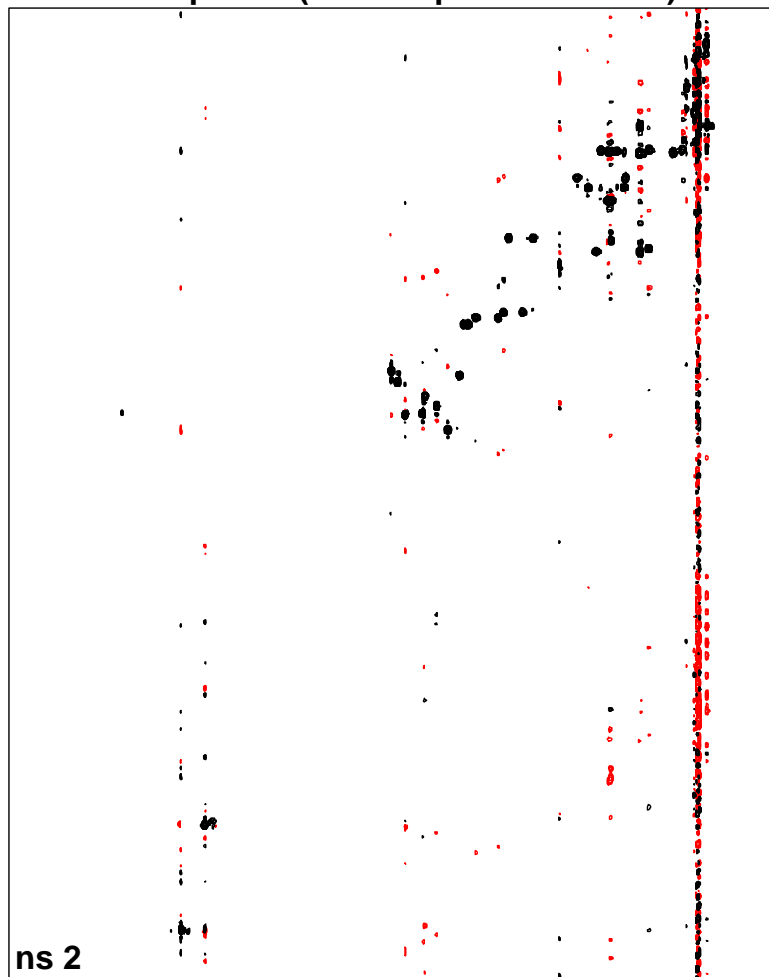


# Applications

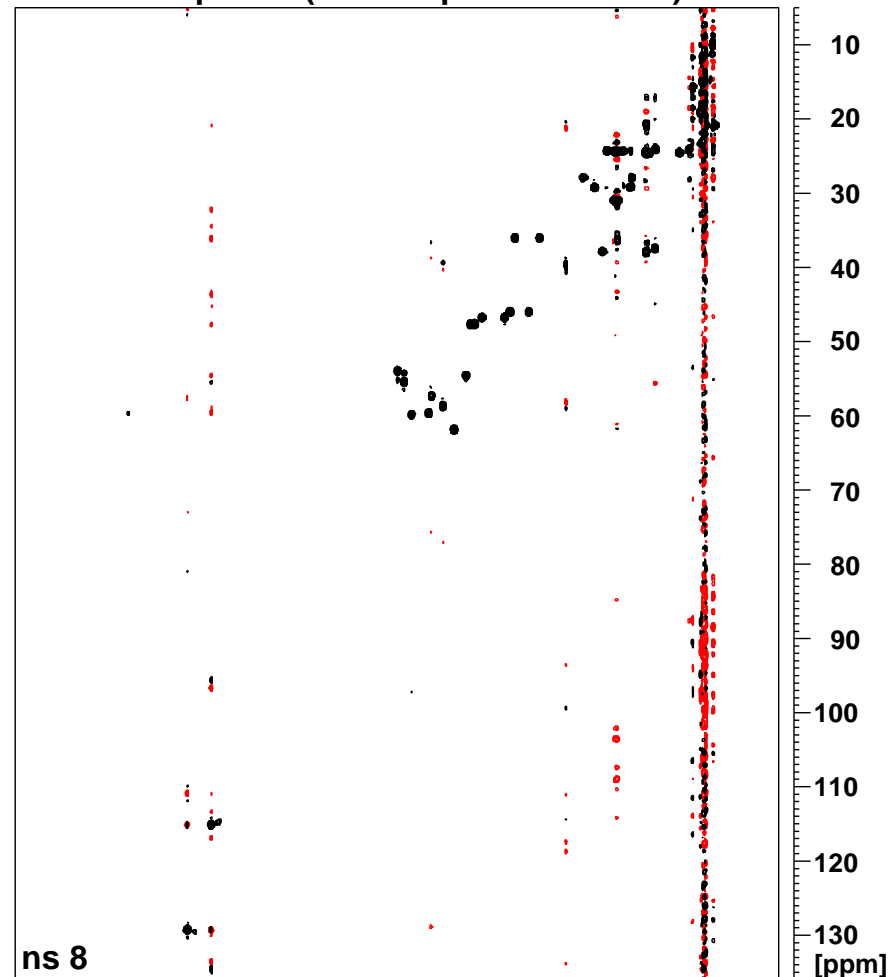
## HSQC



25% of 256 points (nussampler/MDD-NMR)



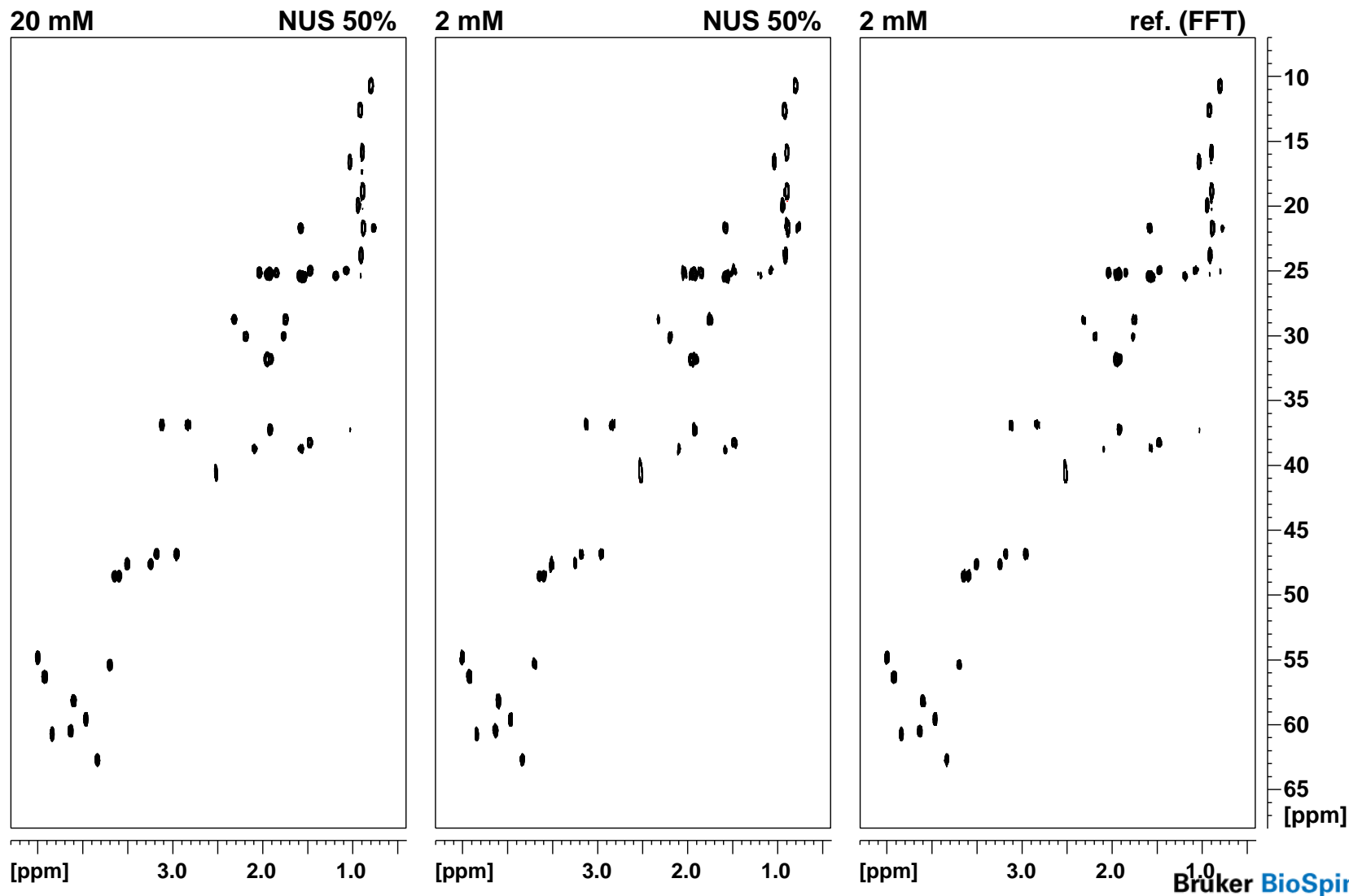
25% of 256 points (nussampler/MDD-NMR)



# Applications



HSQC:  $td = 256$



# Applications



## HSQC

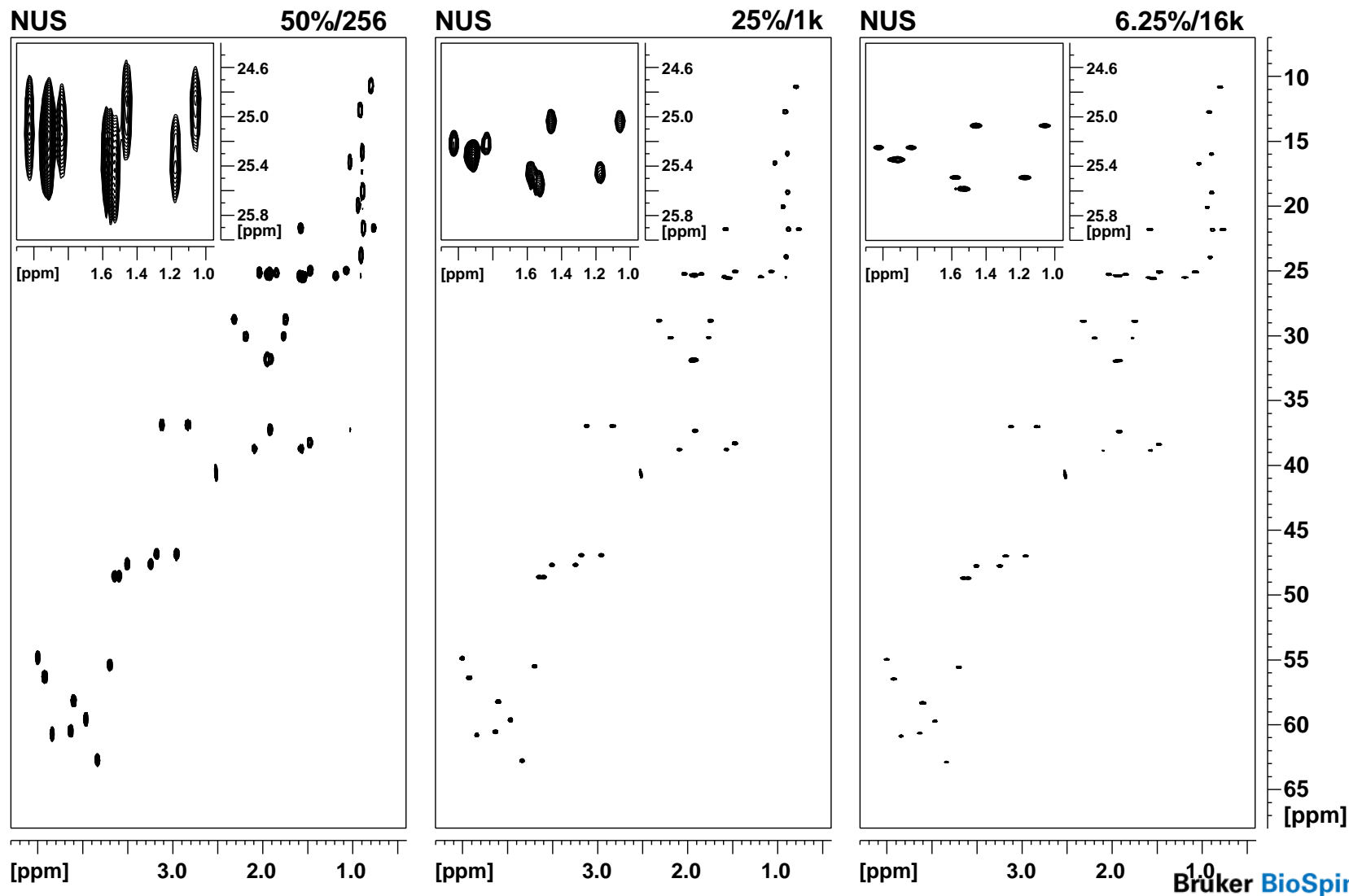
td1	amount	NCP	expt (min)	proc. (FT + mddnmr) (m:s)	si1
256	50%	64	10.5	4:34	512
512	25%	64	10.5	5:06	1k
1k	25%	128	20	11:07	2k
2k	12.5%	128	20	12:18	4k
4k	12.5%	256	38.5	27:31	8k
8k	6.25%	256	38.5	31:24	16k
16k	6.25%	512	76	67:50	32k



# Applications



## HSQC

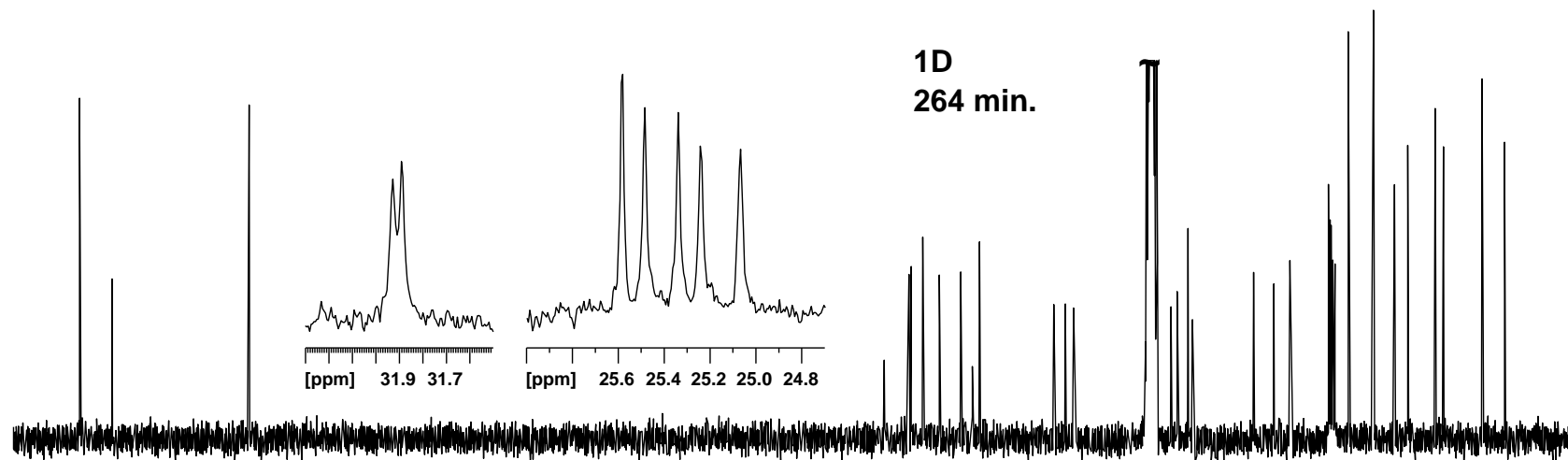


# Applications

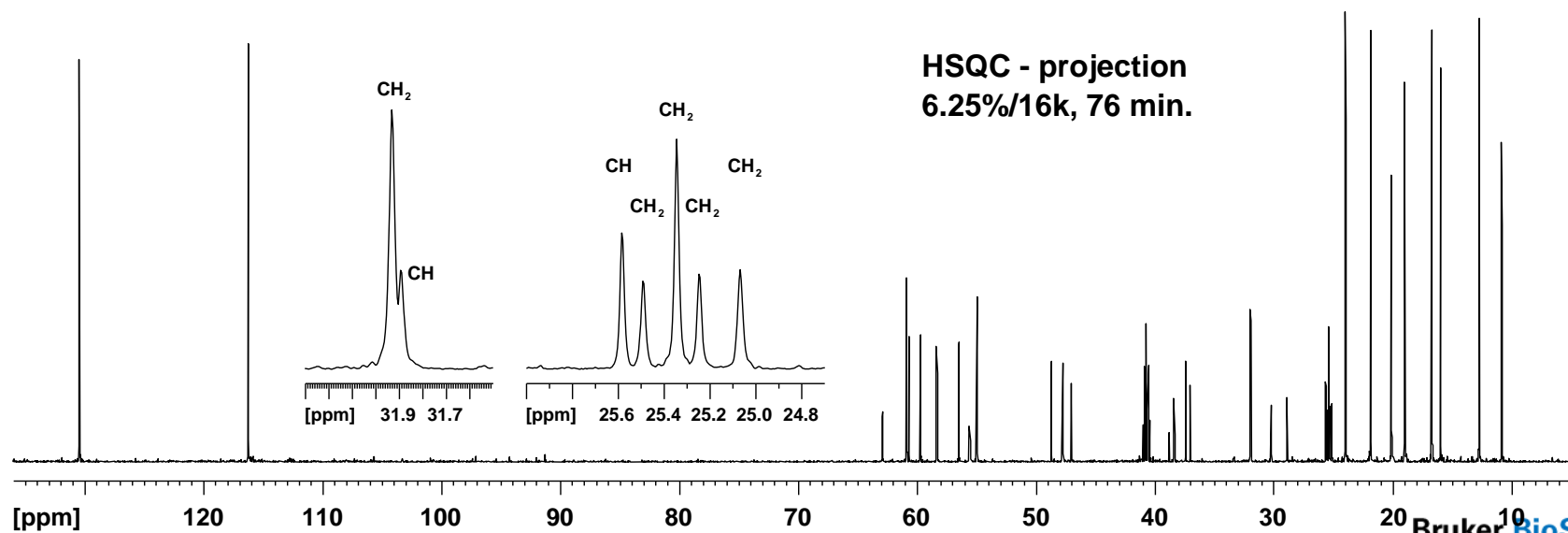


## HSQC

1D  
264 min.



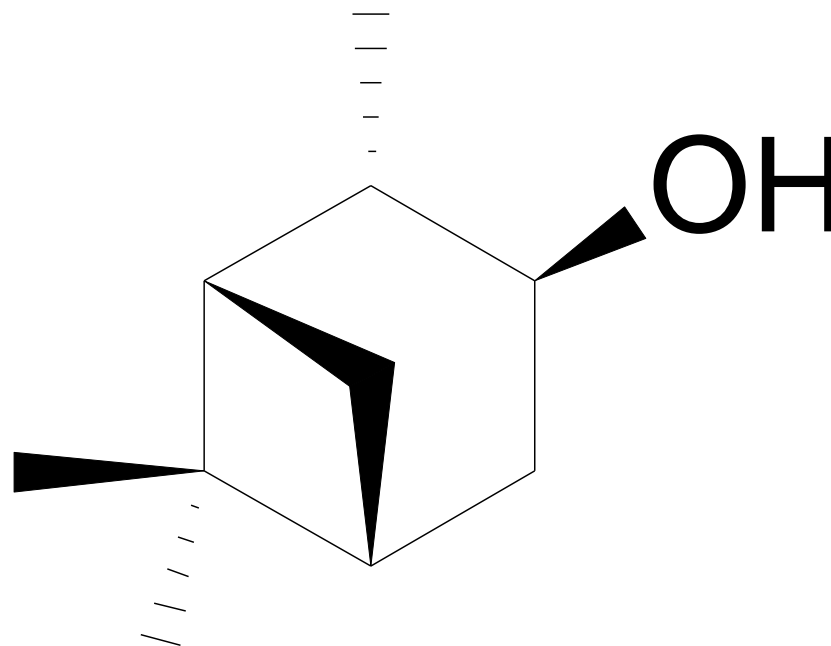
HSQC - projection  
6.25%/16k, 76 min.



# Applications



## (+)-Isopinocampheol ( (+)-IPC )



number of cross peaks  
(estimated maximum):

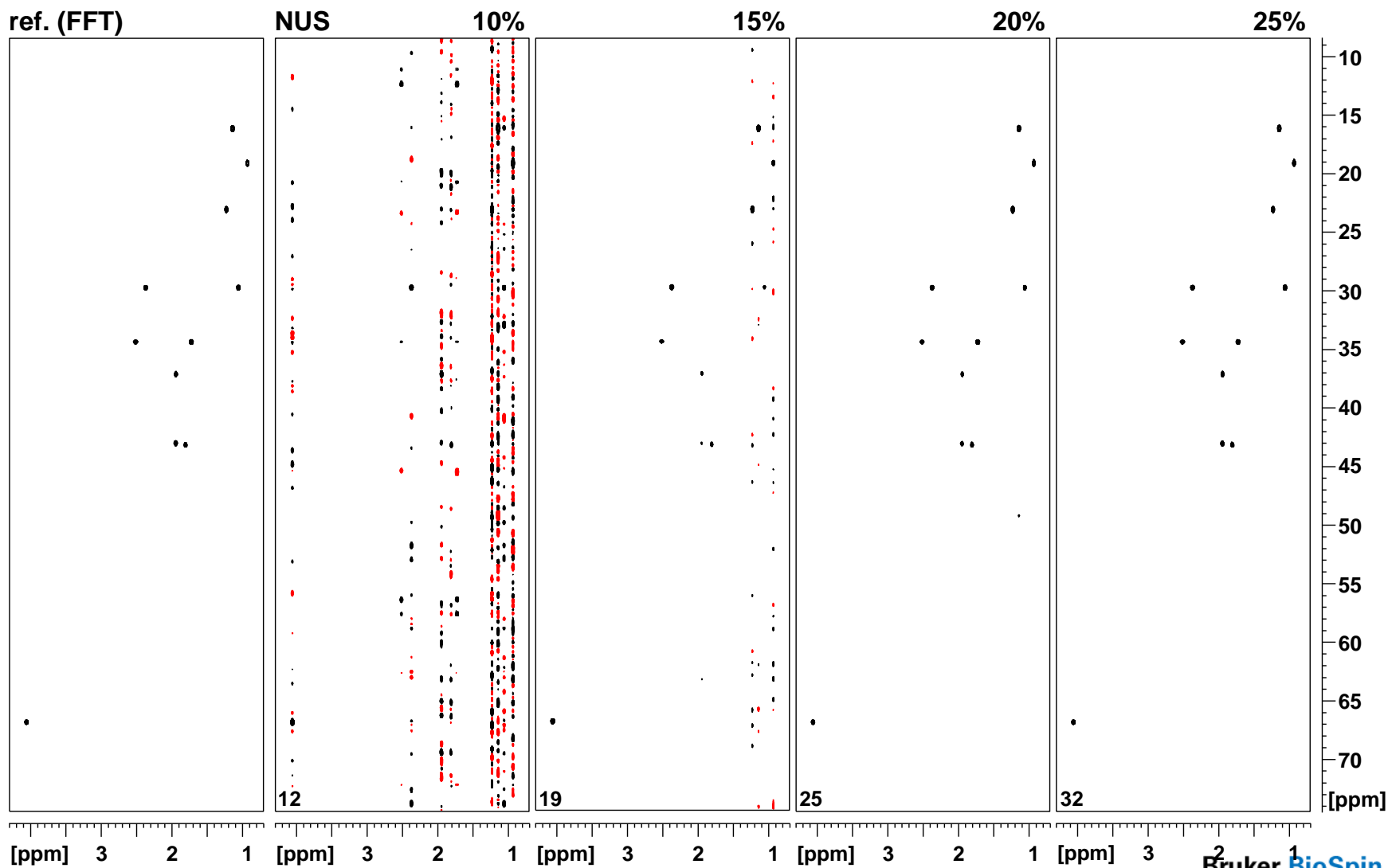
HSQC ( $^{13}\text{C}$ )	11
HMBC ( $^{13}\text{C}$ )	54
COSY	36
TOCSY	83

courtesy C. Thiele

# Applications



HSQC: td = 256

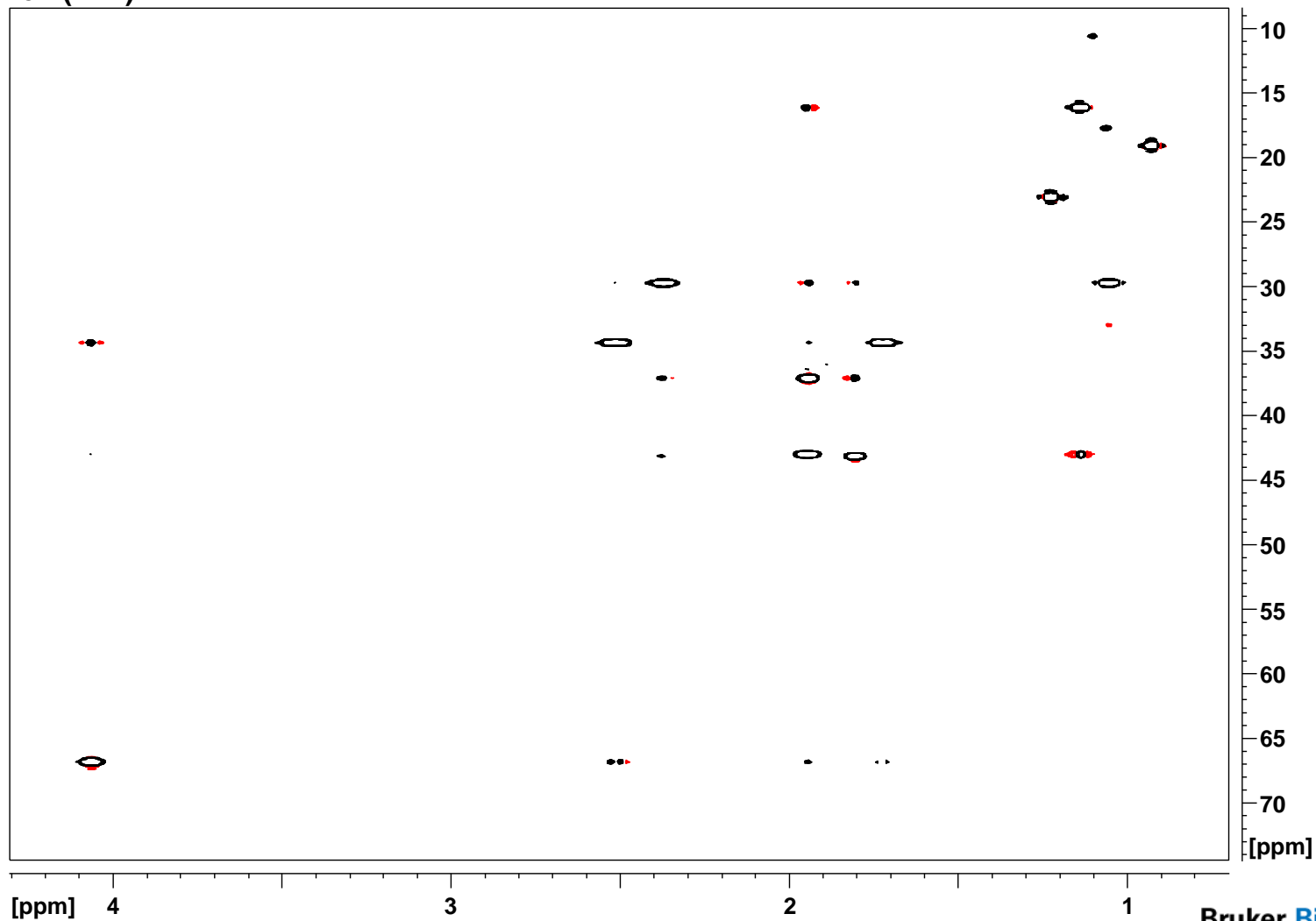


# Applications



## HSQC: COSY peaks in HSQC-si

ref. (FFT)

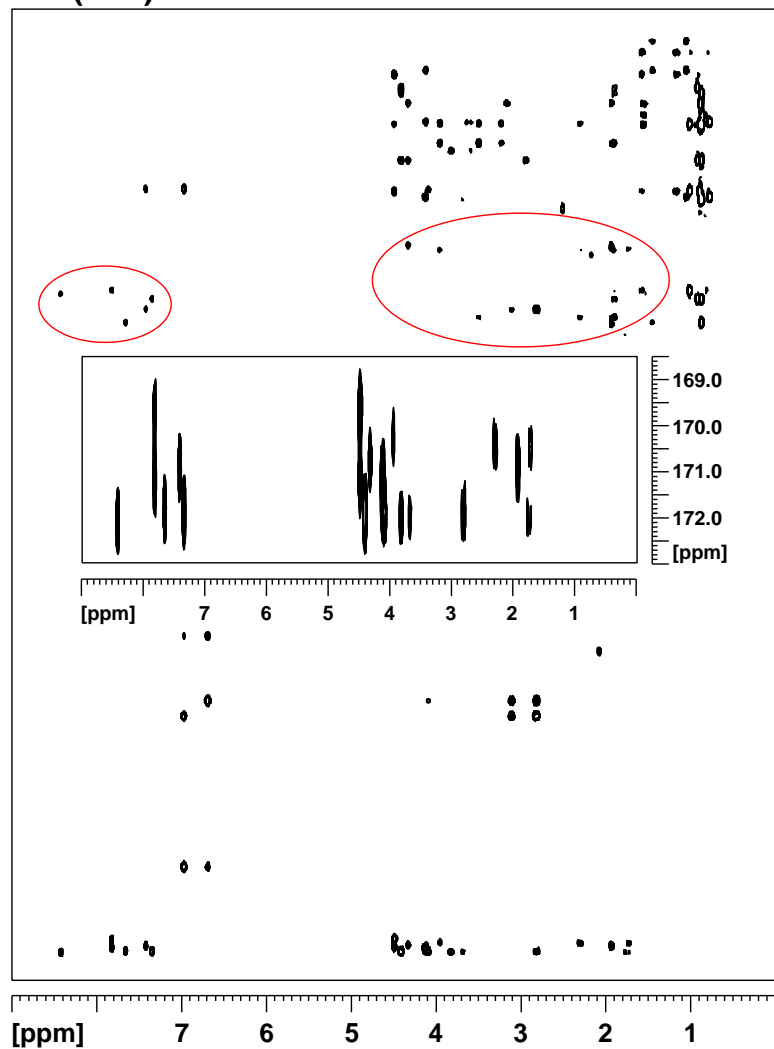


# Applications



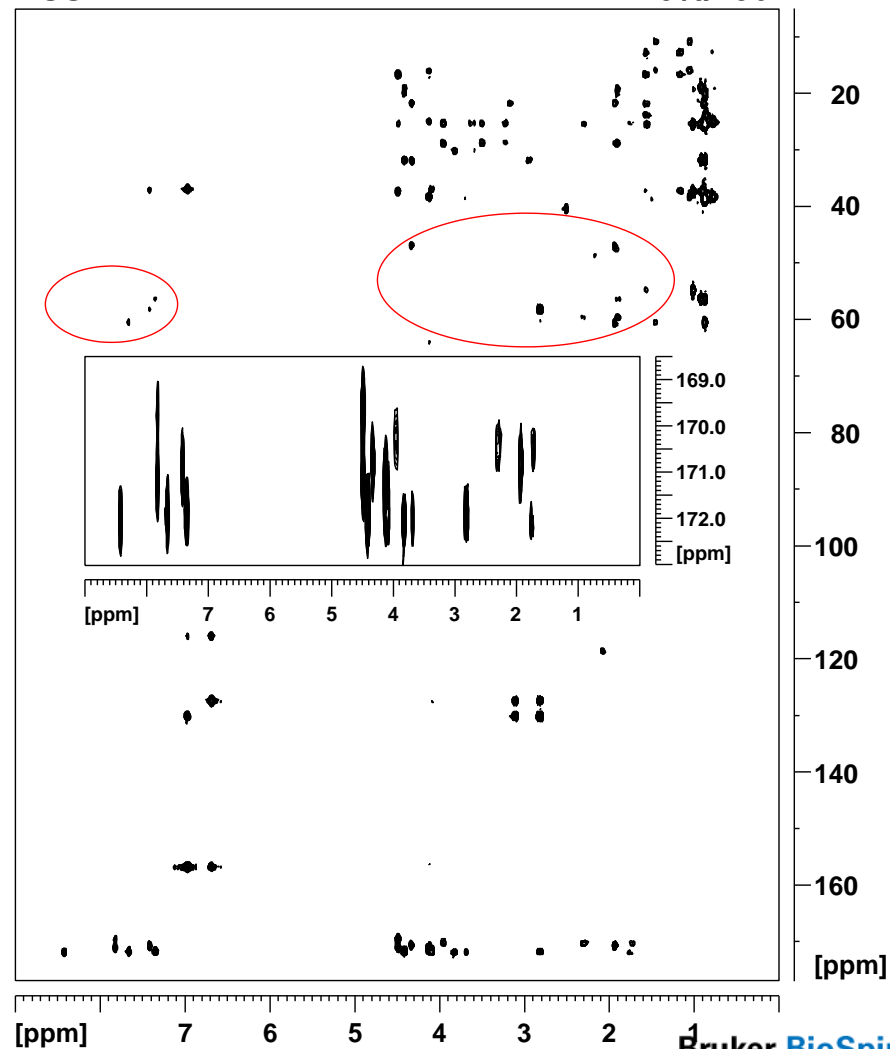
## HMBC

ref. (FFT)



NUS

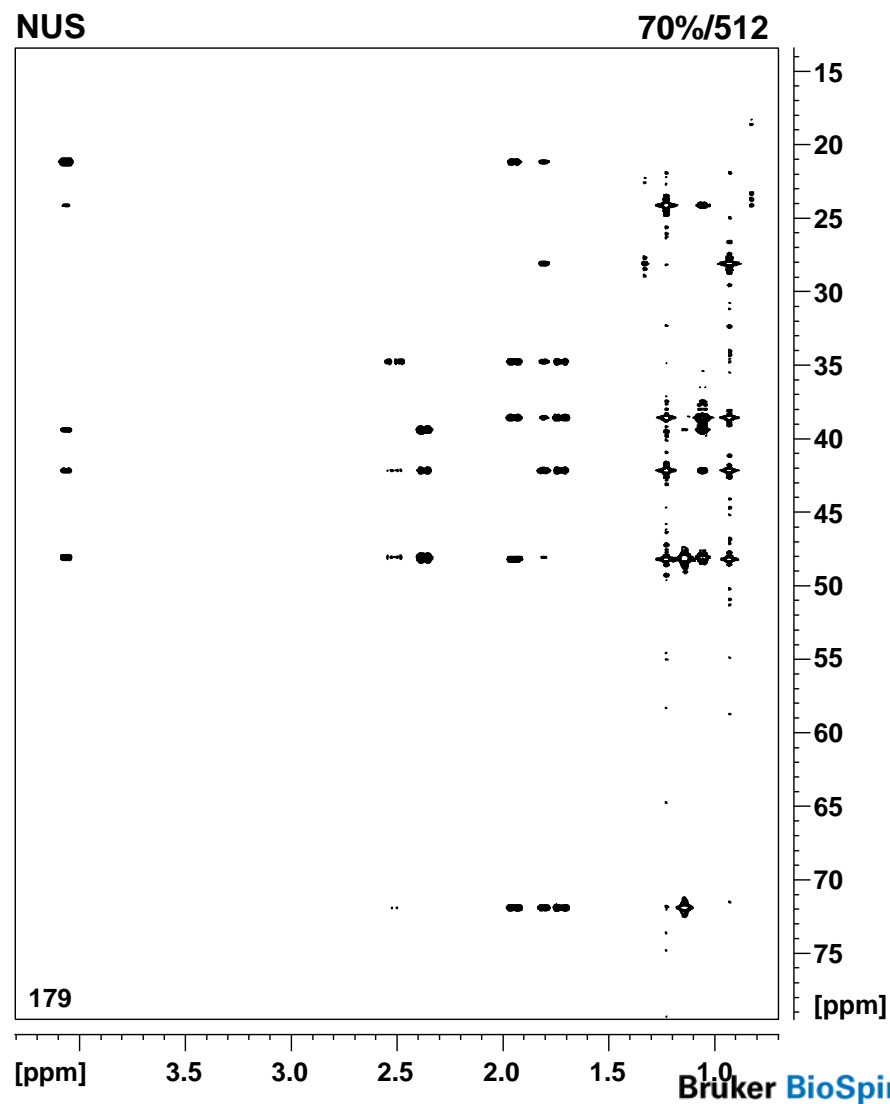
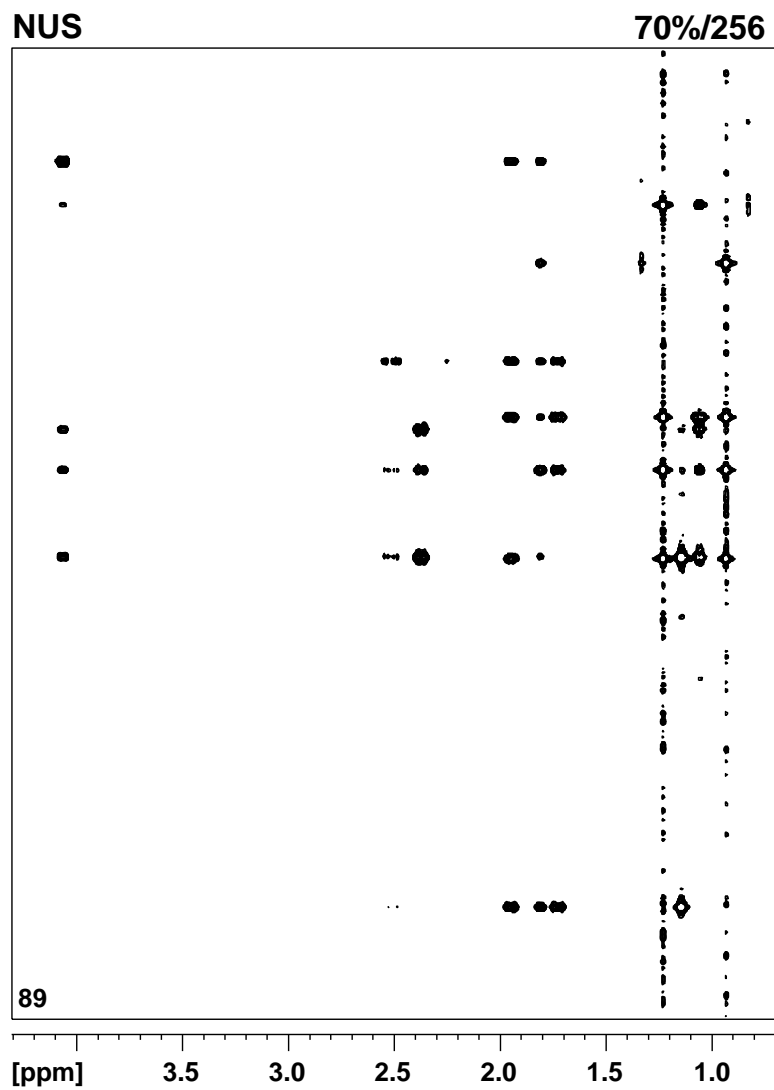
70%/256



# Applications



## HMBC

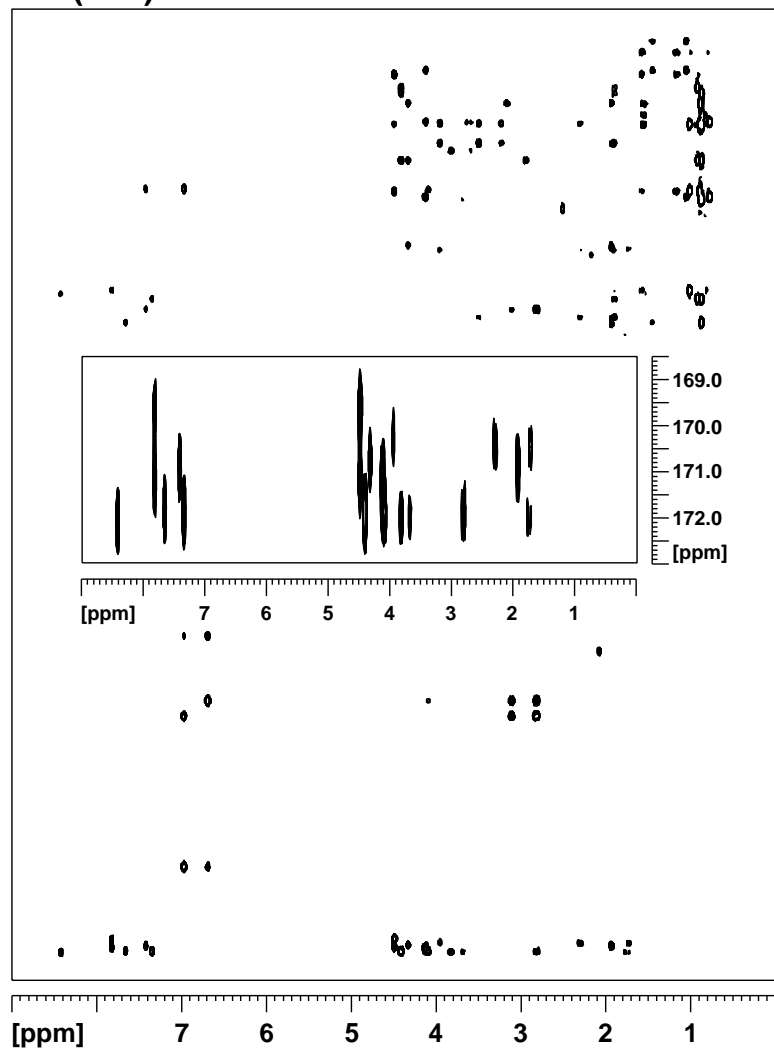


# Applications



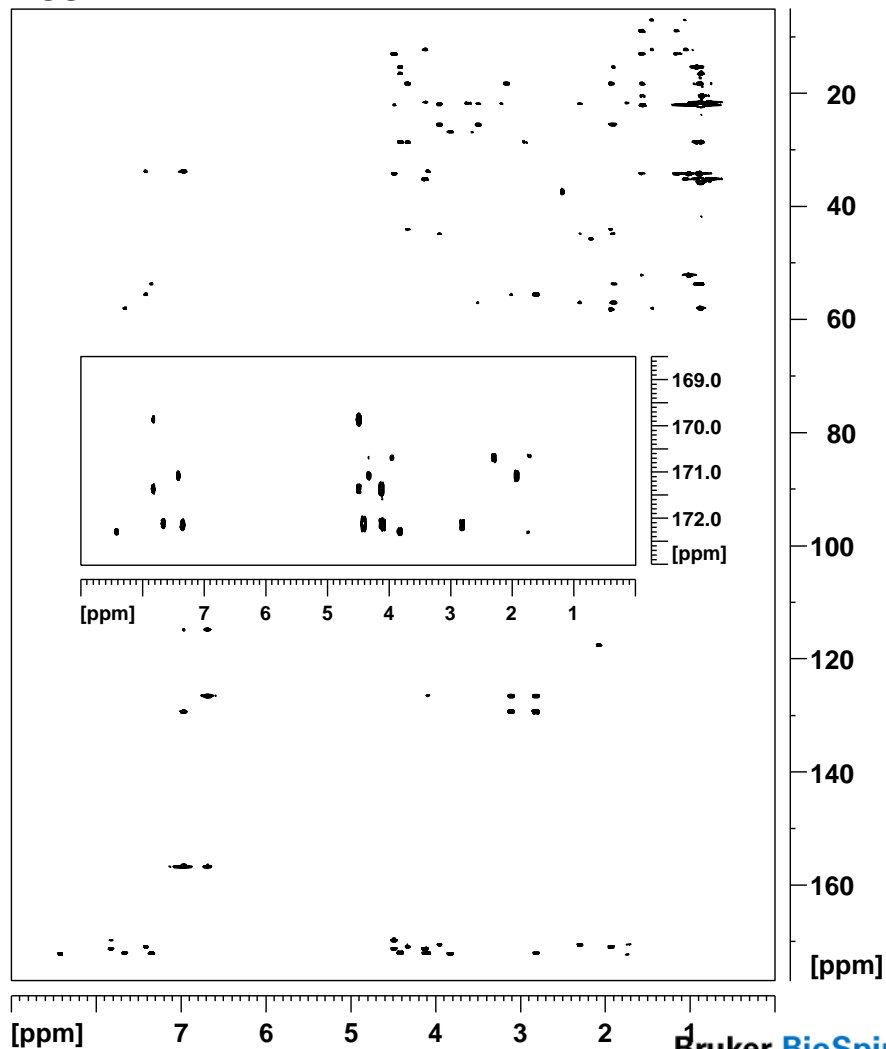
## HMBC

ref. (FFT)



NUS

25%/4k

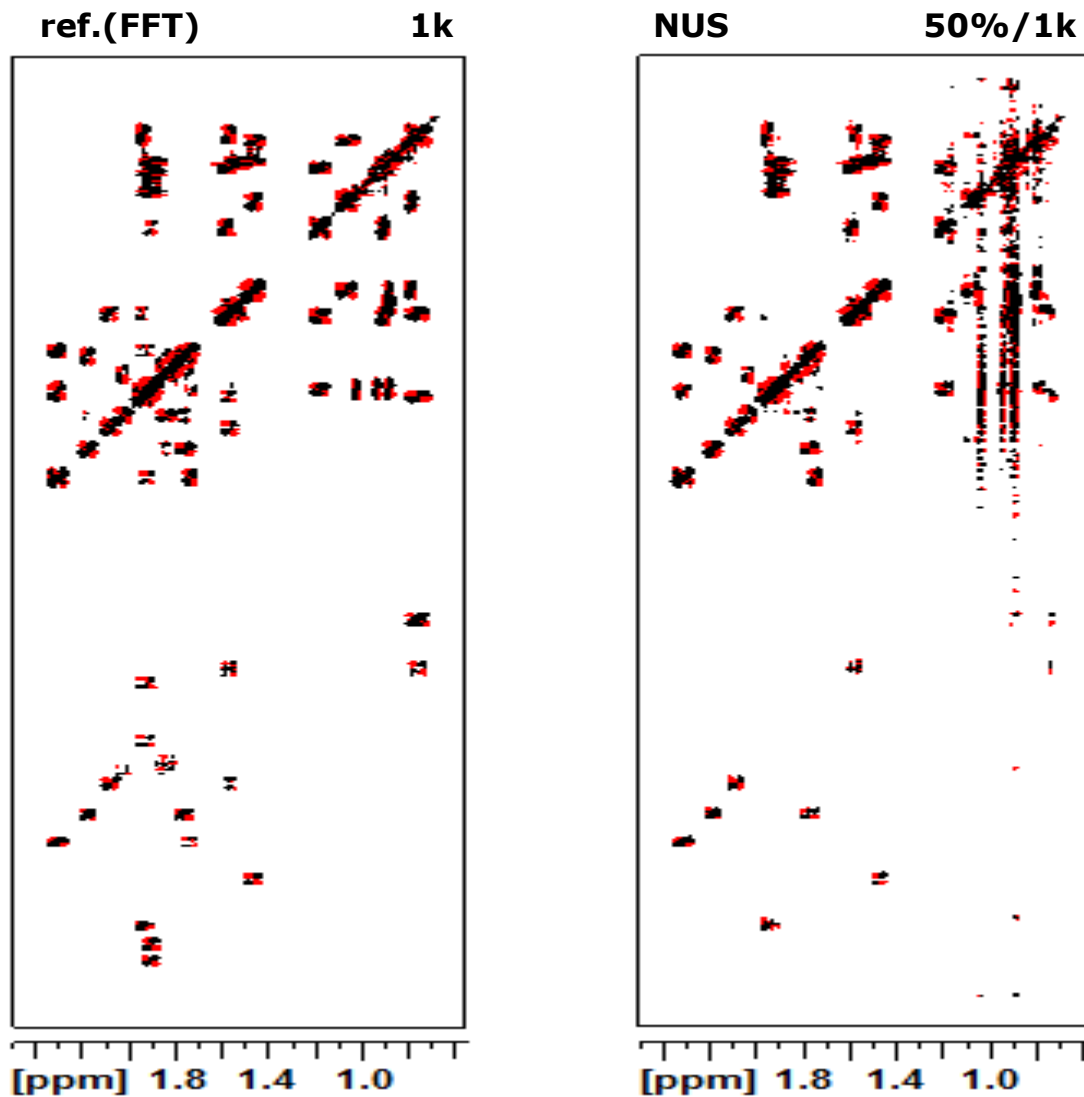




# Applications



COSY - dfph



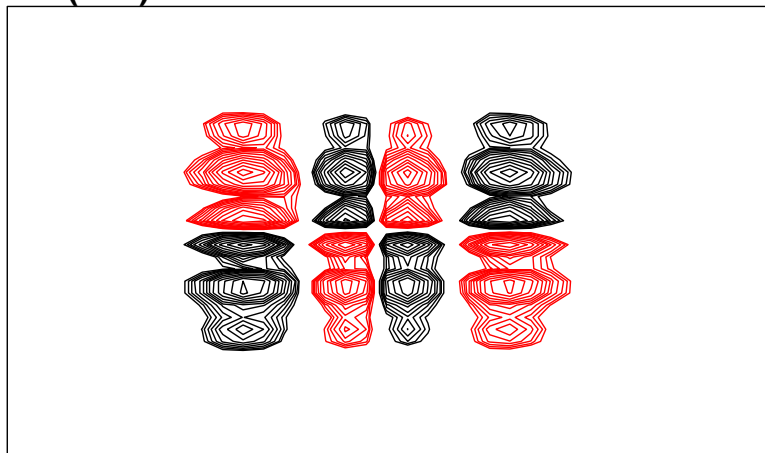
# Applications



## COSY - dfph

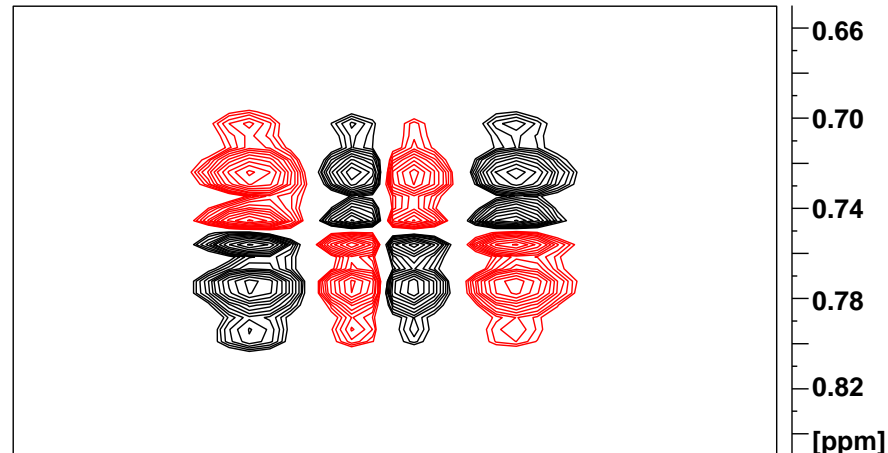
ref. (FFT)

1k



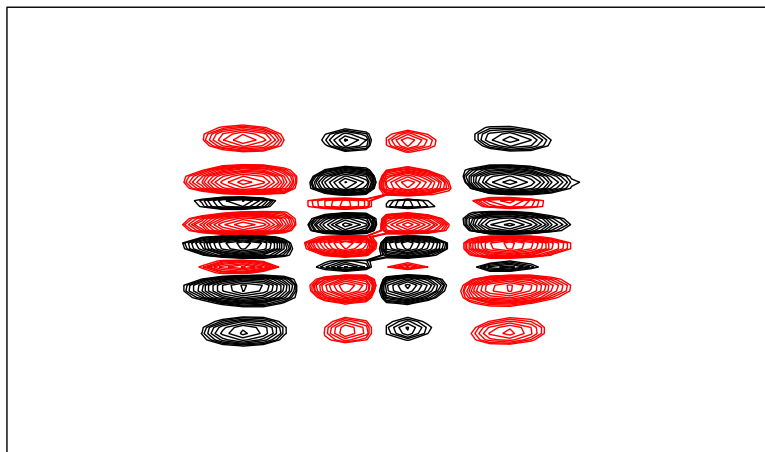
NUS

50%/1k



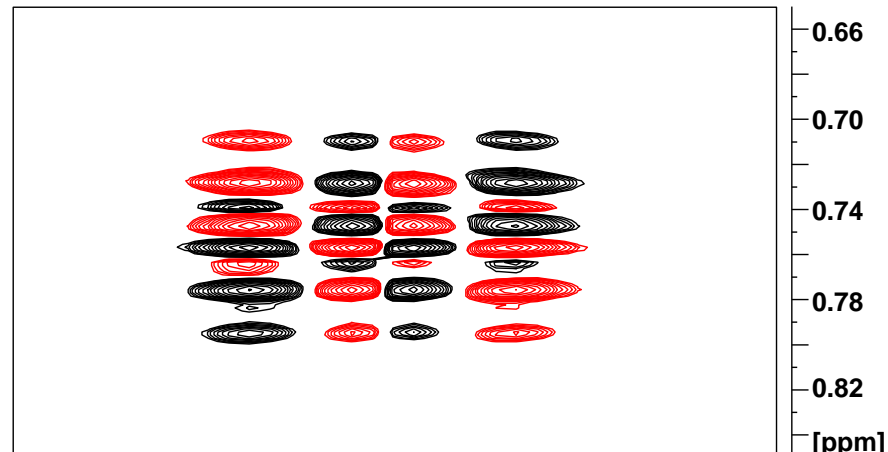
NUS

50%/2k



NUS

50%/4k



[ppm]

2.98

2.96

2.94

2.92

[ppm]

2.98

2.96

2.94

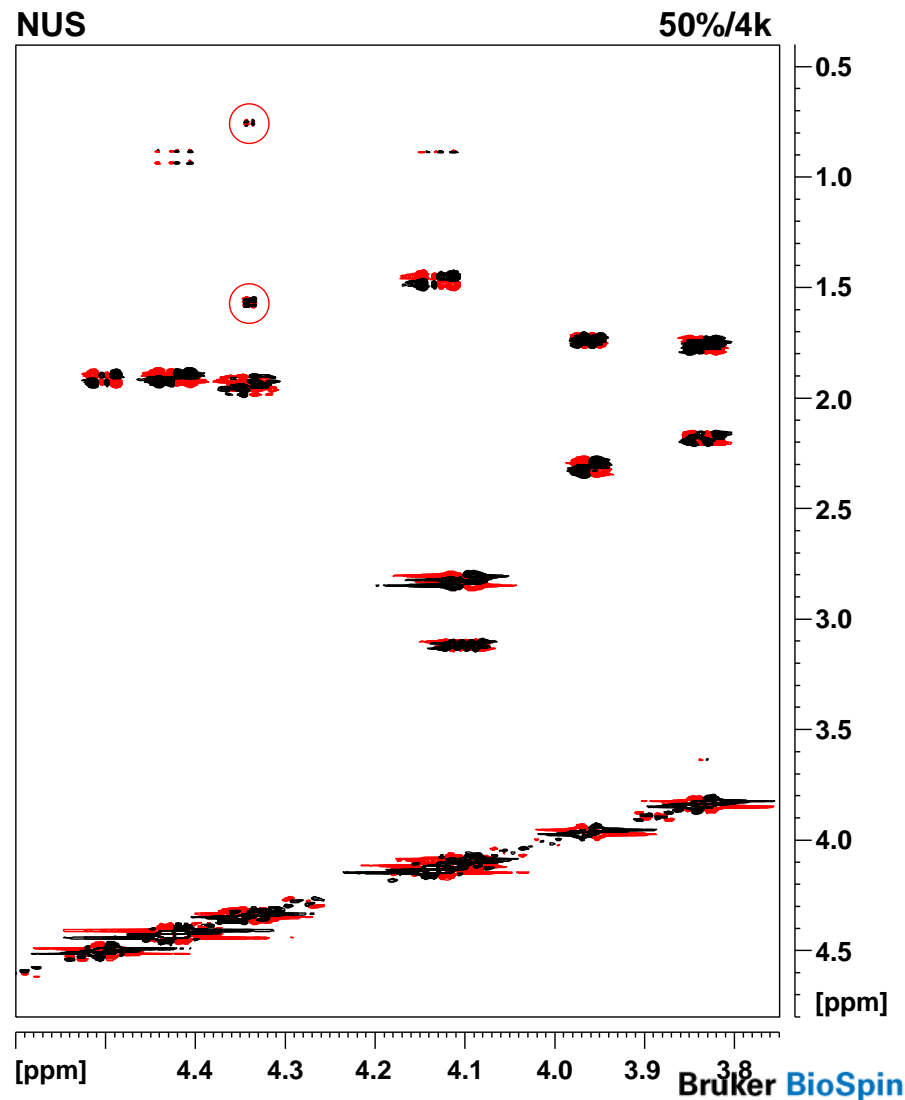
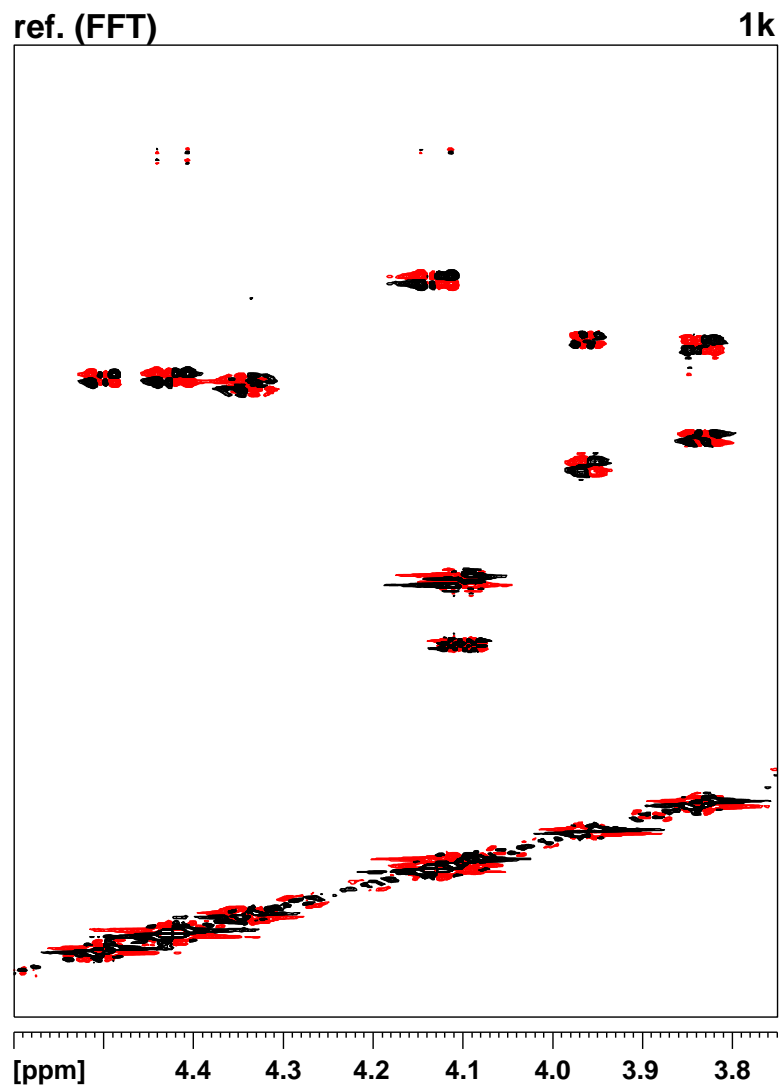
2.92

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# Applications



## COSY - dfph

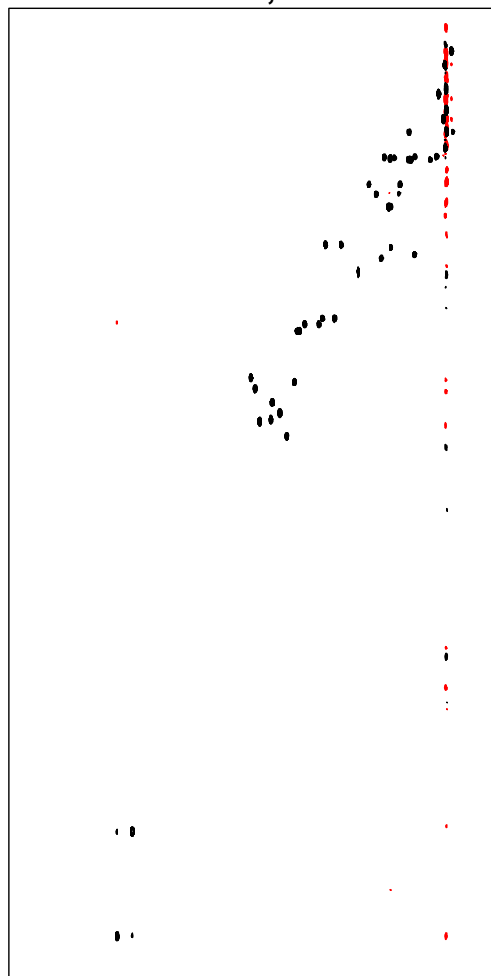


# Applications

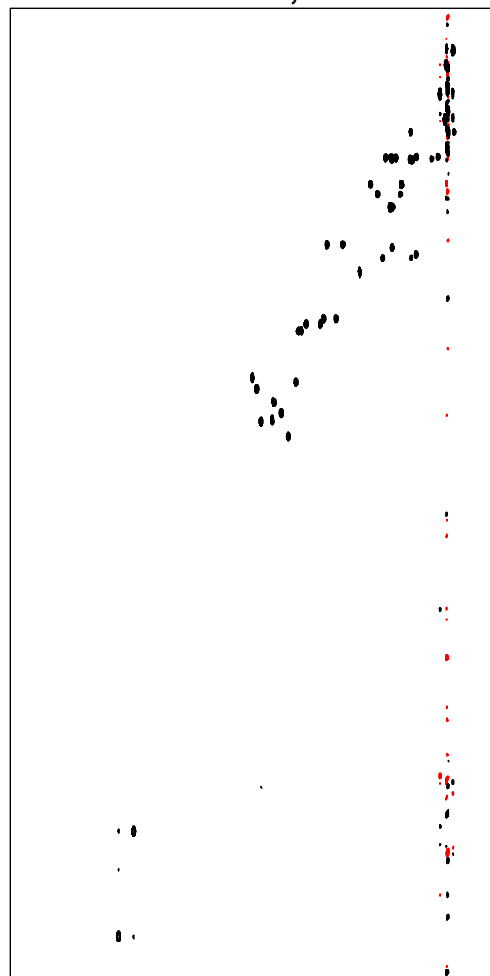


HSQC: td = 256

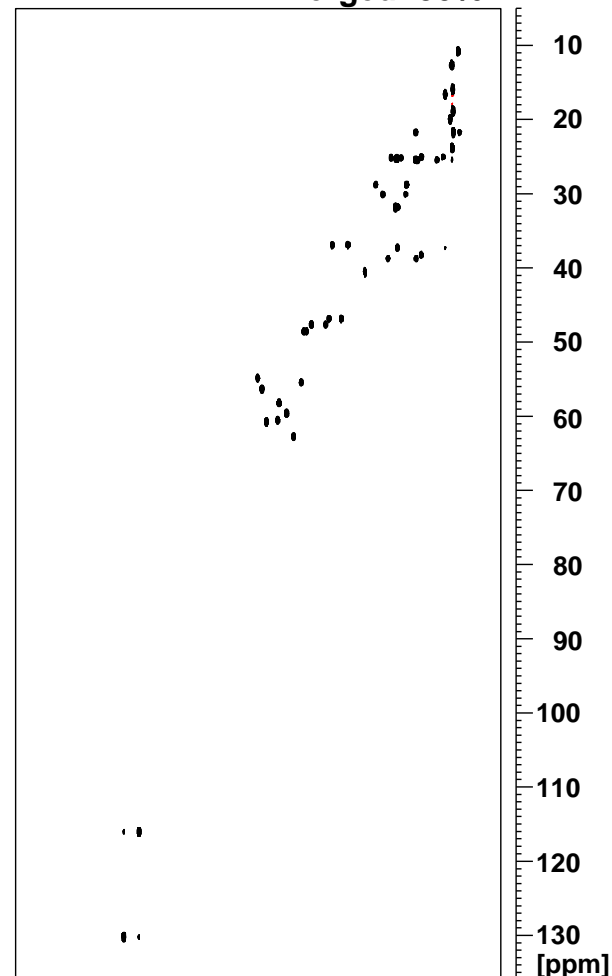
NUS 25%, seed = 6656



NUS 25%, seed = 123



NUS merged: 50%



[ppm] 7 6 5 4 3 2 1

[ppm] 7 6 5 4 3 2 1

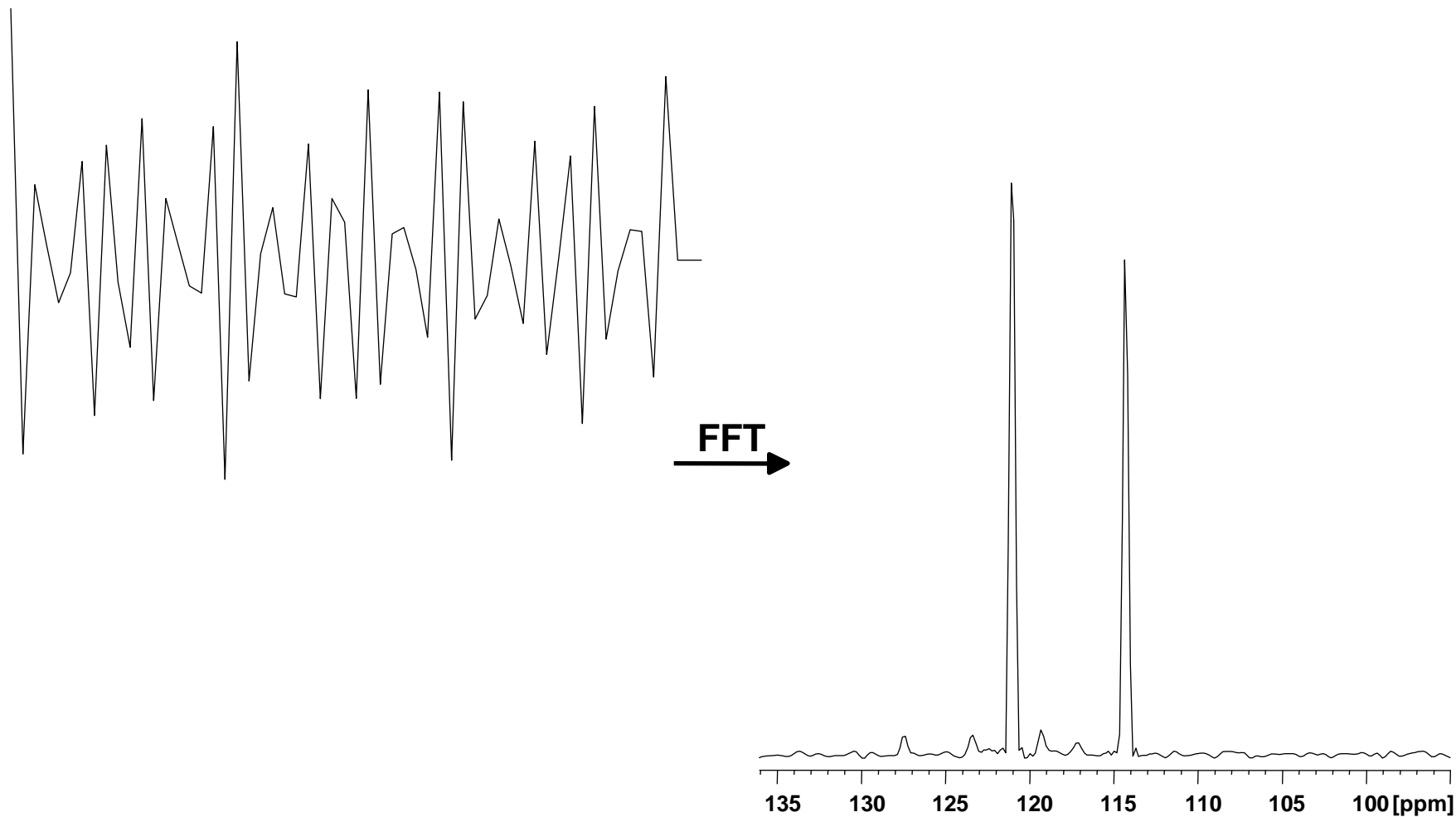
[ppm] 7 6 5 4 3 2 1

10  
20  
30  
40  
50  
60  
70  
80  
90  
100  
110  
120  
130  
[ppm]

# Applications



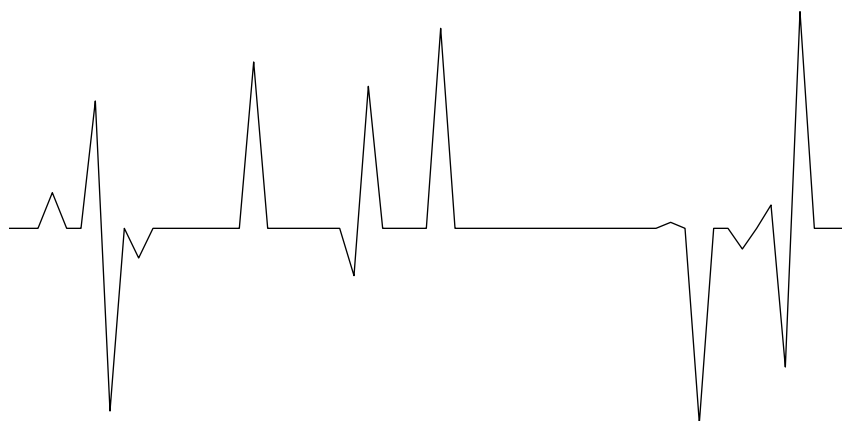
col from first  $t_2F_3$  plane (HNCO)



# Applications

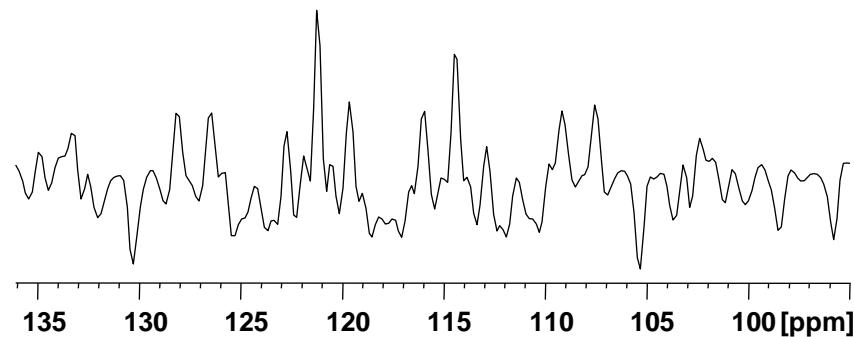


col from first  $t_2F_3$  plane (HNCO)



25% sparse (nussampler)

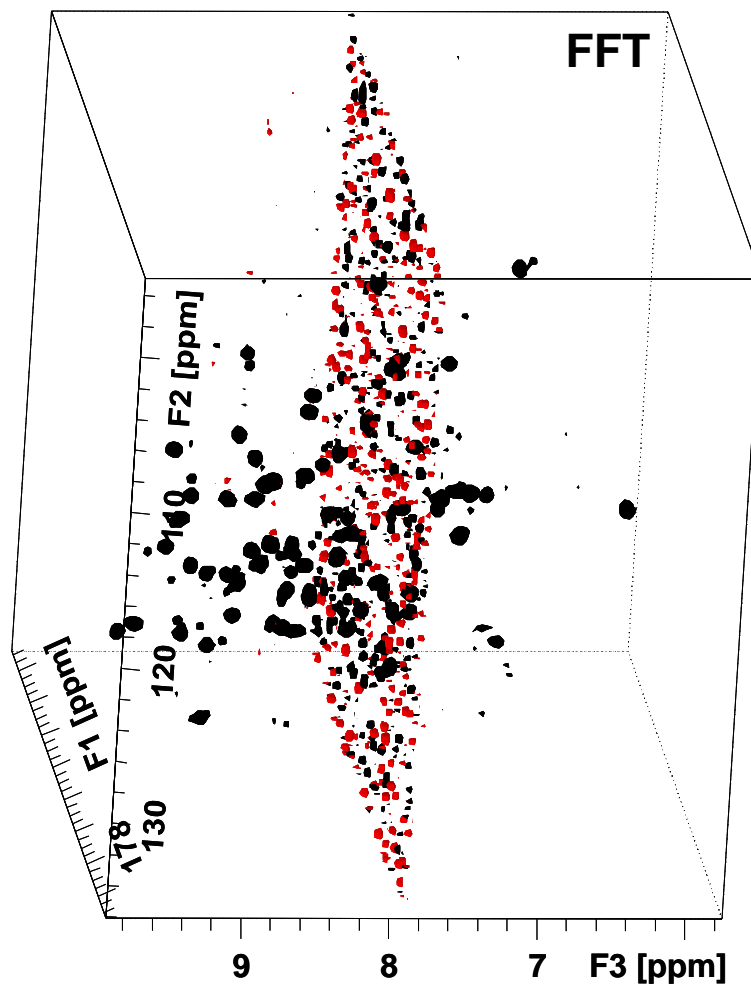
FFT →



# Applications



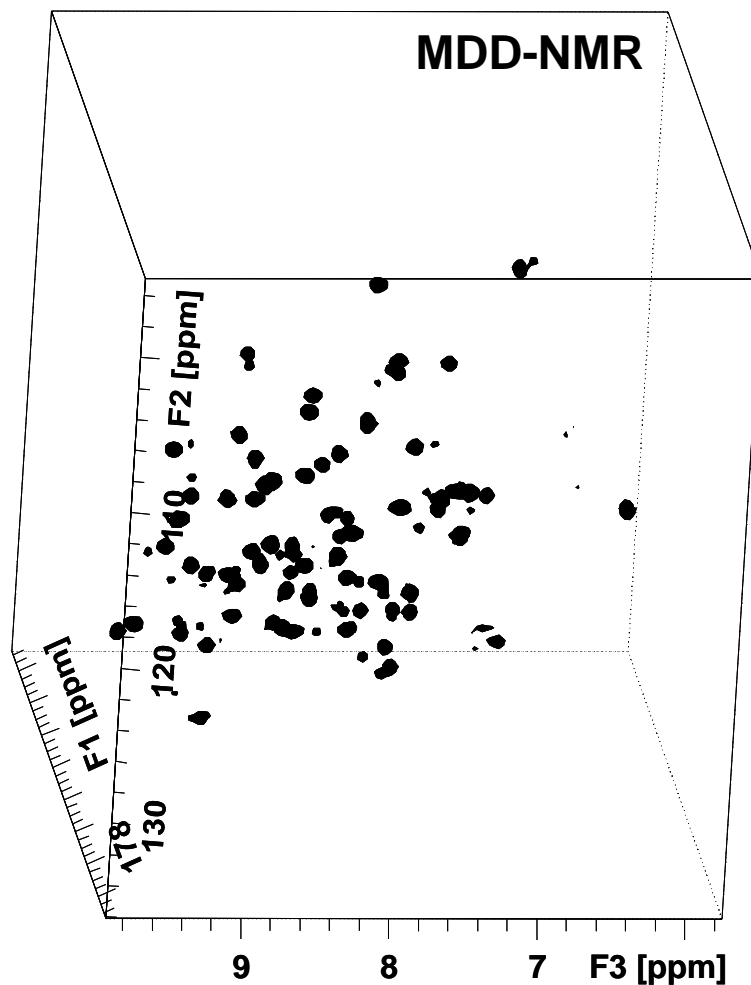
## HNCO - 25% sparse (nussampler)



# Applications



HNCO - 25% sparse (nussampler)

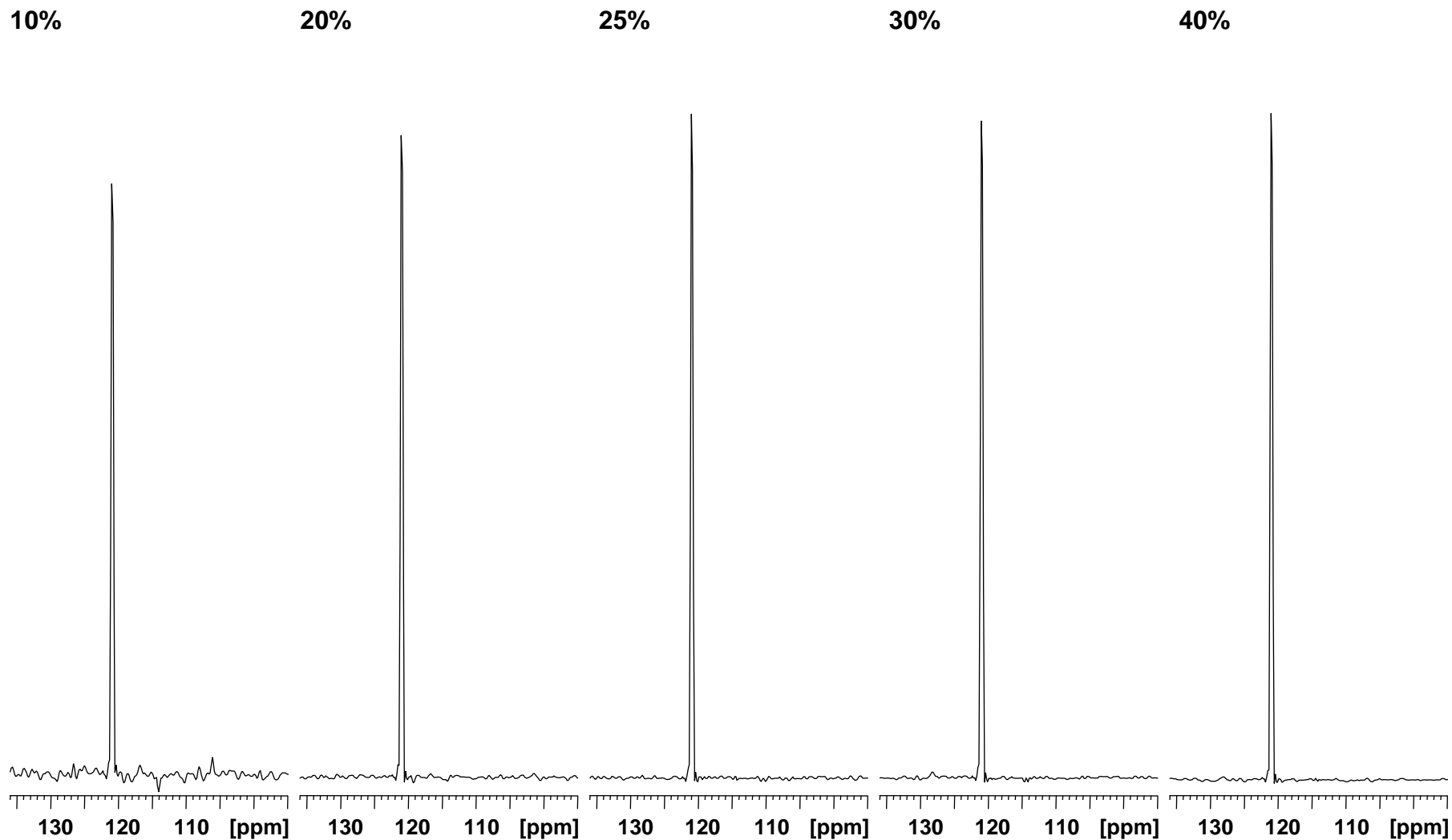




# Applications



HNCO - col from  $F_2F_3$  plane (172.8 ppm) - sparse (nussampler/MDD-NMR)



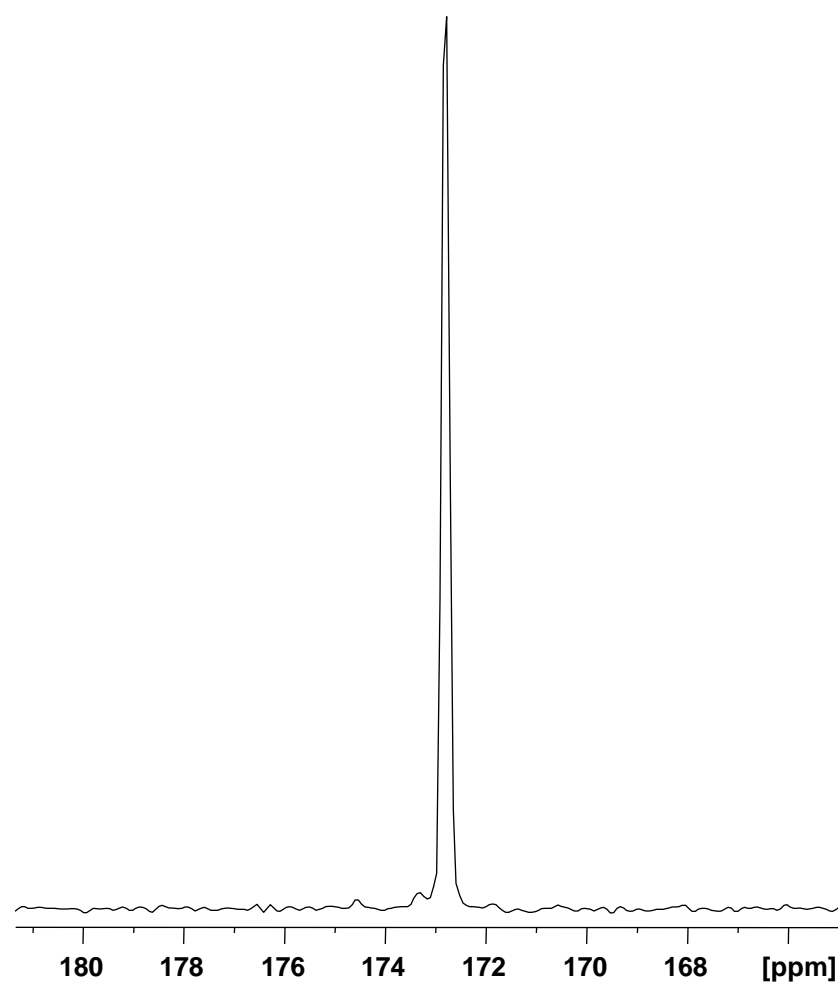
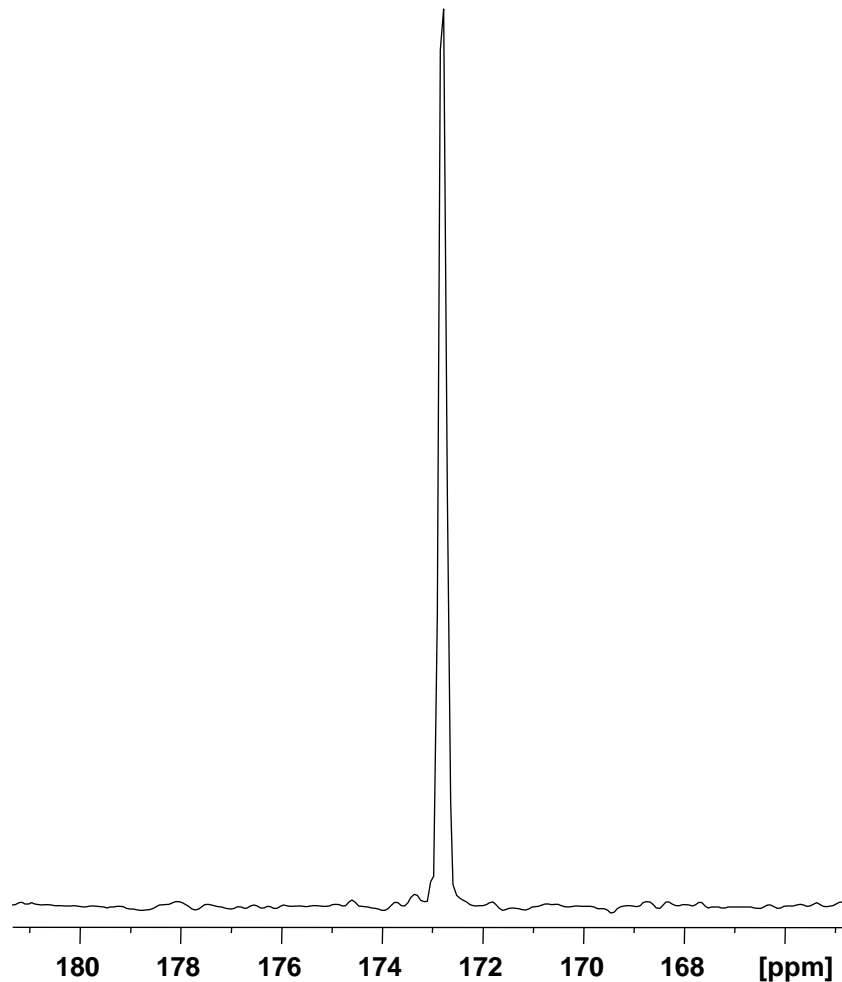
# Applications



col from  $F_1F_3$  plane (121.0 ppm) - 25% sparse (nussampler/MDD-NMR)

not weighted in  $t_1$

exponentially weighted in  $t_1$



# Additional processing parameters



The screenshot shows the Bruker software interface with the 'ProcPars' tab selected. The 'NUS (Non Uniform Sampling) parameters' section is highlighted with a red box. The 'MddNCOMP' parameter is circled in red.

Parameter	Value	Description
Mdd_mod	mdd	MDD mode
MddCEXP	FALSE	RMDD/MDD flag
MddCT_SP	FALSE	Constant time
MddF180	FALSE	Delayed sampling flag
MddNCOMP	0	Number of components
MddPHASE	0	Phase
MddSRSIZE [ppm]	0	Sub region size

## Number of components

- default is 15
- can be increased if peaks are missing
- processing times can get very long

# Additional processing parameters



HNCO: F1F3 projection

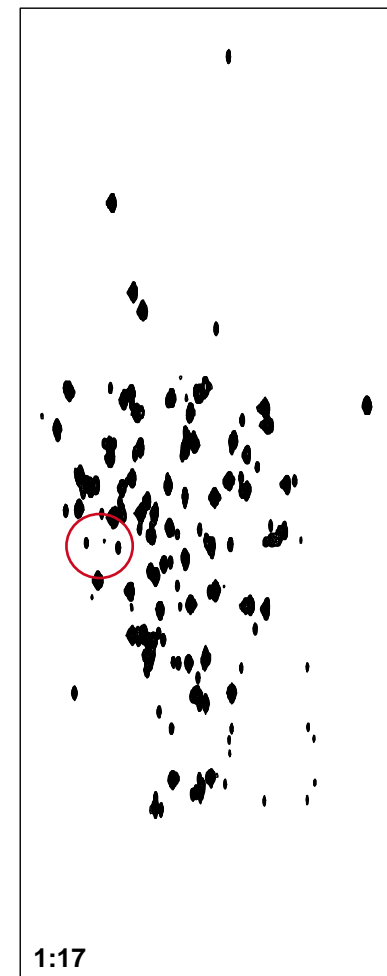
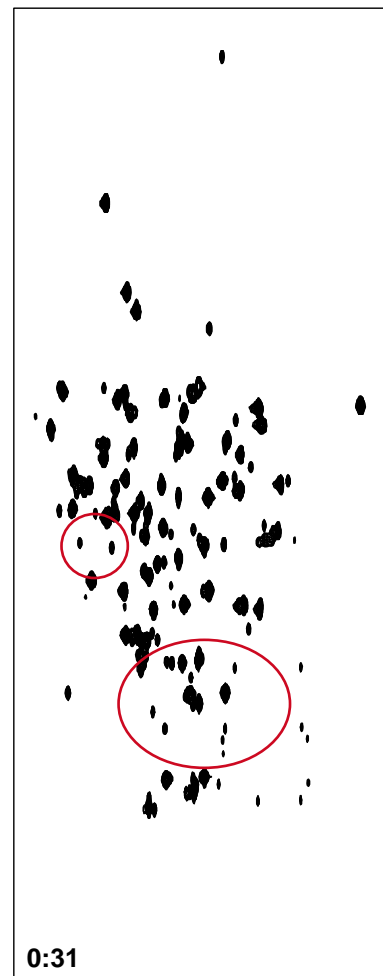
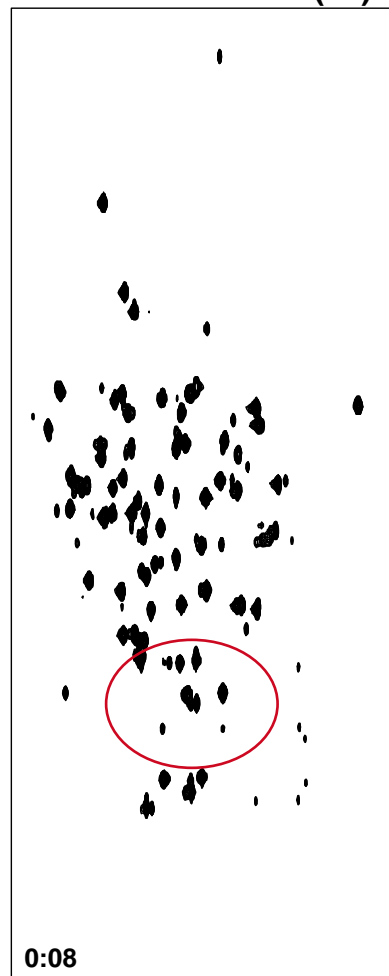
NUS 25%, CEXP: nnn

ref. (FFT)

NCOMP = 0 (15)

NCOMP = 30

NCOMP = 60



166  
168  
170  
172  
174  
176  
178  
180  
[ppm]

[ppm] 8.5 8.0 7.5 7.0 6.5 6.0

[ppm] 8.5 8.0 7.5 7.0 6.5 6.0

[ppm] 8.5 8.0 7.5 7.0 6.5 6.0

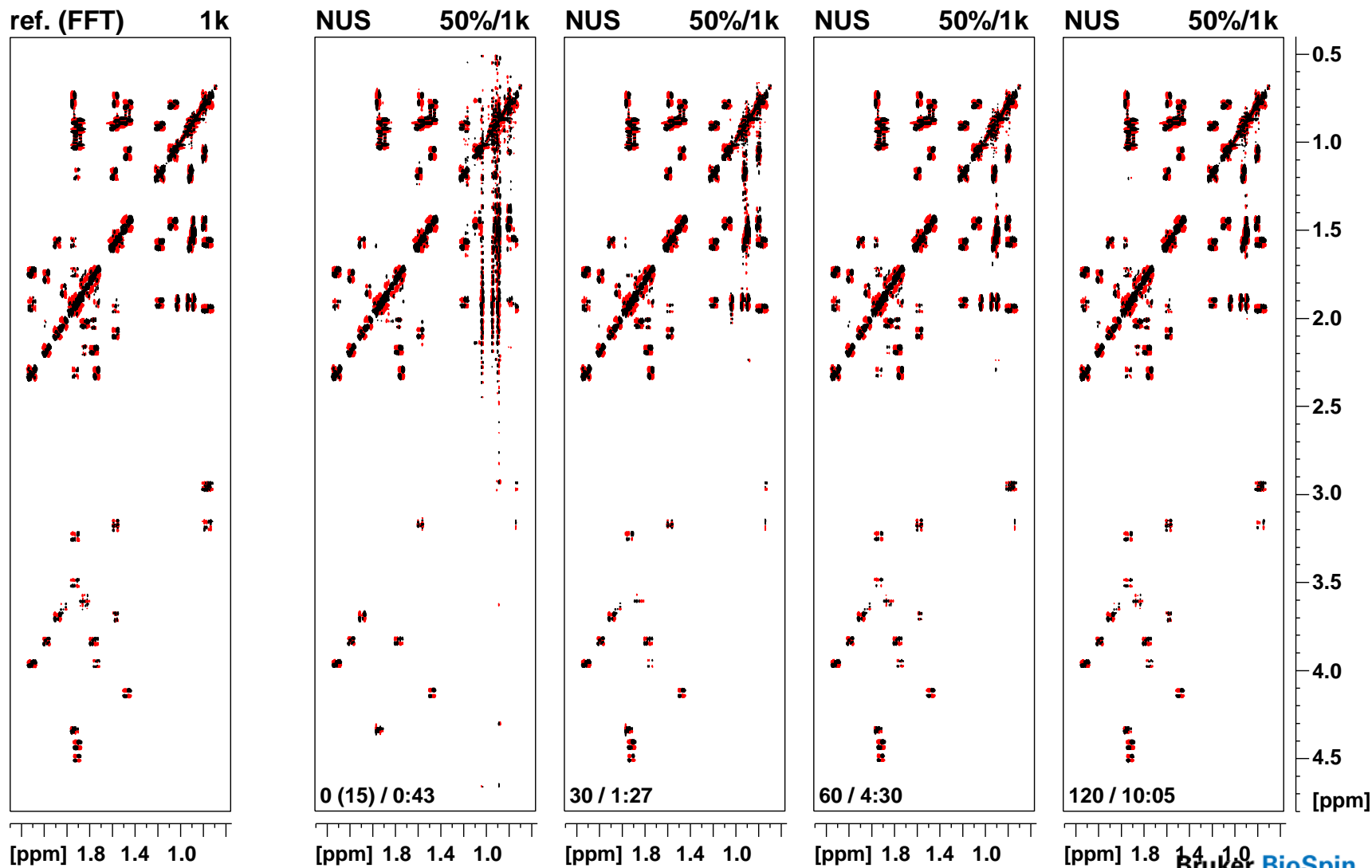
[ppm] 8.5 8.0 7.5 7.0 6.5 6.0

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# Additional processing parameters



## COSY - dfph



# Additional processing parameters



Spectrum ProcPars AcqPars Title PulseProg Peaks Integrals Sample Structure Plot Fid

S 12.. M

Reference  
Window  
Phase  
Baseline  
Fourier  
NUS  
Peak  
Automation  
Miscellaneous  
User

^ NUS (Non Uniform Sampling) parameters

Mdd_mod	mdd		MDD mode
MddCEXP	FALSE	FALSE	RMDD/MDD flag
MddCT_SP	FALSE	FALSE	Constant time
MddF180	FALSE	FALSE	Delayed sampling flag
MddNCOMP	0		Number of components
MddPHASE	0	0	Phase
MddSRSIZE [ppm]	0		Sub region size

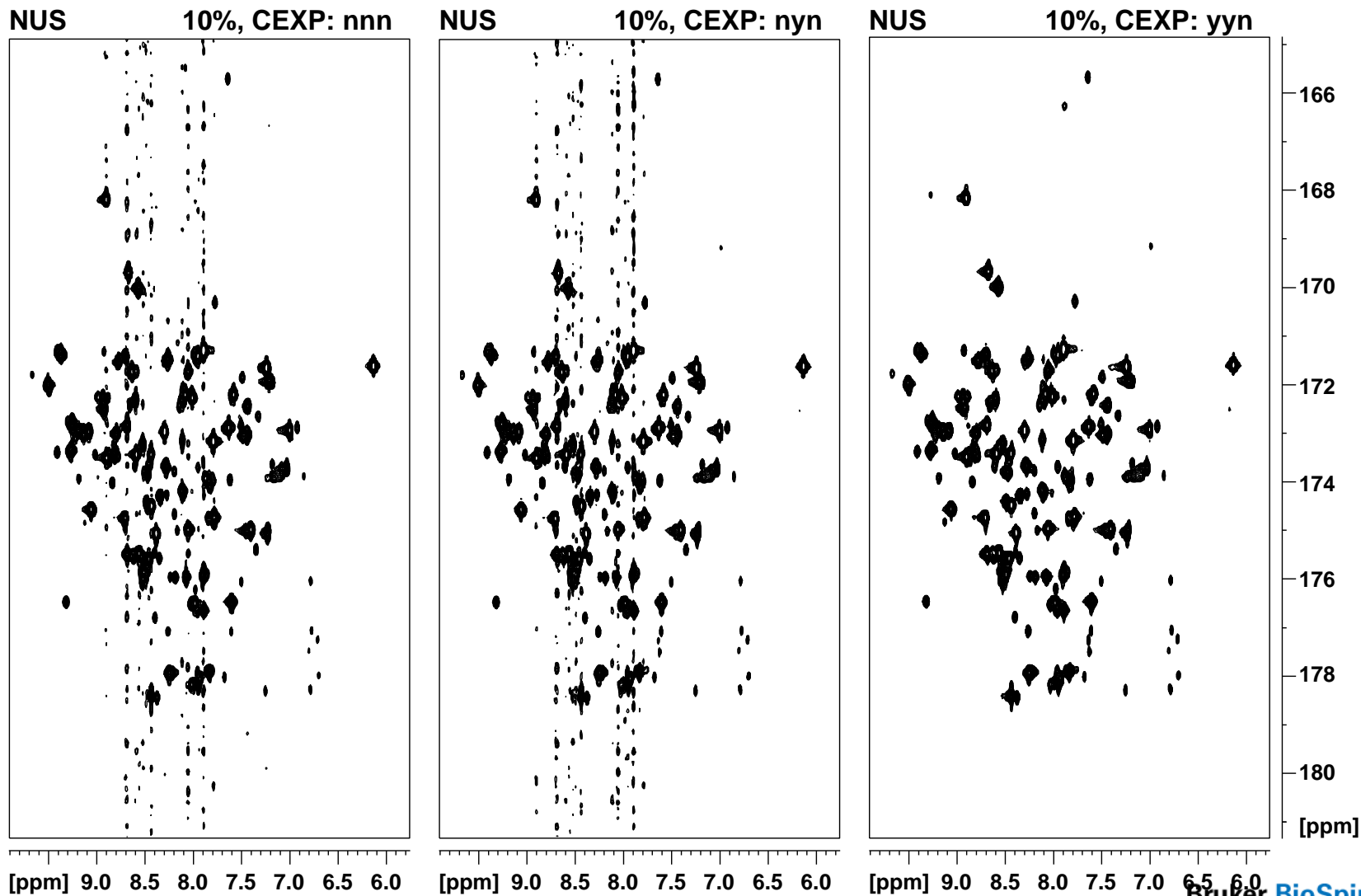
## Recursive MDD

- required for 2D
- can also help with nD
- processing times are longer

# Additional processing parameters



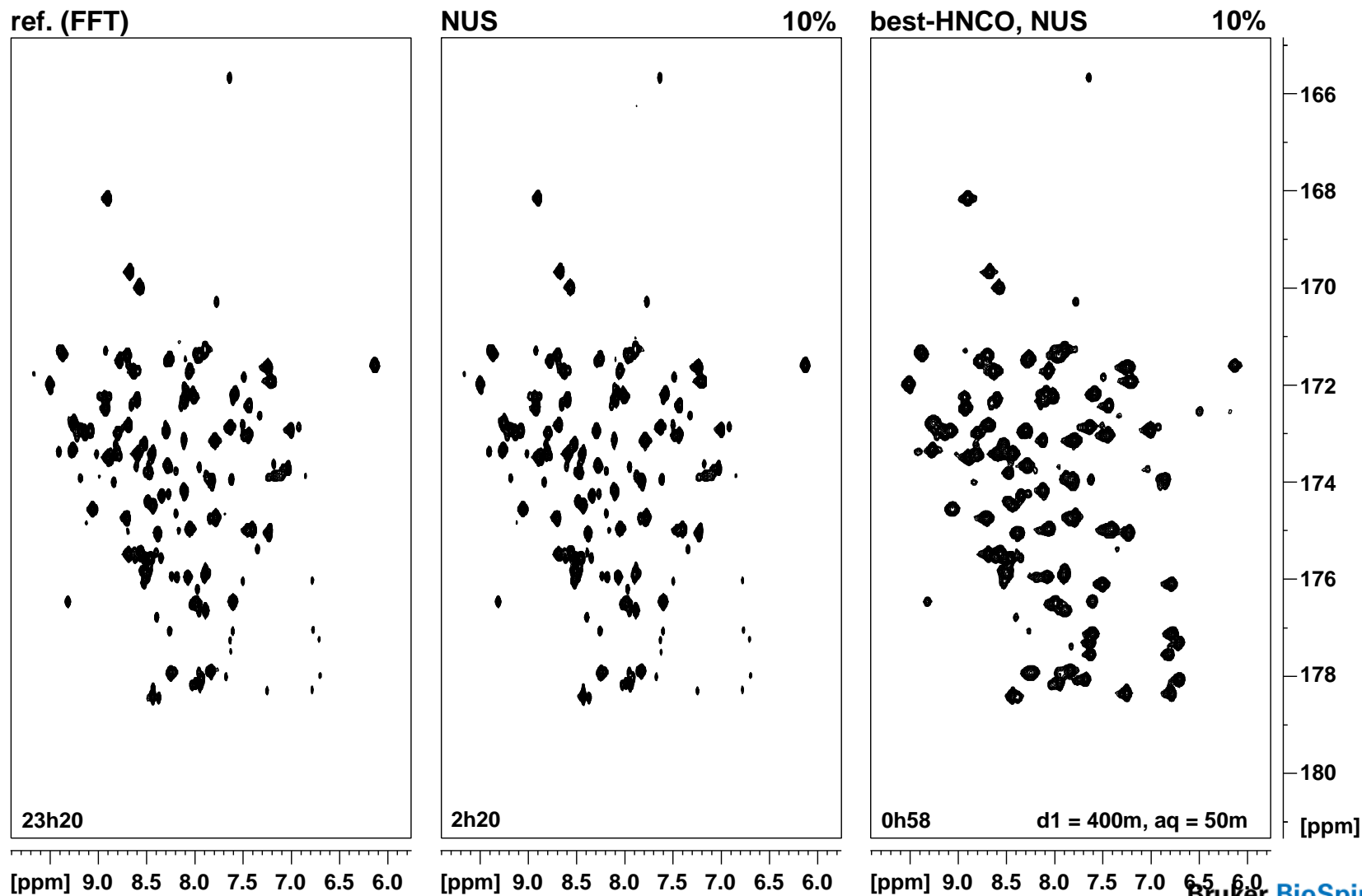
## HNCO: F1F3 projection



# Implementation



## HNCO: F1F3 projection

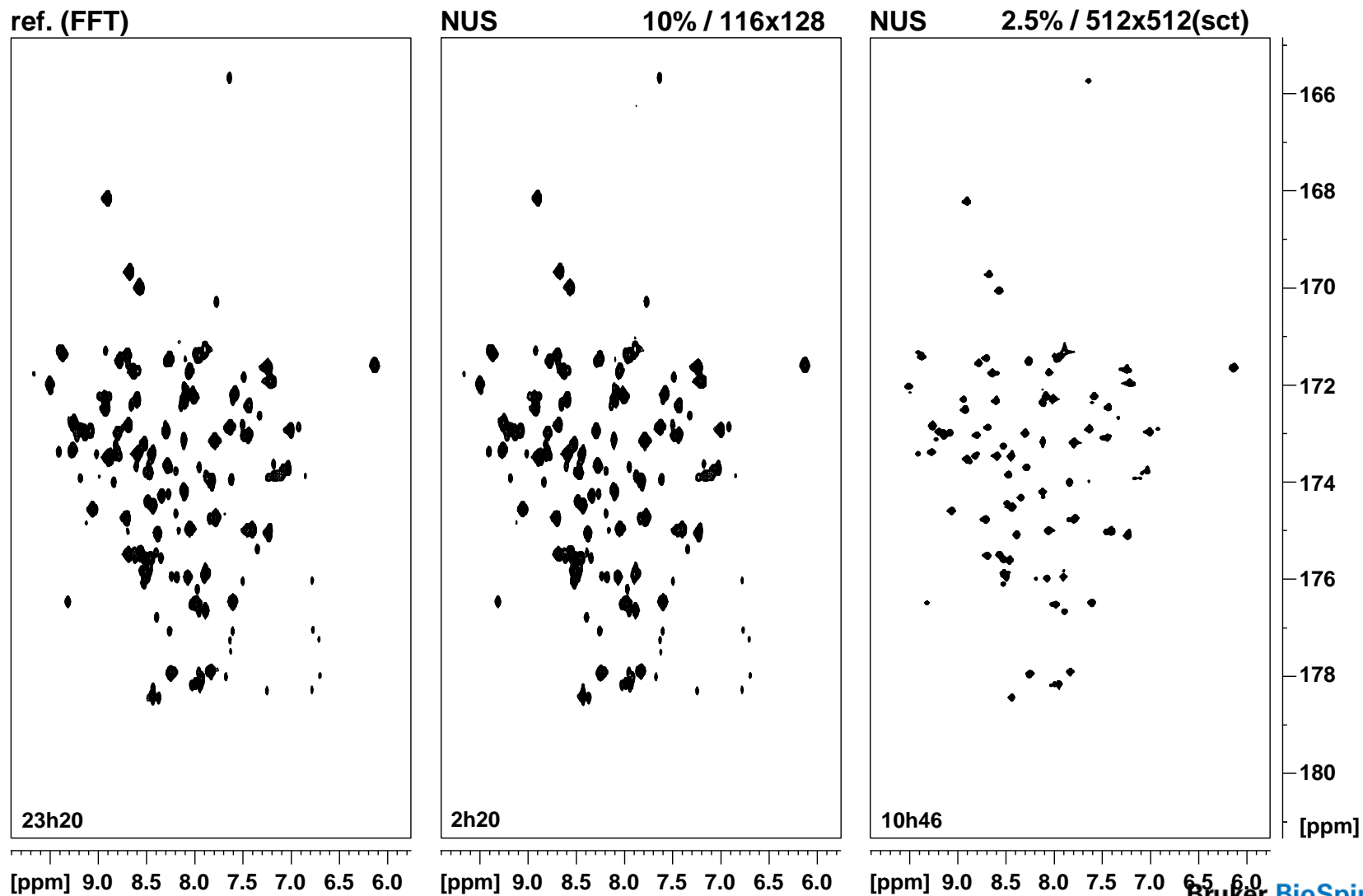




# Implementation



## HNCO: F1F3 projection



# New processing algorithm



The screenshot shows the Bruker software interface with the 'ProcPars' tab selected. The 'NUS (Non Uniform Sampling) parameters' section is highlighted with a red box. The 'Mdd\_mod' dropdown menu is open, showing 'mdd' and 'cs' options. 'cs' is circled in red. The 'NUS (Non Uniform Sampling) parameters' section is highlighted with a red box.

Parameter	Value	Flag	Description
Mdd_mod	mdd		MDD mode
MddCEXP	FALSE	▼	RMDD/MDD flag
MddCT_SP	FALSE	▼	Constant time
MddF180	FALSE	▼	Delayed sampling flag
MddNCOMP	0		Number of components
MddPHASE	0	0	Phase
MddSRSIZE [ppm]	0		Sub region size

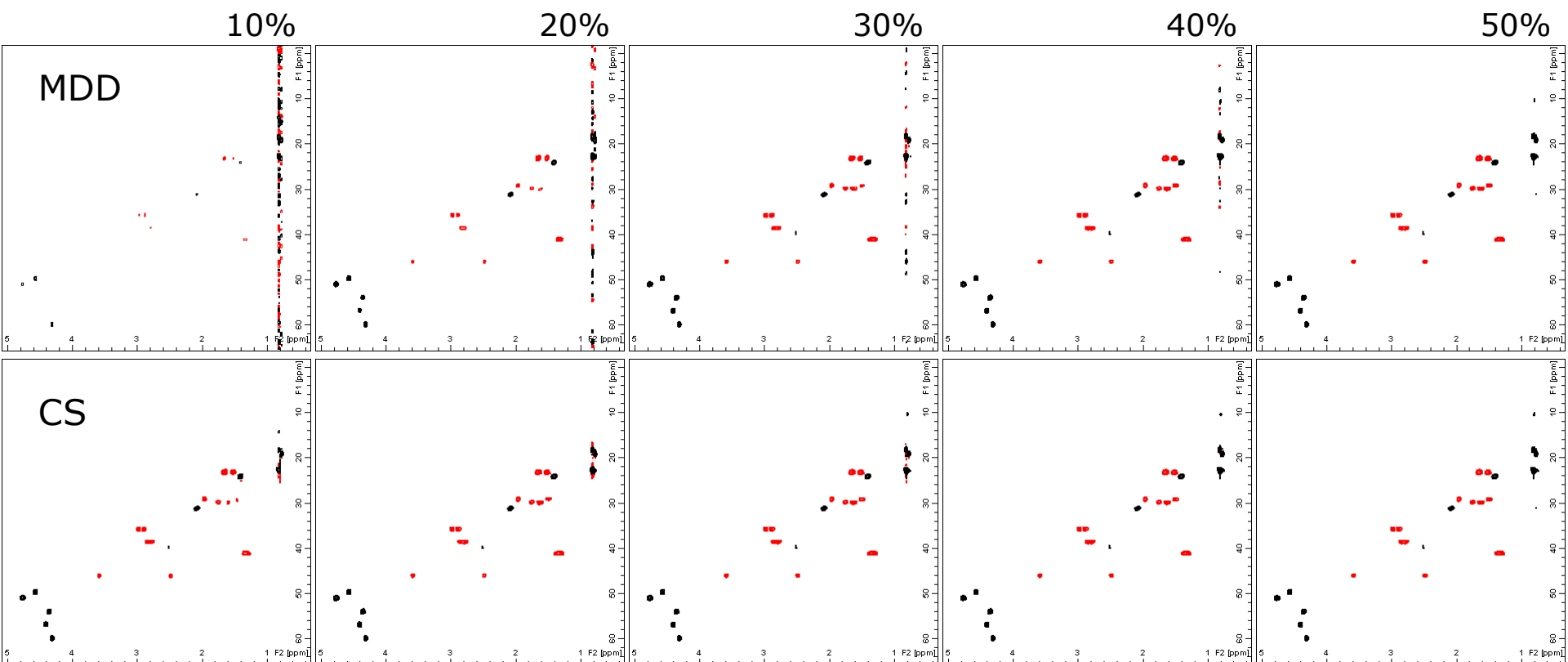
## CS - Compressed Sensing

- significantly improves 2D processing
- can be helpful for nD as well
- additional license needed

# MDD vs. CS processing



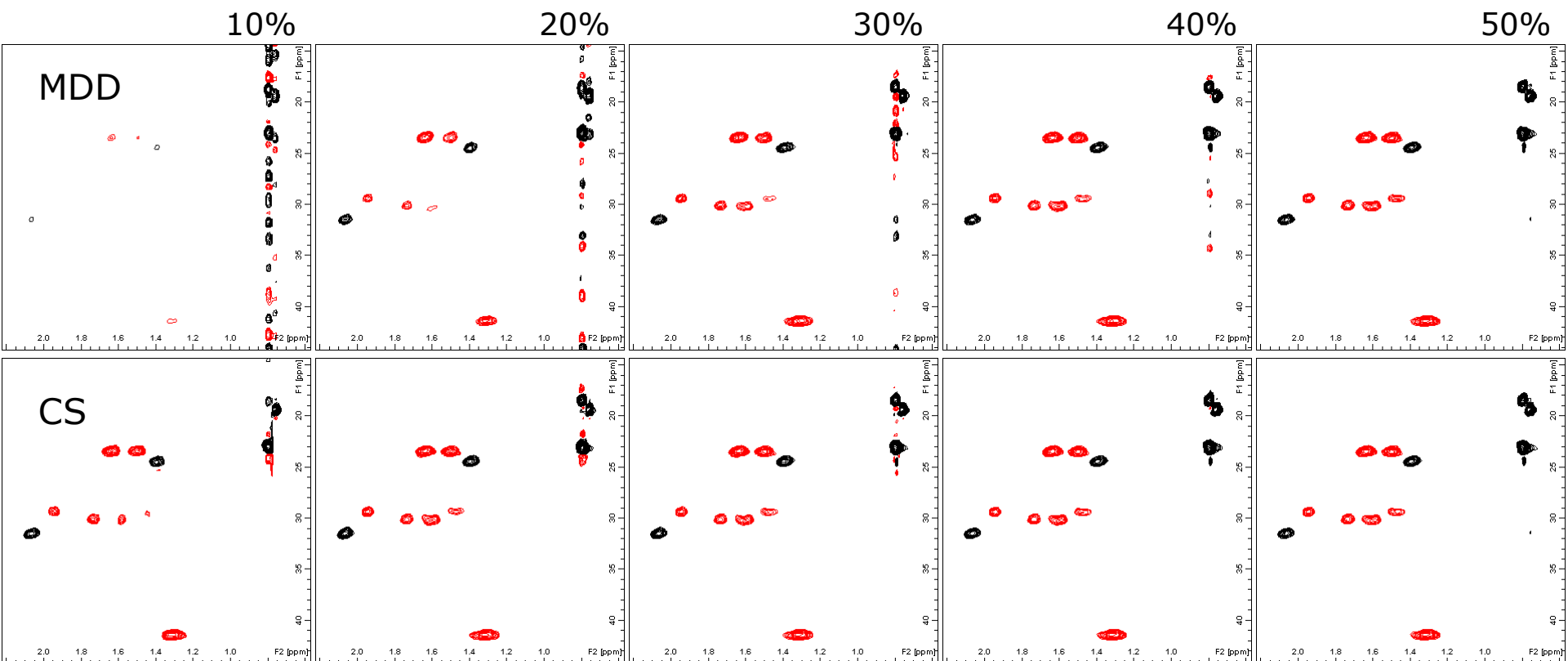
50mM Gramicidin  
edited HSQC  
td=256



# MDD vs. CS processing



50mM Gramicidin  
edited HSQC  
td=256



# Pushing the limits



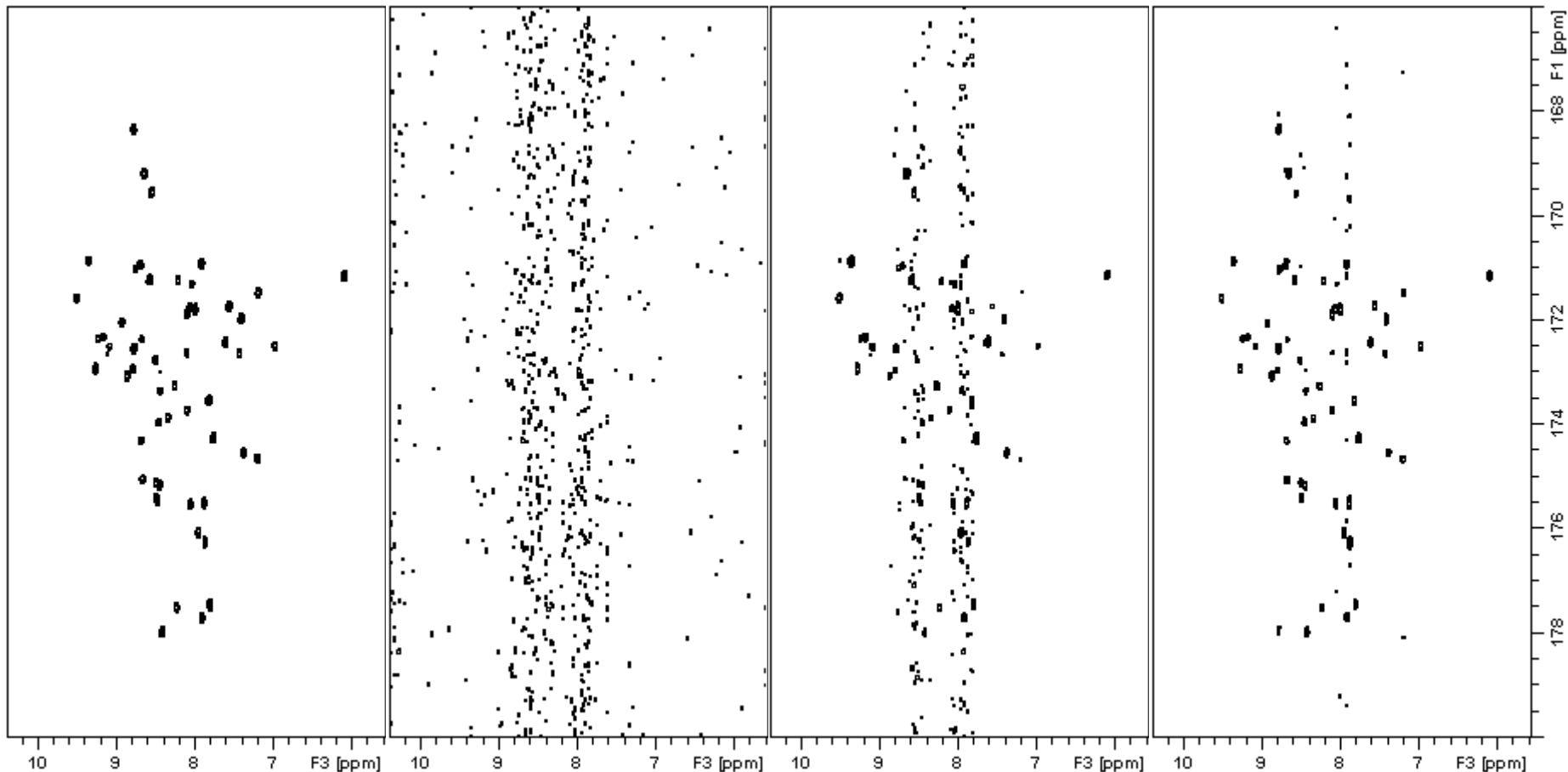
## HNCO: F1F3 projection

ref. (FFT)

MDD

RMDD

CS



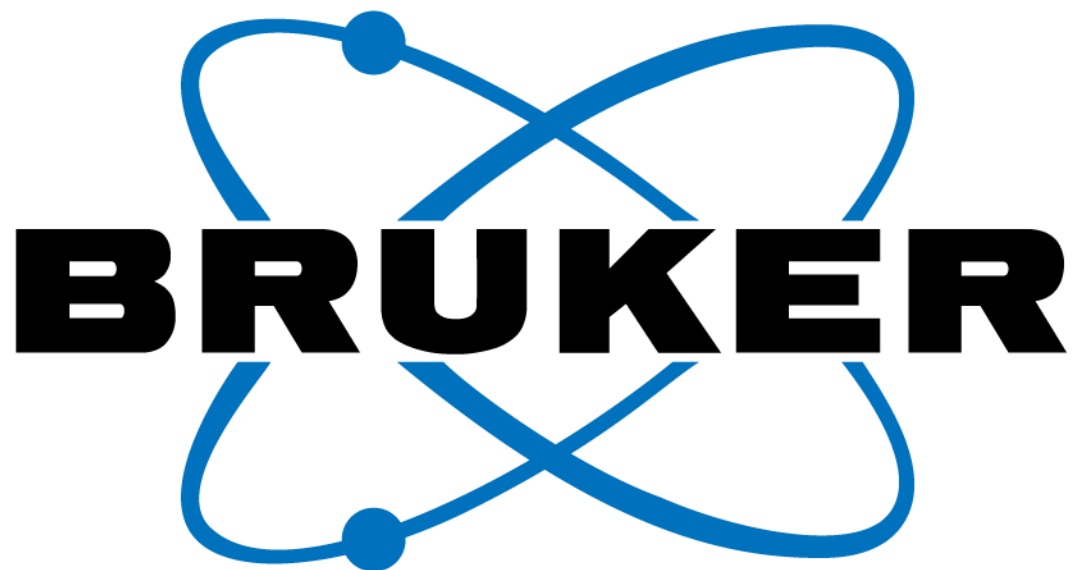
Ubiquitin

NUS 4% / 80x128

17min acquisition

**Bruker BioSpin**

**Thank  
You**



[www.bruker-biospin.com](http://www.bruker-biospin.com)