Fast Data-Acquisition in NMR Spectroscopy

Detlef Moskau (2008)
Bruker Biospin AG

The different methods …

Reduced number of Increments in *nD* experiments:

- Non linear sampling	(Wagner, …)
- Reduced dimensionality (GFT /MWD / APSY)	(Szyperski,Gronenborn,Brutscher, Billeter,Wüthrich..)
- Projection Reconstruction	(Kupce & Freeman)
- Spectrum folding	(Sidebottom, Sakhaii)
- Covariance	(Brüschweiler,..)

Slice selection:

- Single scan	(Frydman, Pelupessy)

Enhanced Repetition rate:

- Rapid Pulsing	(Ross, Pervushin, Brutscher)

Pseudo-2D Representation of multiple selective 1D-experiments:

- Hadamard	(Kupce & Freeman)
- …	

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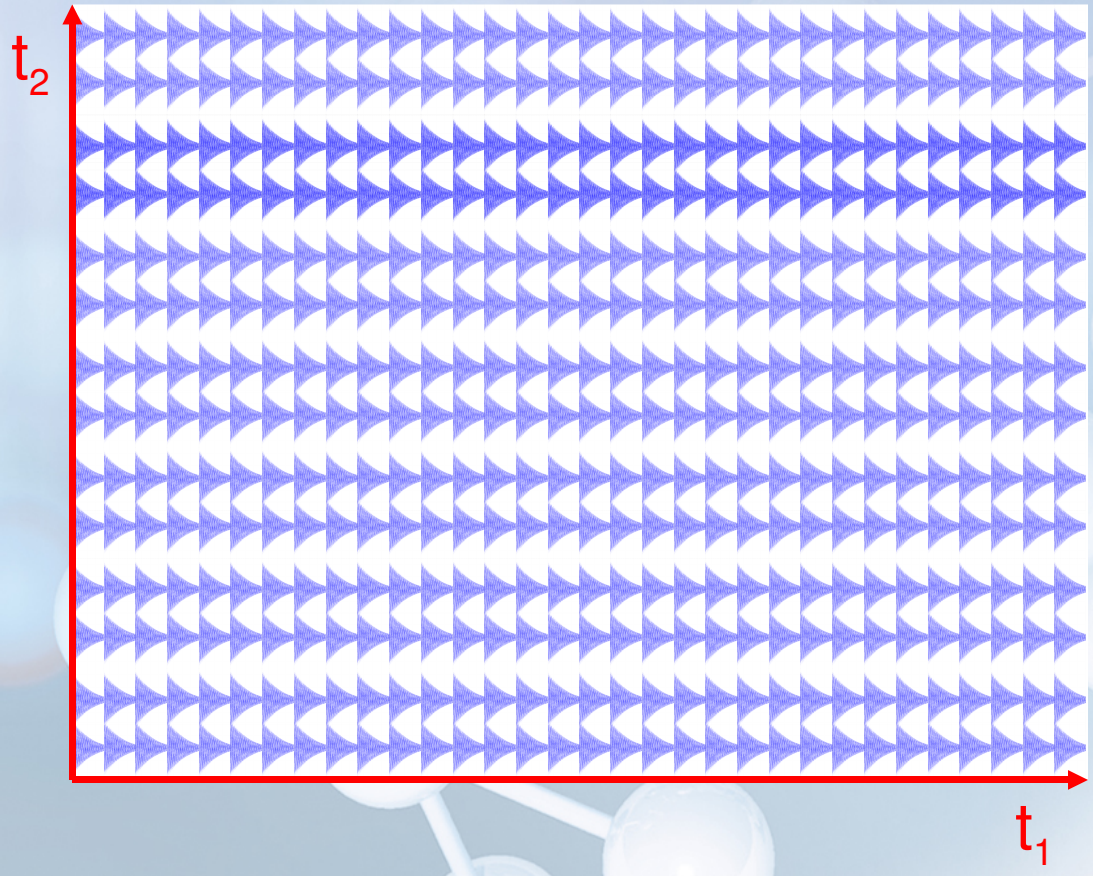
Reduced Number of Increments

Full Sampling



Time consuming

Reduced Number of Increments

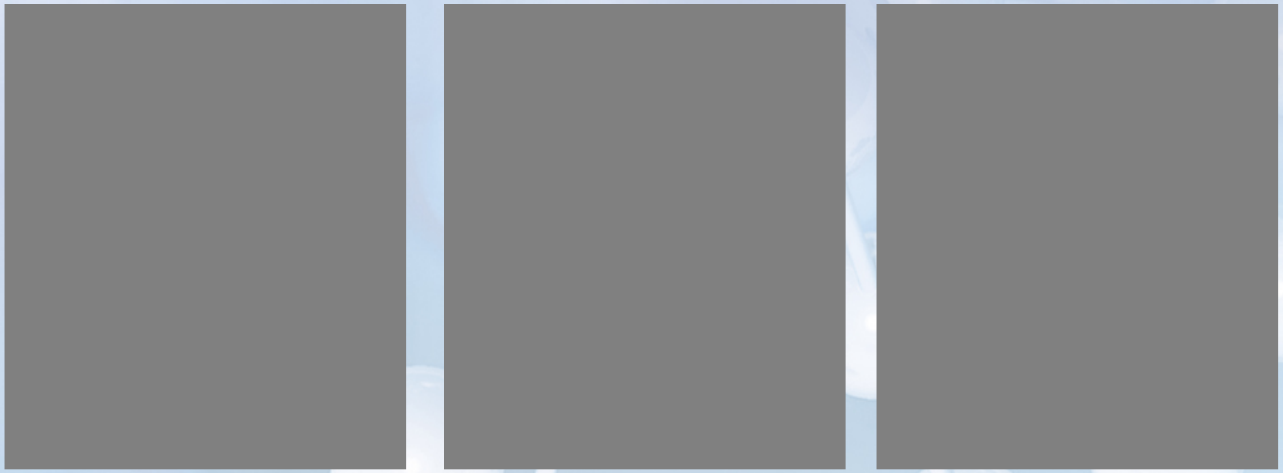
General Approach:

Acquisition: apply a ‘mask’
number of increments is reduced according to ‘mask’

Processing: different mathematical data treatment depending on the ‘mask’ that was used

Reduced Number of Increments

‘Masks’ being used:



Reduced Number of Increments

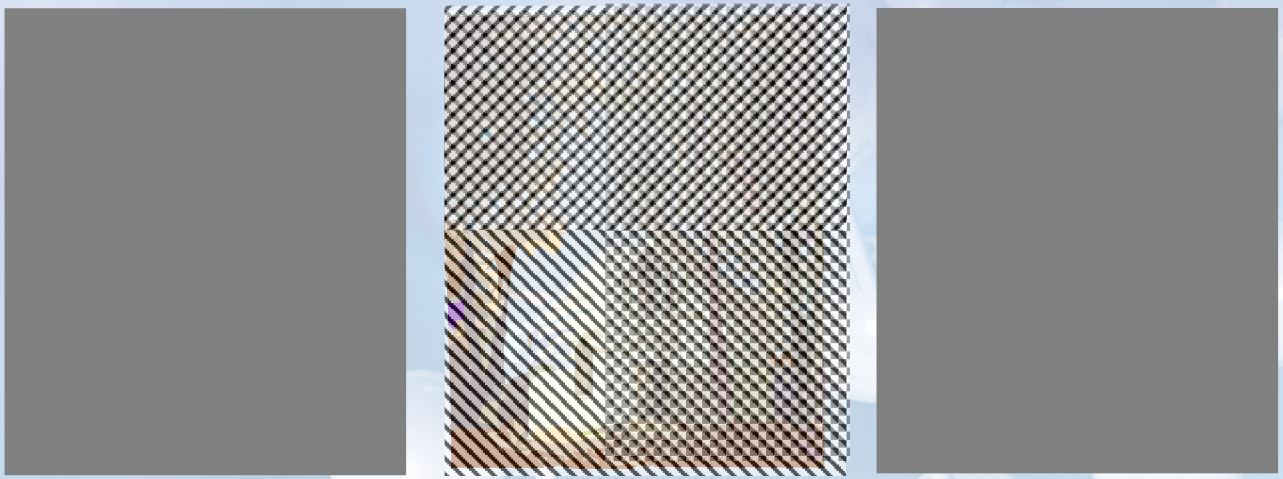
‘Masks’ being used:

Small window

Reduced Number of Increments

‘Masks’ being used:

random pattern

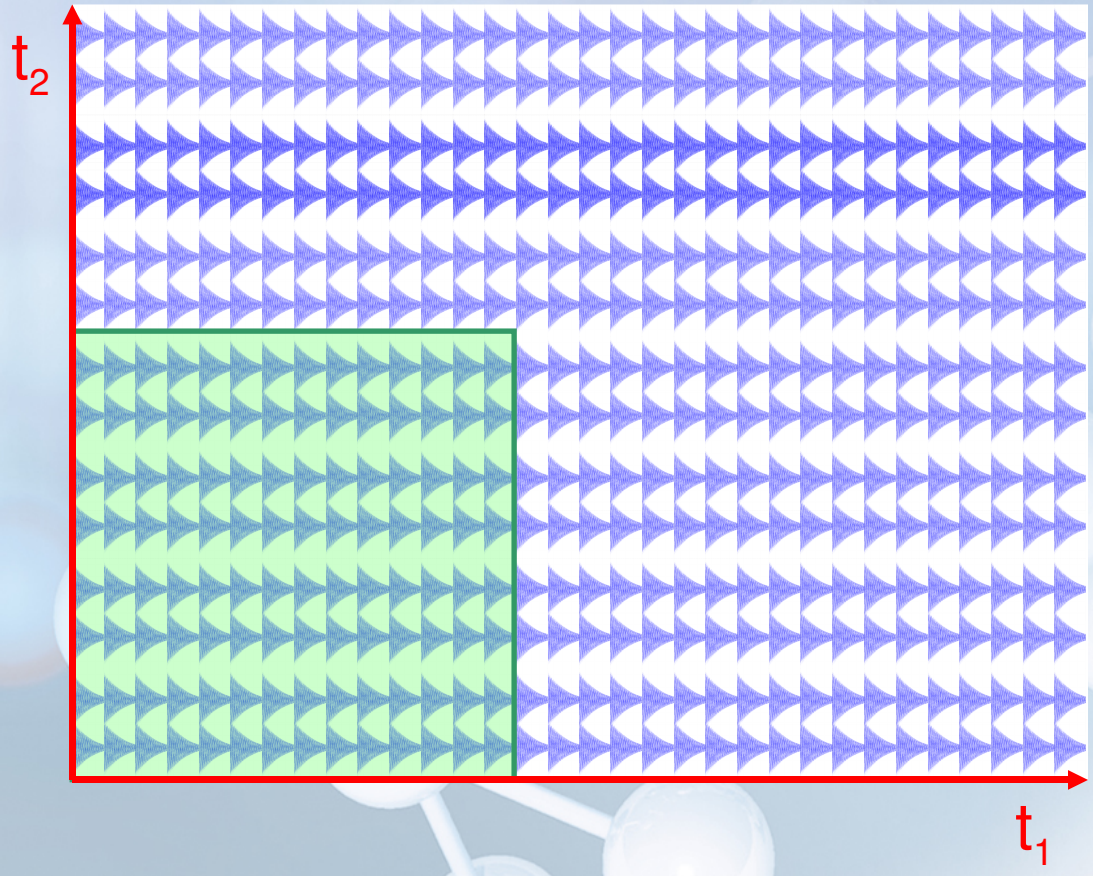


Reduced Number of Increments

‘Masks’ being used:

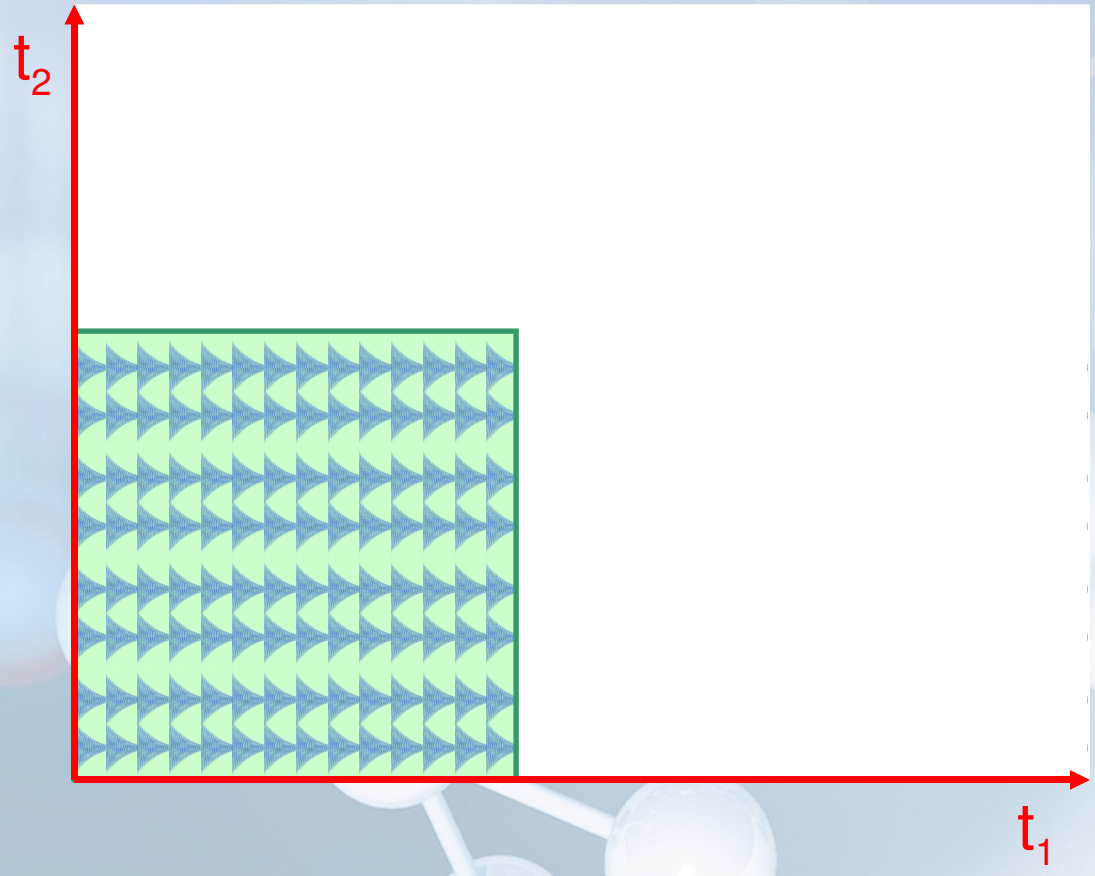
Reduced Number of Increments

1) Reduced, equidistant samples



Reduced Number of Increments

1) Reduced equidistant samples Used by:



- Spectral folding
  Reduced indirect SW
- Covariance
  ‚Transfer‘ resolution of direct dimension to indirect dimension

Covariance

Principle

After FT in direct dimension:

Compare all columns (indirect dimension)

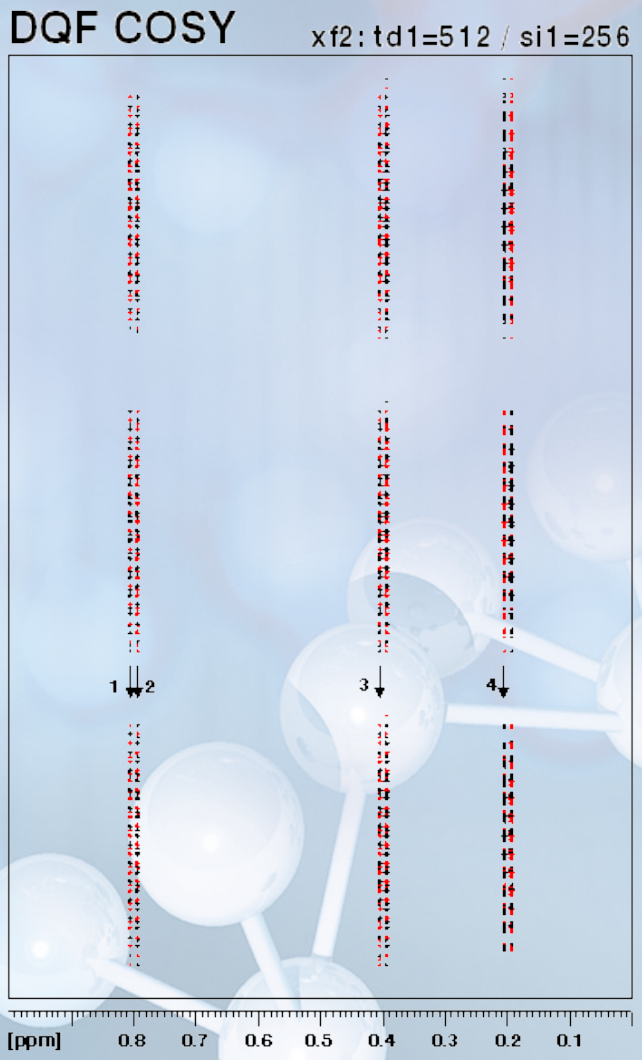
For columns which are similar:

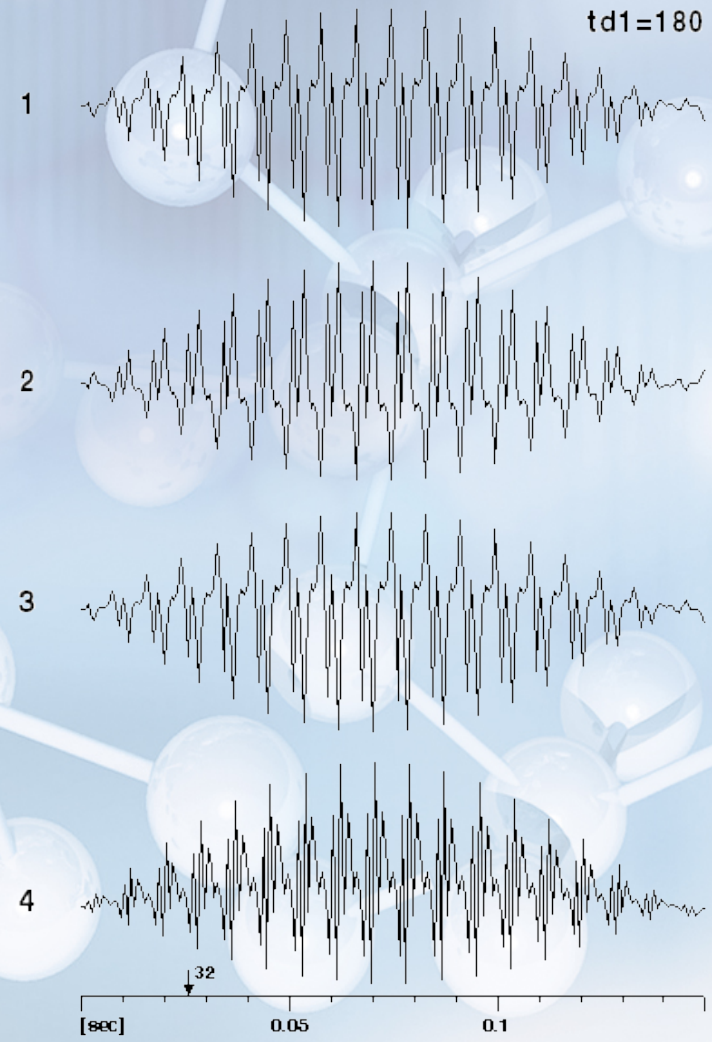
transfer info of frequency in direct dimension to the indirect dimension

No further FT applied

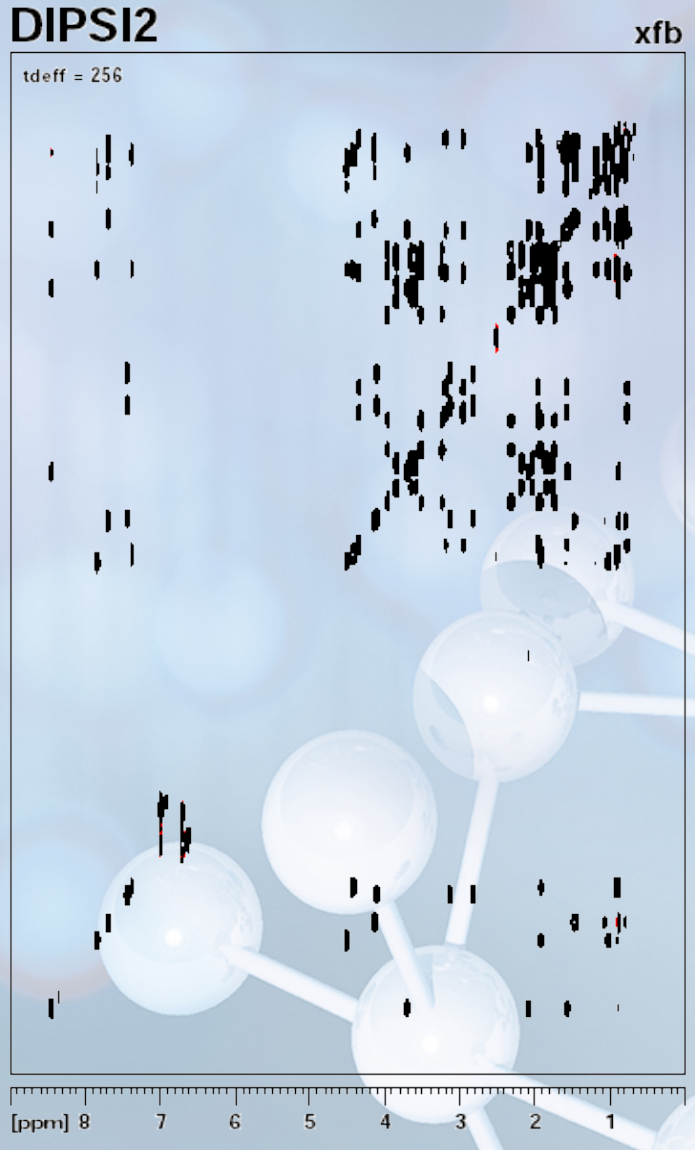
Advantage: enhanced resolution in indirect dimension

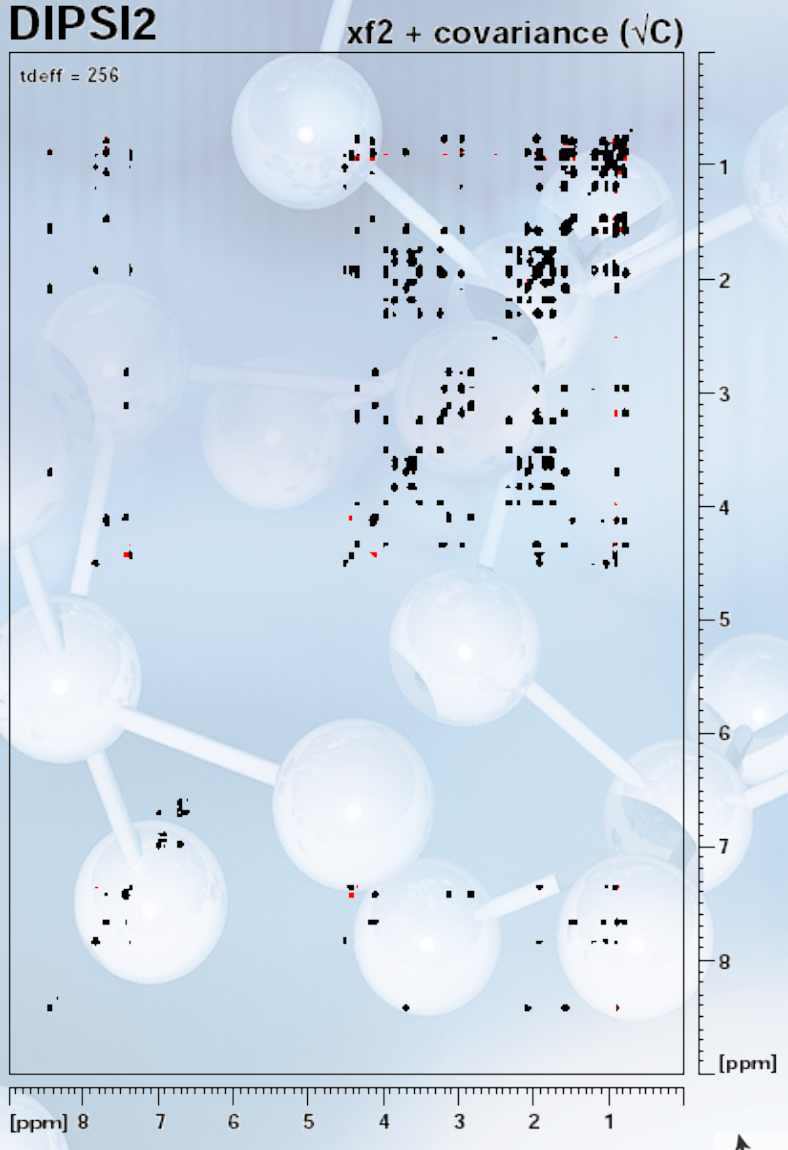
Covariance


DQF COSY
xf2: td1=512 / si1=256
1
2
3
4
[ppm]
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1


td1=180
1
2
3
4
32
[sec]
0.05
0.1

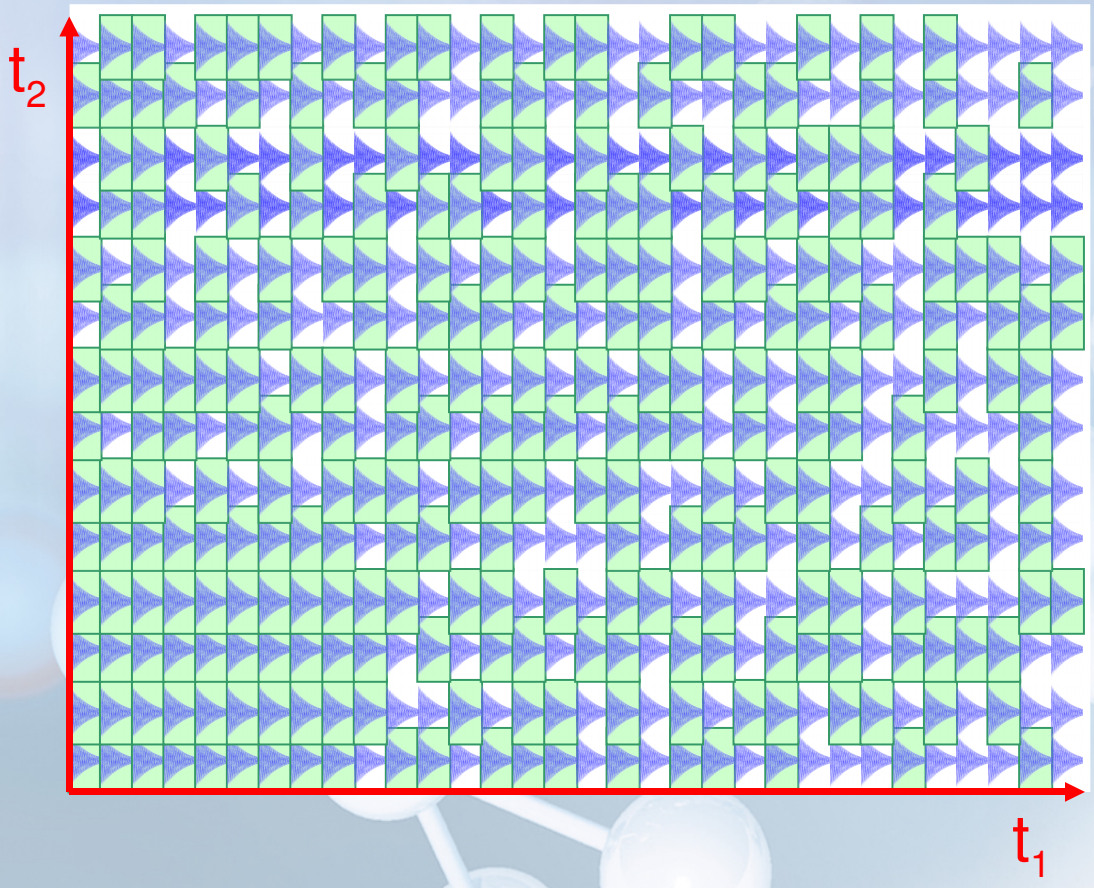
Covariance


DIPSI2
xfb
tdeff = 256
[ppm] 8 7 6 5 4 3 2 1


DIPSI2
xf2 + covariance (√C)
tdeff = 256
[ppm] 8 7 6 5 4 3 2 1
1 2 3 4 5 6 7 8
[ppm]

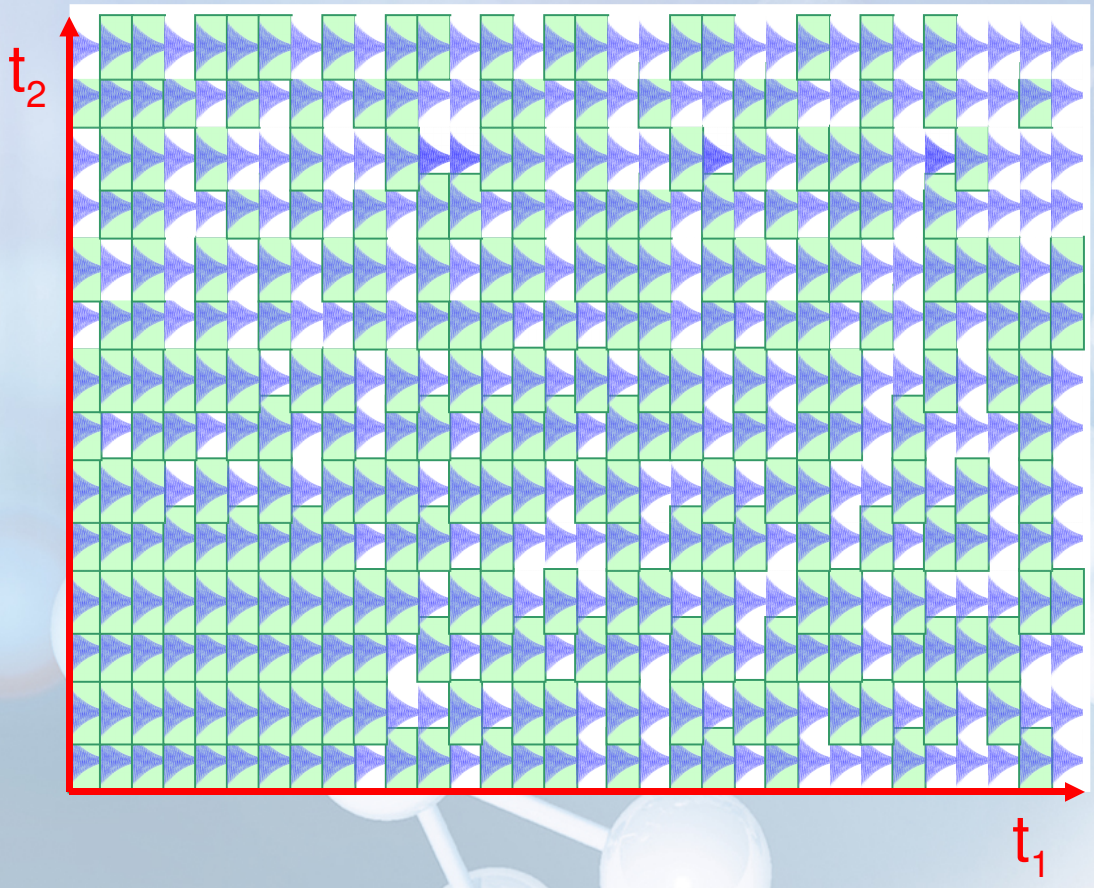
Reduced Number of Increments

3) Non-linear sampling



Reduced Number of Increments

3) Non-linear sampling

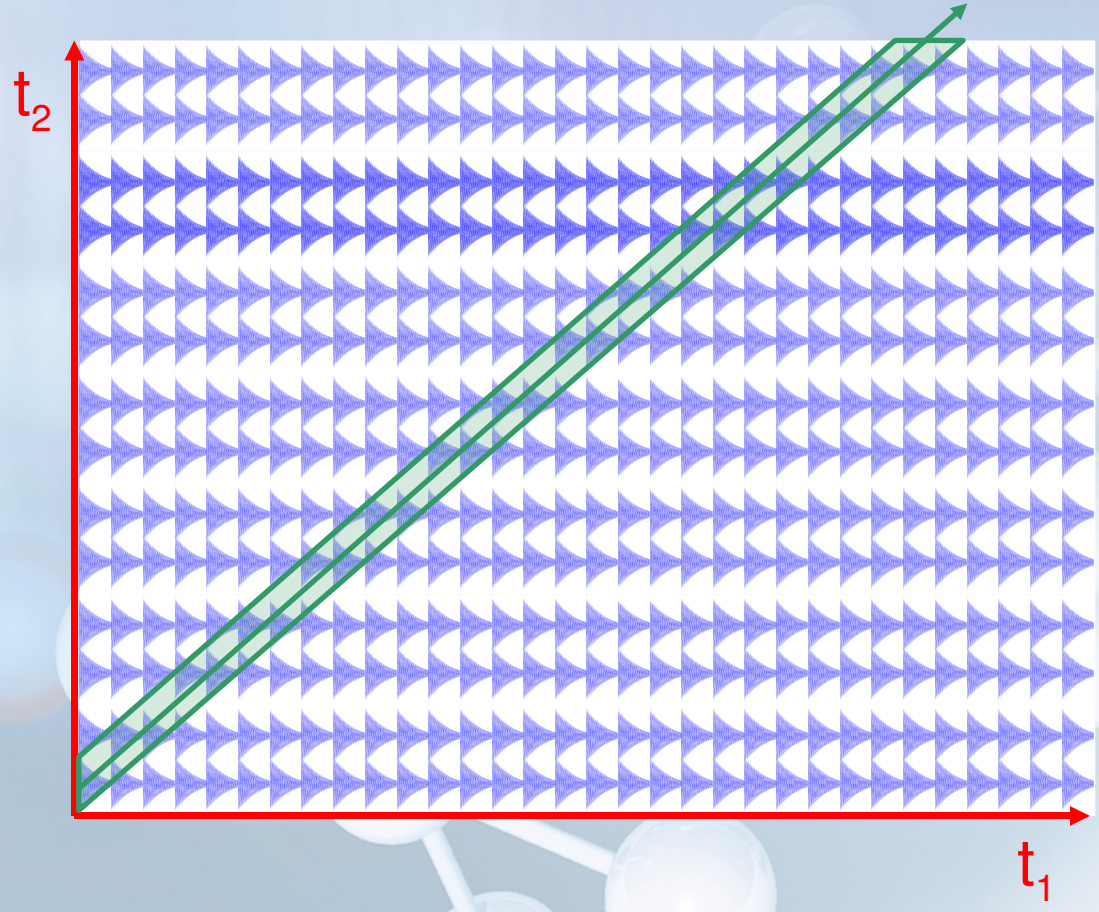


Challenge:

- Processing
  e.g. Maximum entropy methods

Reduced Number of Increments

3) Reduced Dimensionality / Projection Spectroscopy



Reduced Number of Increments

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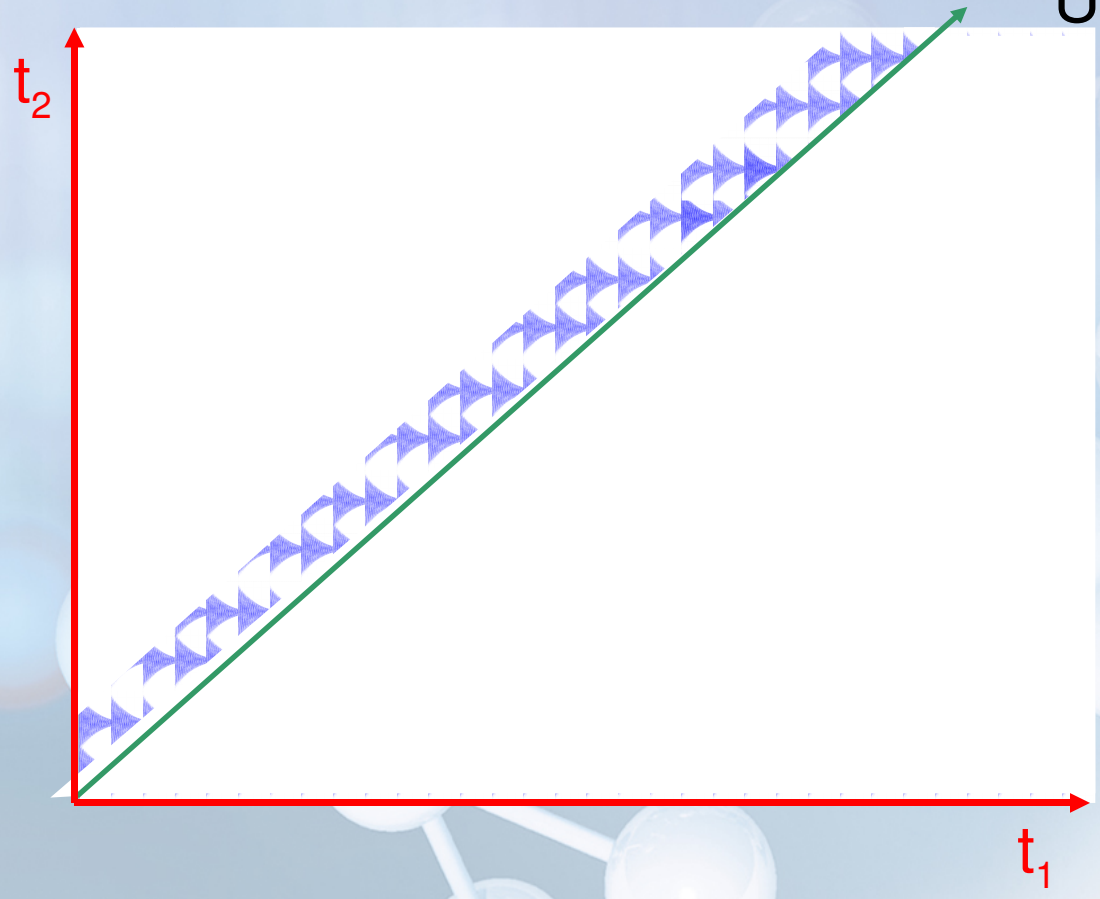

Used by:

- GFT
- Proj. Reconstruction
  Result: spectrum
- APSY
  Result: peak list

APSY

APSY: Automated Projection SpectroscopY

Automated recording of a discrete set of projections for *N*-dimensional experiments *(N ≥ 3)*

Projection angles: default or user defined values

Number of projections:

a) Fixed number

b) Until convergence of peak list

Automated identification of correlation peaks ***GAPRO***

Result: a peak list

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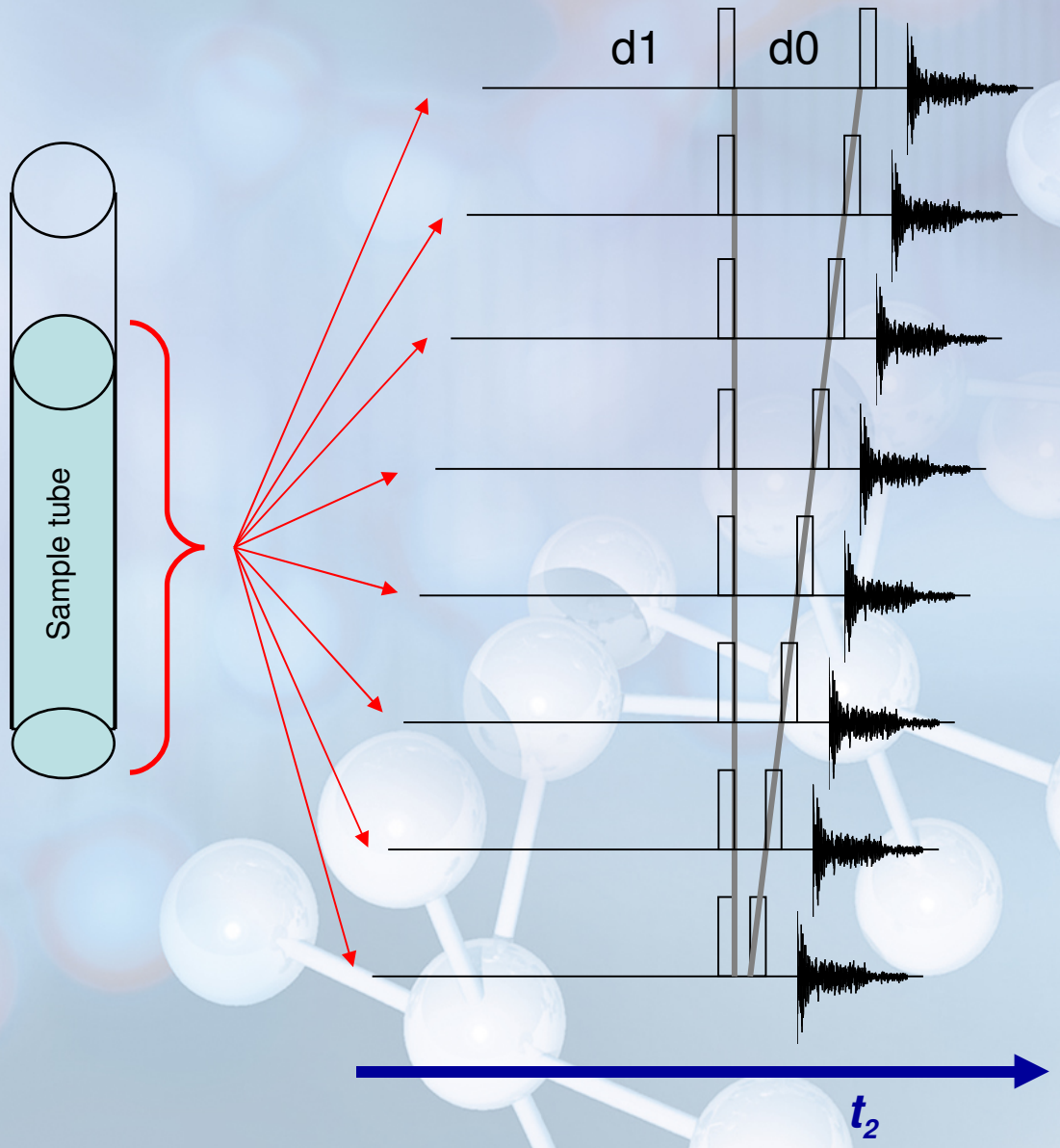
Single Scan: Slice Selection

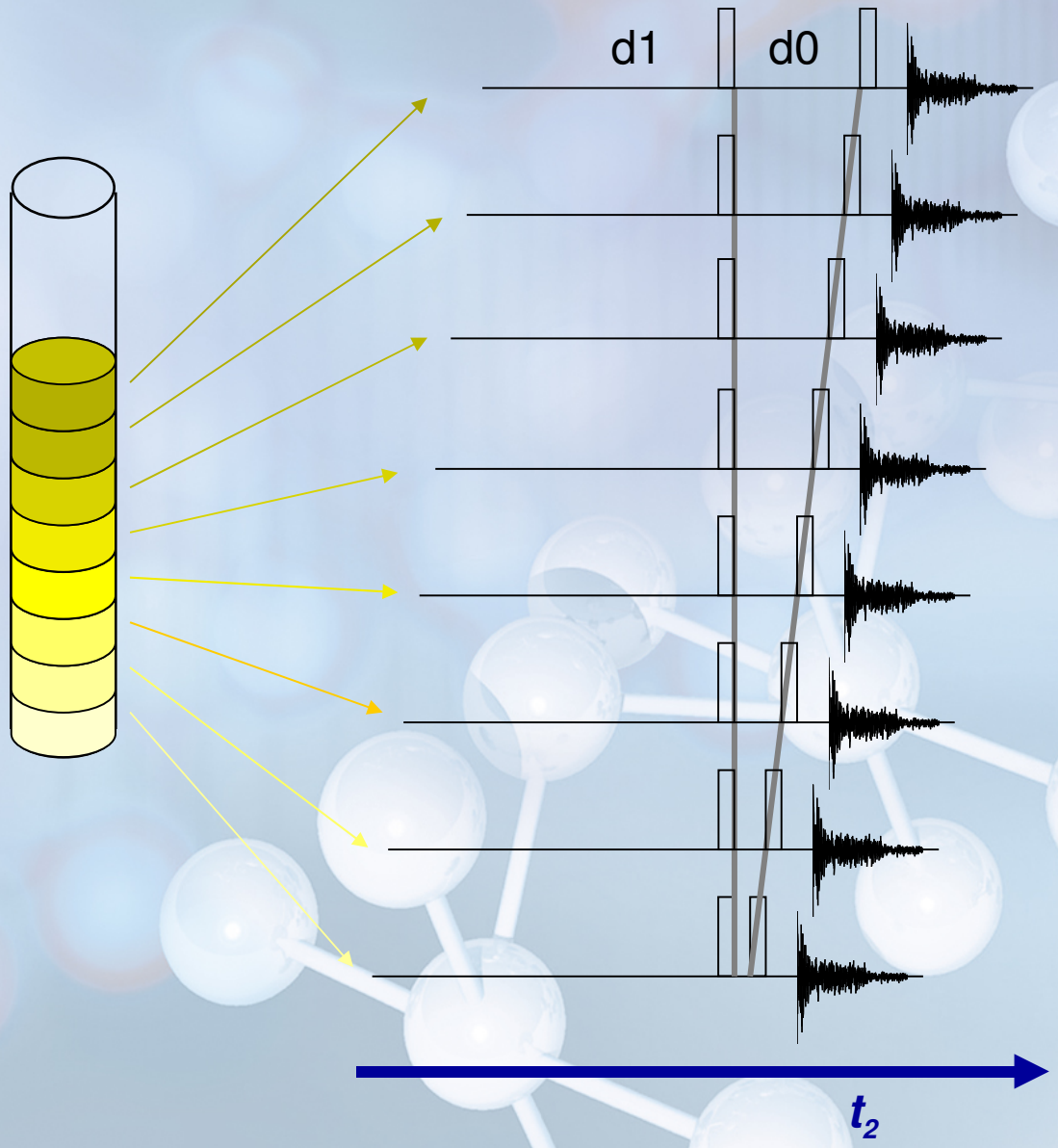


Standard Approach:

3. The entire sample is excited

5. Relaxation delay between individual scans / increments

Single Scan: Slice Selection



Slice Selection:

3. Each slice corresponds to one increment
5. No need for a relaxation delay
7. Pulse sequence: EPI

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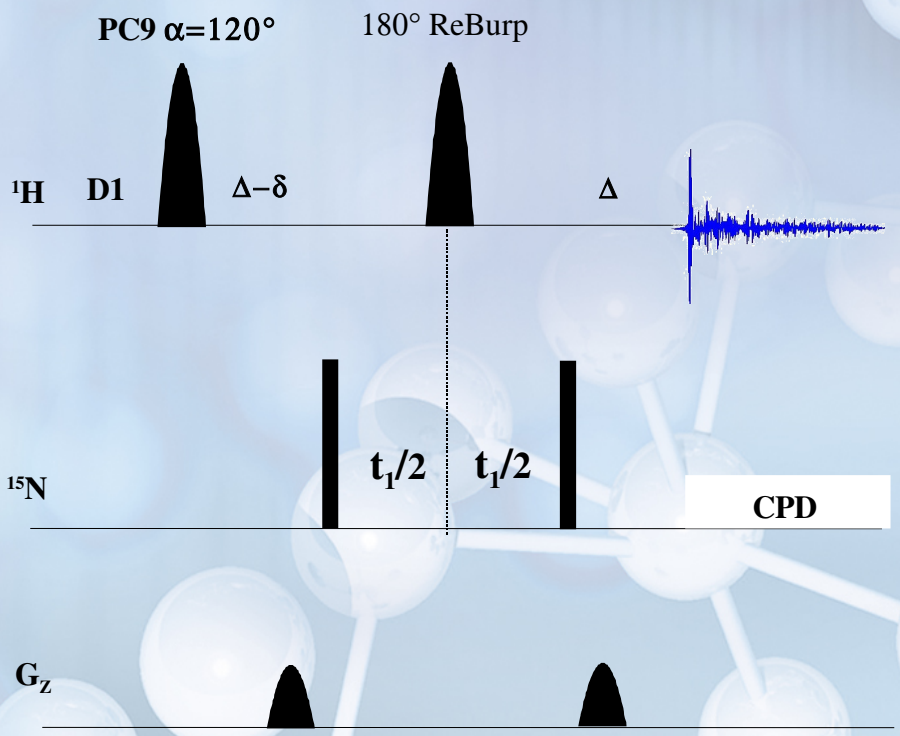
So-Fast HMQC: Principles



Rapid Pulsing:

- Experiment is based on very fast repetition rate
- Extreme cases: D1 = 1ms
- Selective excitation of NH protons only, keep $C_{aliphatic}$ along +Z axis
- Enhanced T_1 relaxation of NH protons
- Use of the Ernst angle:

Selective pulse on NH protons:
120° - 180° = -60°

P. Schanda and B. Brutscher, J. Am. Chem. Soc., 127, 8014, 2005

A. Ross, M. Salzmann and H. Senn, J. Biomol. NMR, 10, 389, 1997

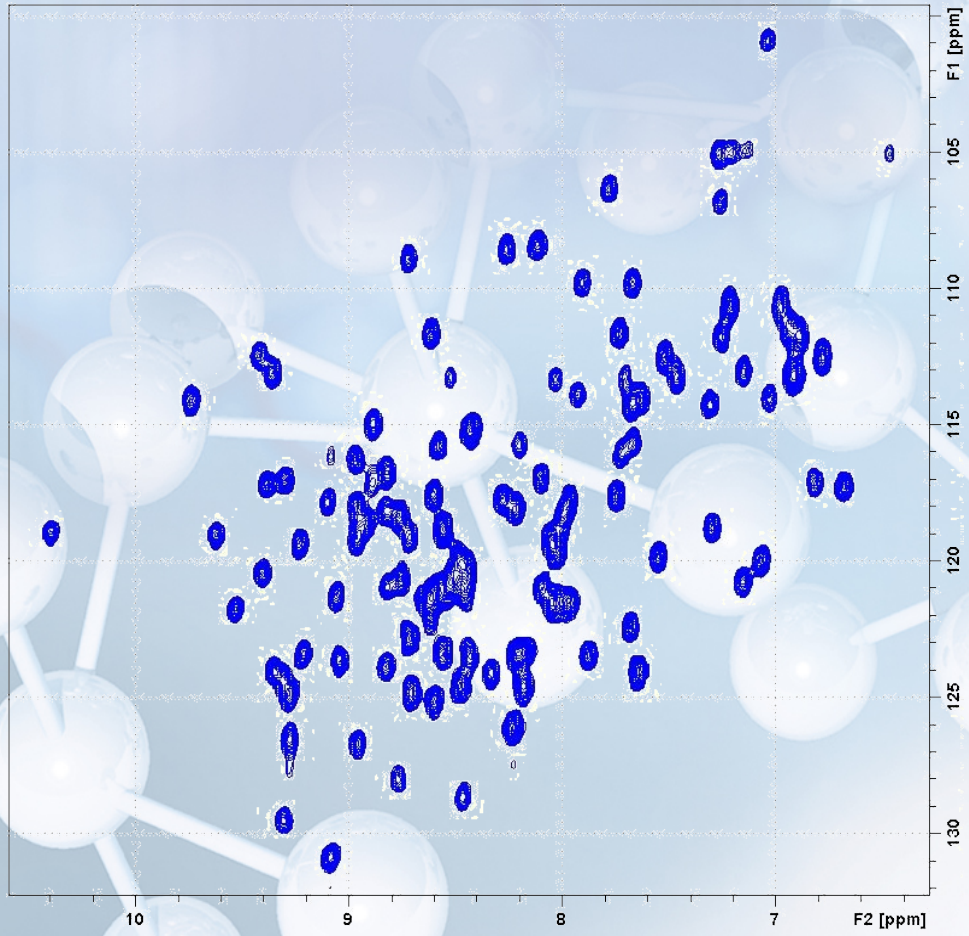
So-Fast HMQC: 2 mM Ribonuclease (TCI Cryoprobe 600 MHz)

Experiment time 65s

D1= 0.3 s

AQ(f2)=41 ms / 700 complexes points

AQ (f1)=13 ms / 40 complex points

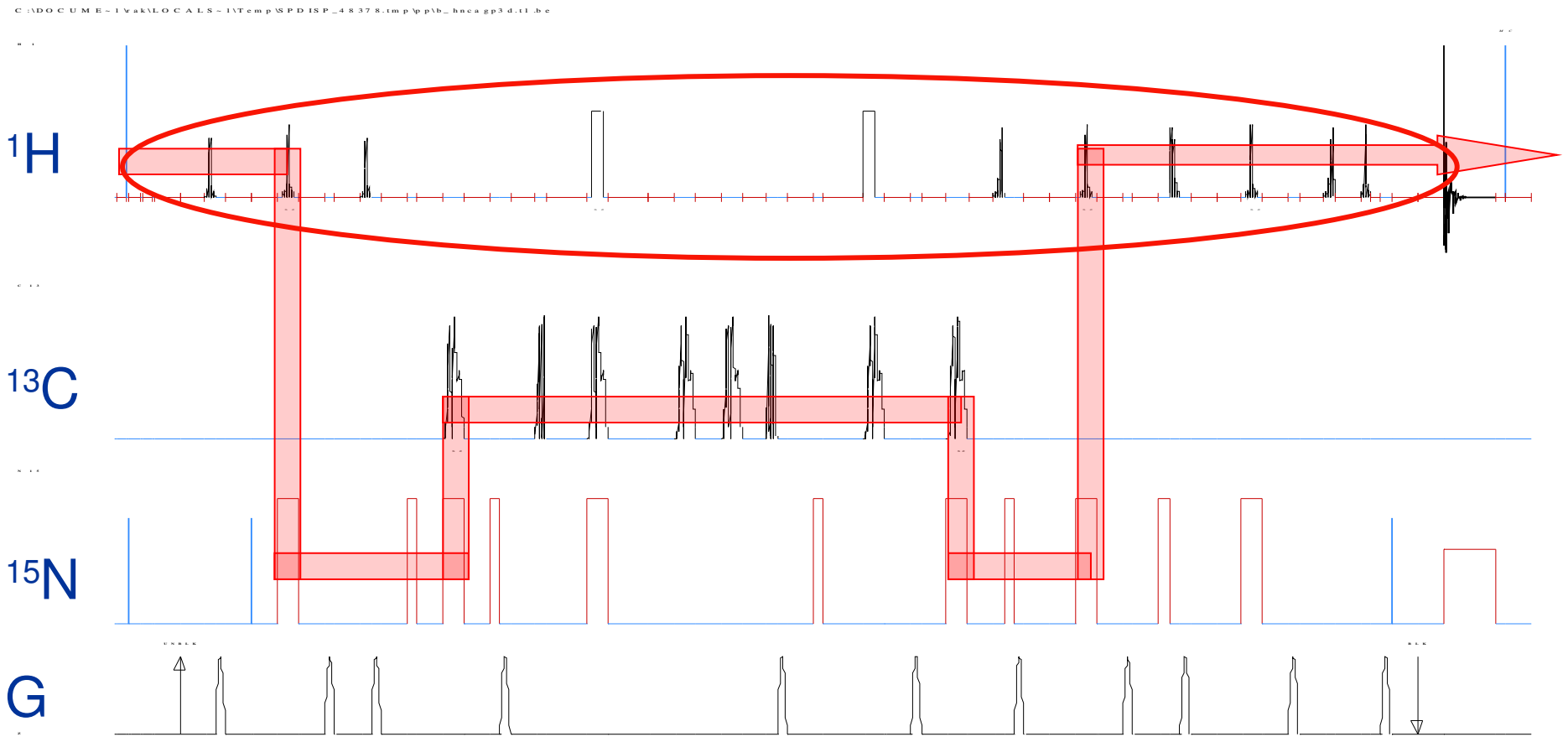


So-Fast HMQC

- Allows to study very rapid phenomena (protein folding)
- Increase the speed for HTS
- Important RF power deposited in the probe

700 MHz TCI CryoProbe: BEST-NMR

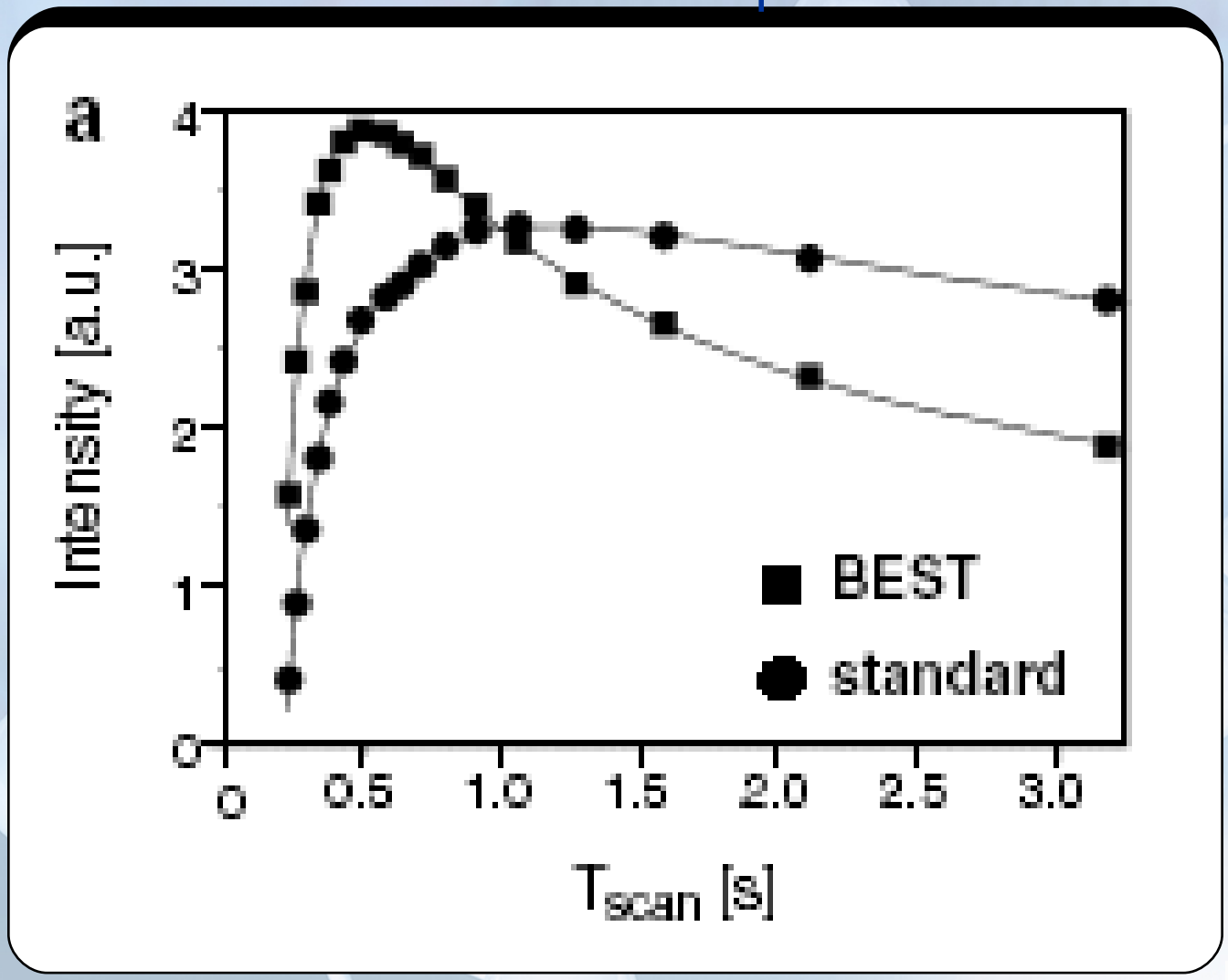
BEST-HNCA



Brutscher et al. JMR 187, 2007, 163

700 MHz TCI CryoProbe: BEST-NMR

BEST vs. standard implementation



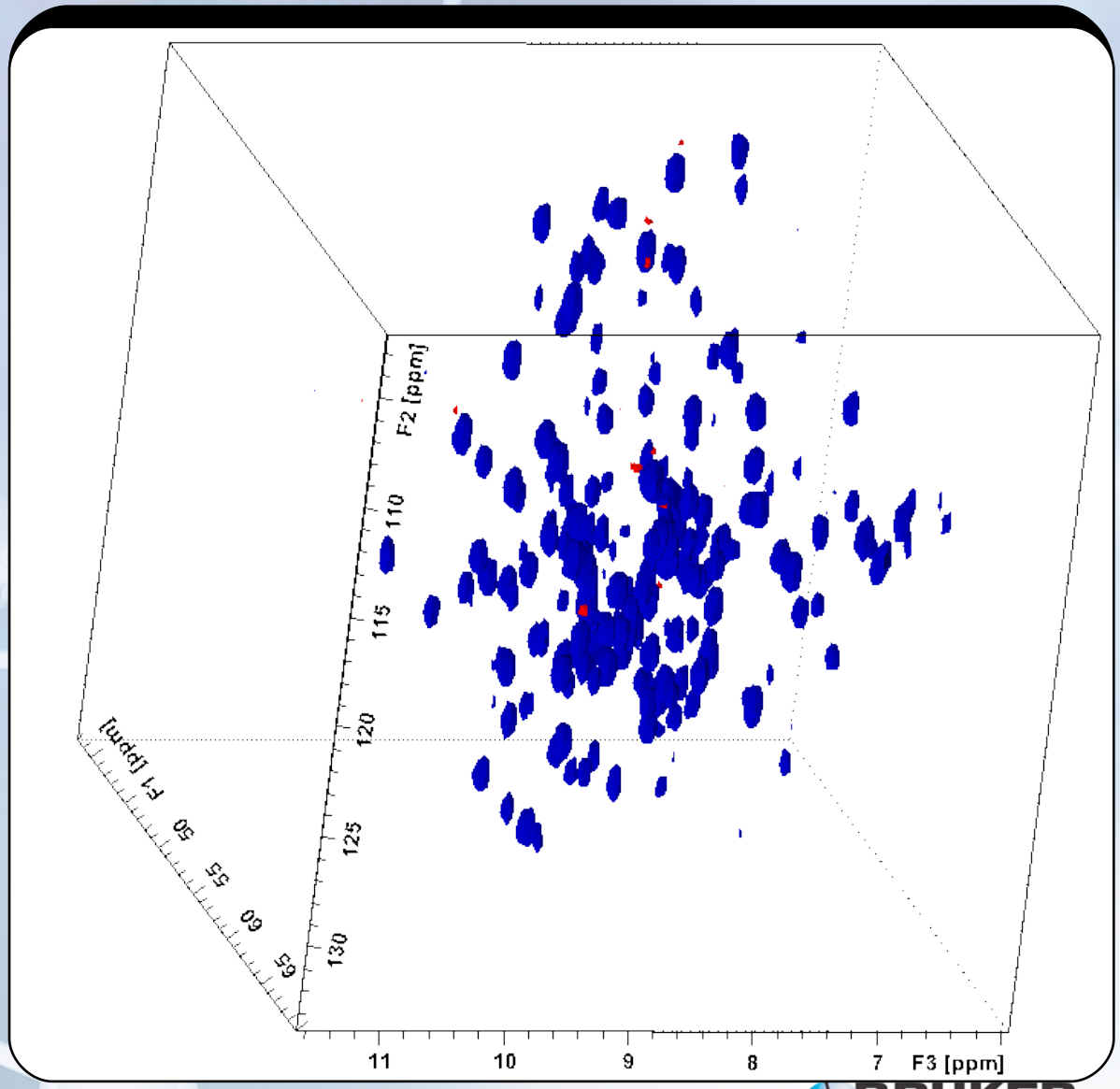
Brutscher et al. JMR 187, 2007, 163

700 MHz TCI CryoProbe: BEST-NMR

T1RNAse ($^{13}C/^{15}N$) in
90% H_2O / 10% D_2O

BEST-HNCA

ns = 2; 1k x 40 x 128
d1 = 1m



29 min. acquisition time !

Brutscher et al. JMR 187, 2007, 163

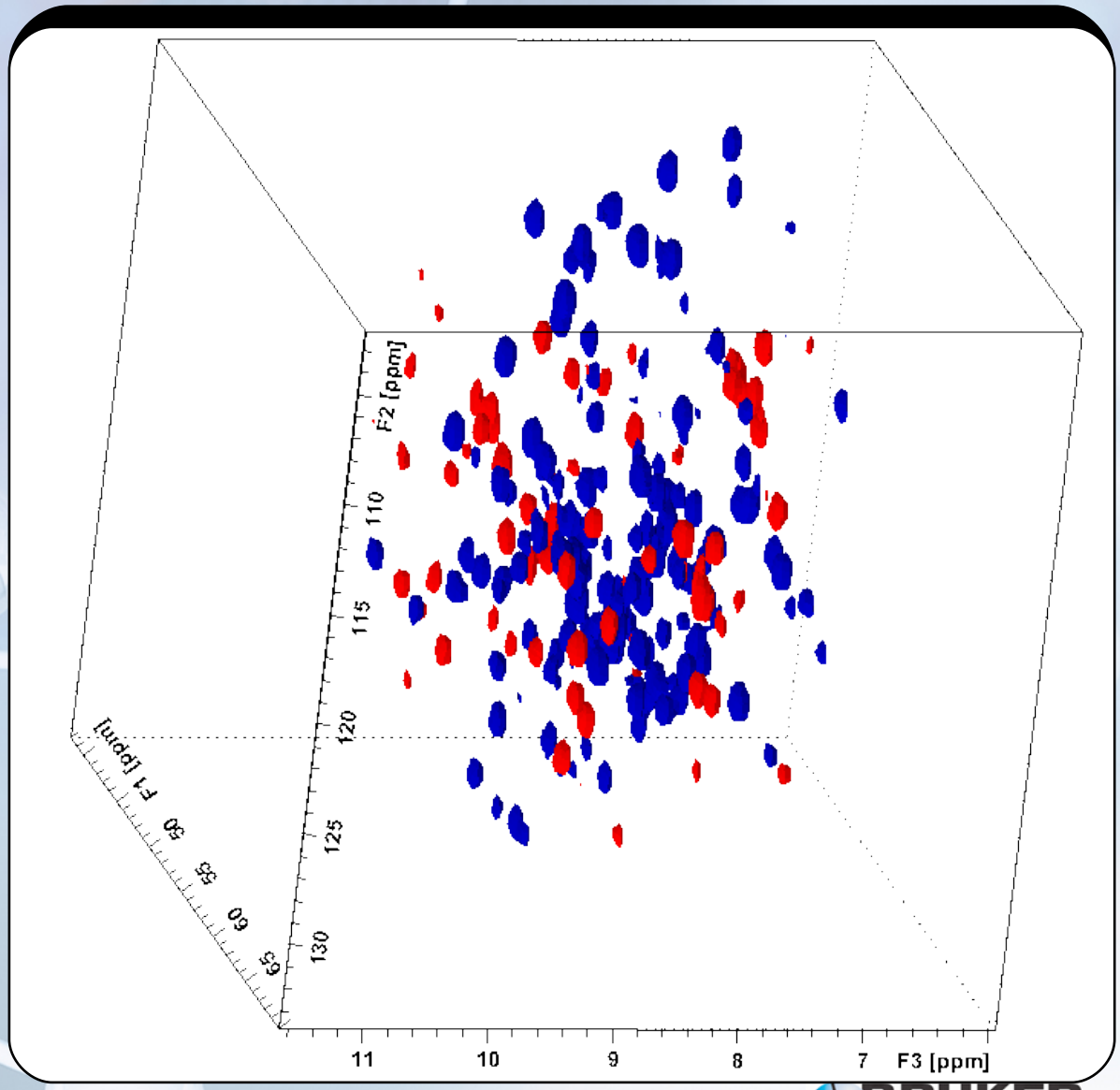
700 MHz TCI CryoProbe: BEST-NMR

T1RNAse ($^{13}C/^{15}N$) in
90% H_2O / 10% D_2O

BEST-HNCACB

ns = 2; 1k x 40 x 96
d1 = 100m;

1 hour 12 min.
acquisition time !



Brutscher et al. JMR 187, 2007, 163

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Pseudo-2D Representation of multiple selective 1D-experiments:

- Hadamard +	(Kupce & Freeman)

Hadamard spectroscopy

Principle:

3. It is a series of selective excitation experiments

5. Instead of individual selective 1D-experiments, all peaks are excited according to Hadamard scheme

7. Use the Hadamard matrix to separate individual peaks

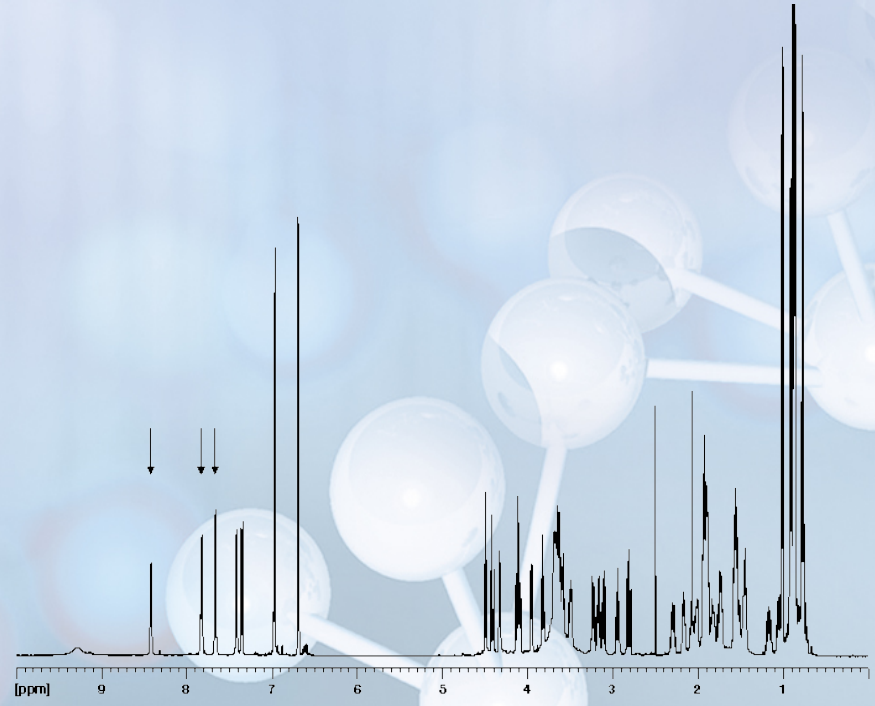
9. Pseudo-2D representation of 1D selective spectra

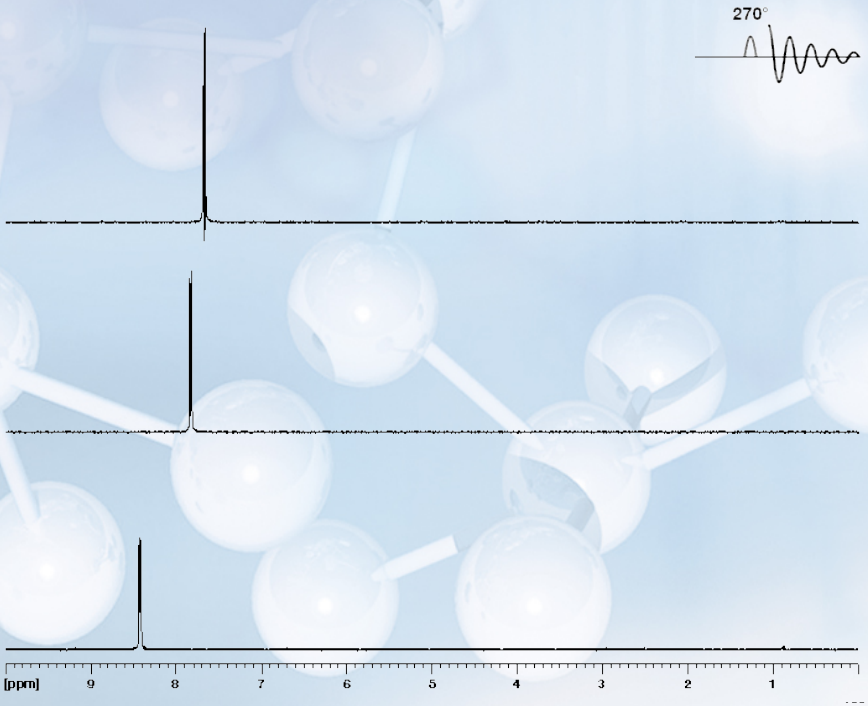
E. Kupce, T. Nishida and R. Freeman, Prog. NMR Spec., 42, 95, 2003

Hadamard spectroscopy

nonselective

3 selective excitations

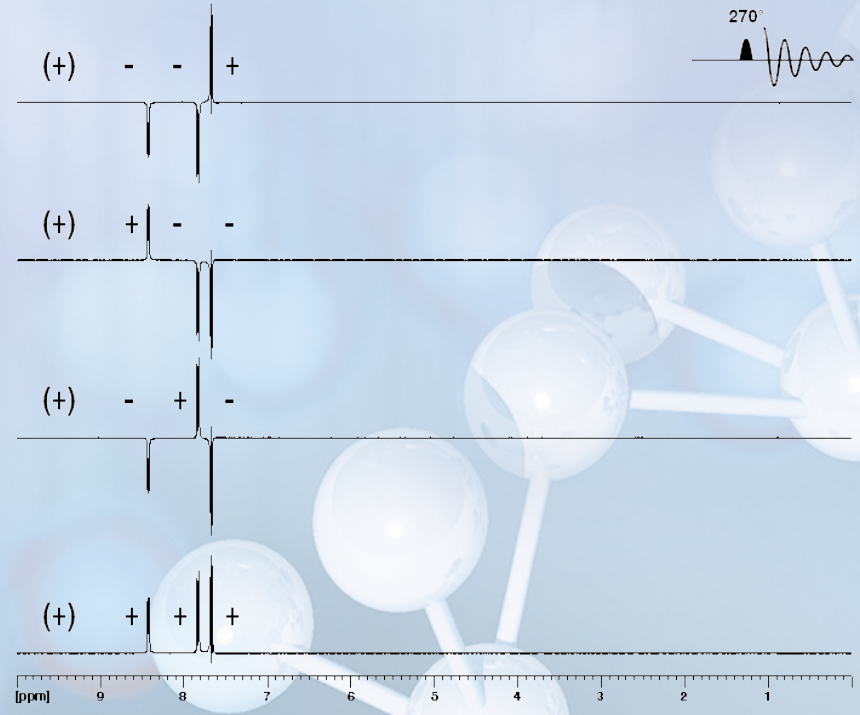


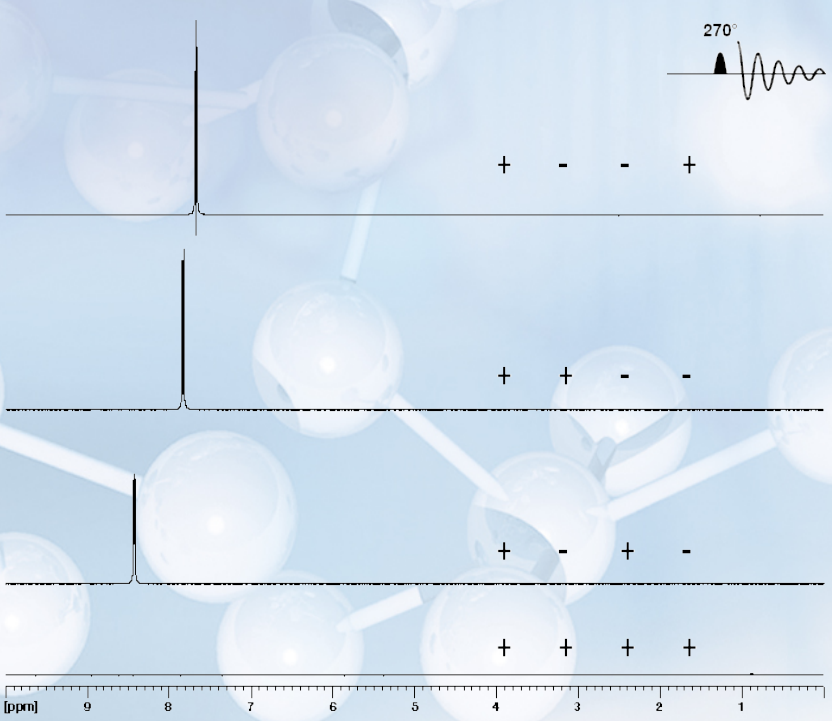


Hadamard spectroscopy

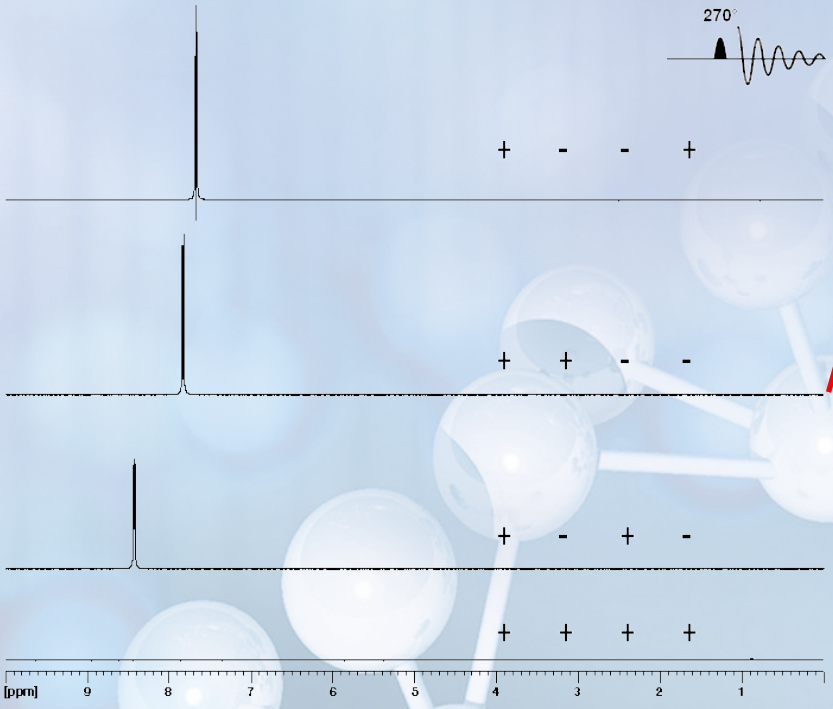
Multiple-selective excitation

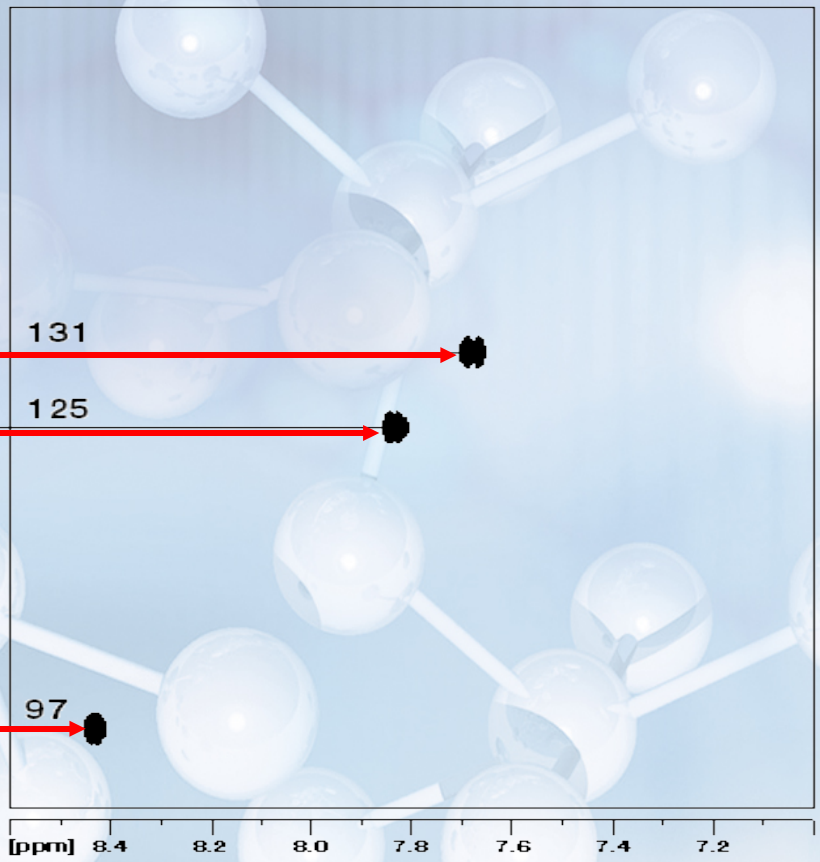
Linear combination with Hadamard matrix





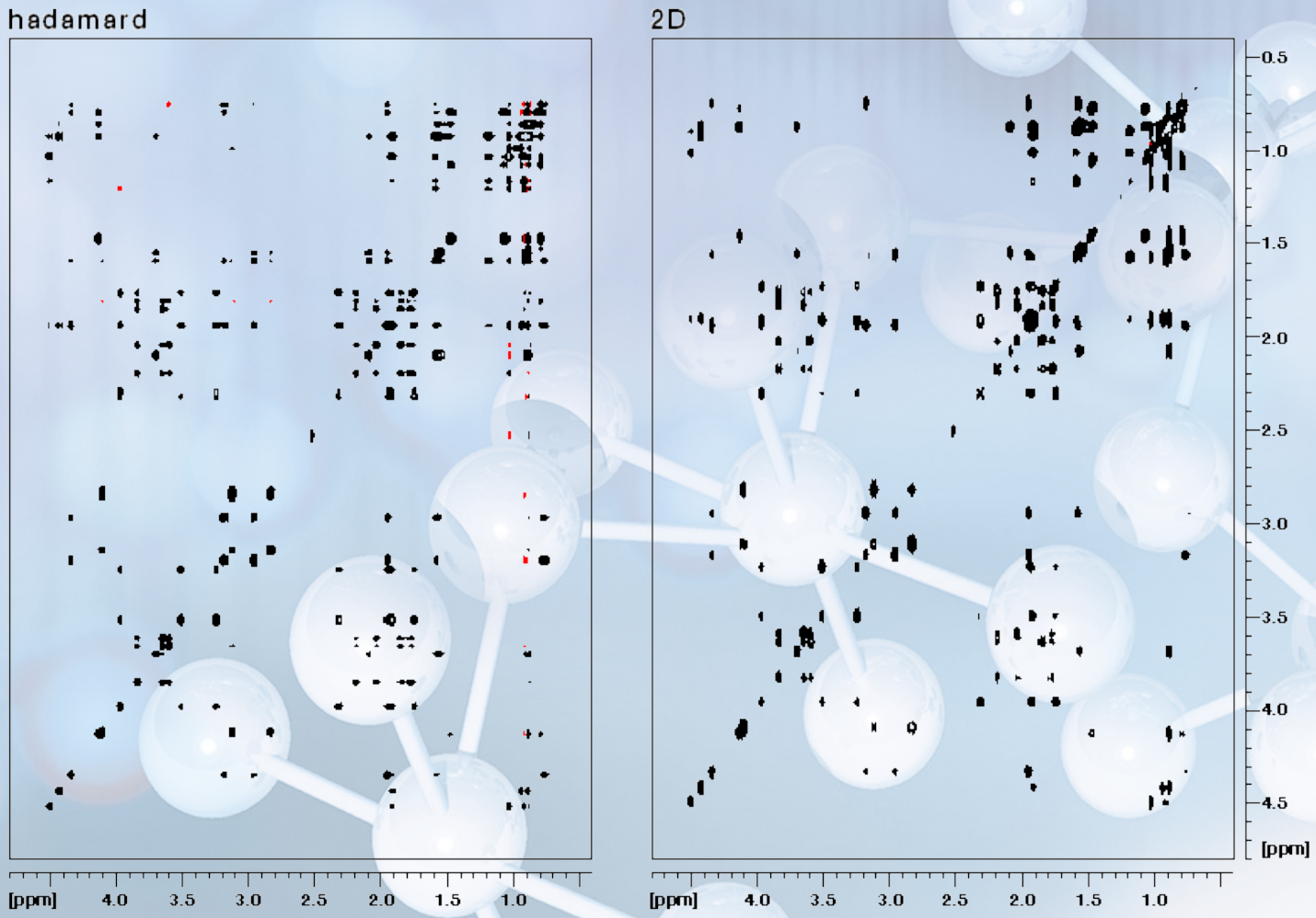
Hadamard spectroscopy





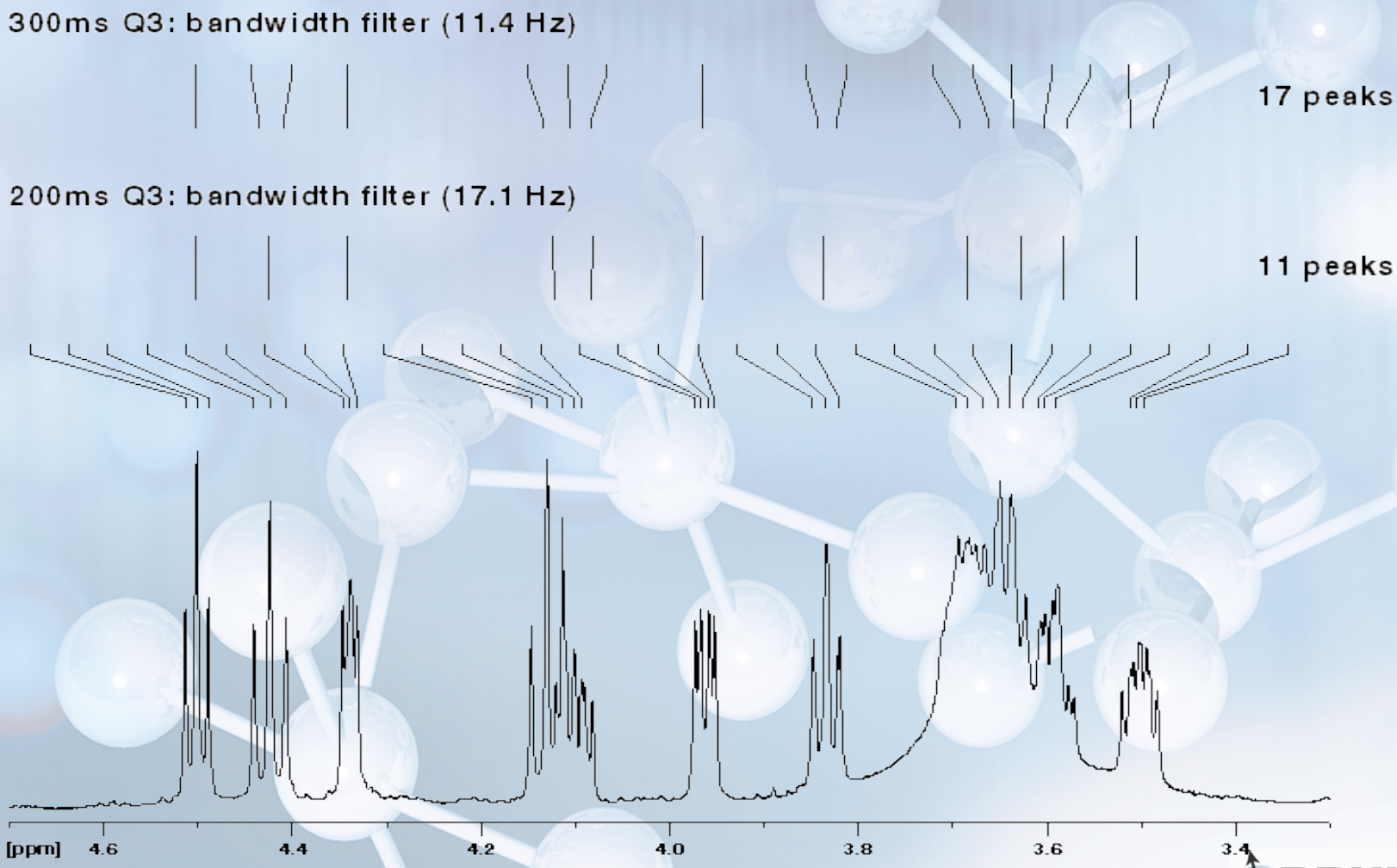
Hadamard spectroscopy

TOCSY experiments



Hadamard spectroscopy

peak picking: bandwidth filter



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+ Software available - Special software (n.a.) * Patented

Acknowledgment

ETH Zürich

K. Wüthrich
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