Can we improve solid-state NMR sensitivity without DNP ?

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15/06/2023 – GERM 2023 – Résonance Magnétique aux Extrêmes


Photo challenge

Context

Sensitivity problem

“There are three problems in NMR: sensitivity, sensitivity and sensitivity”, 2020
Dr Ulrich Scheler, Institute for Polymer Research, Dresden, Germany

Dynamic nuclear polarization, M€

Magnetic field, M€

$$PSNR_{max} \propto B_0^{1.5}$$

Ultra-fast MAS, 100 k€

Can we improve solid-state NMR sensitivity without DNP ? → extremely low cost limit → 7 T, 4-7 mm

Sensitivity definition

Ability to distinguish slight concentration differences
Proportional to Signal-to-Noise Ratio (SNR)
Increases as square root of time

$$SNR = \frac{\sigma^2_{signal+noise} - \sigma^2_{noise}}{\sigma^2_{noise}} = SNNR - 1$$ electronics

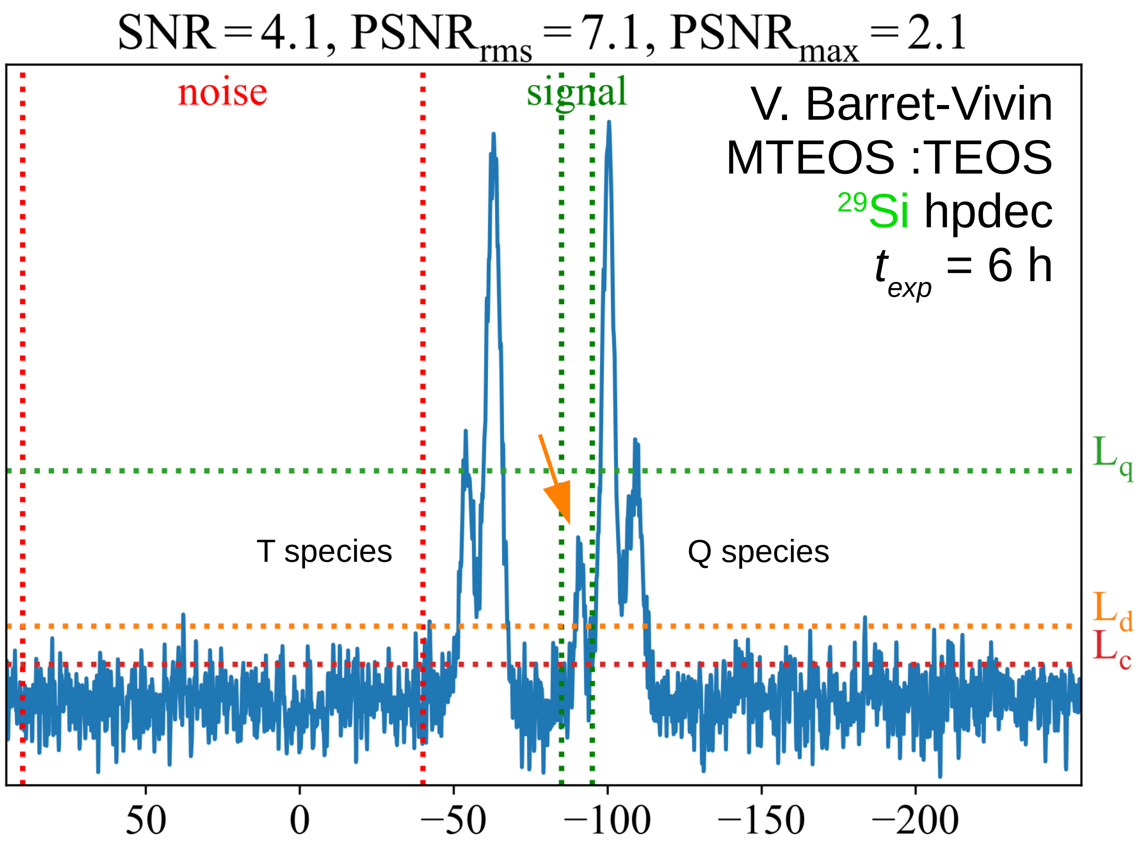
$$PSNR_{rms} = \frac{H_{signal}}{h_{noise\_rms}} = \frac{H_{signal}}{\sigma_{noise}}$$ spectroscopies

$$PSNR_{max} = \frac{H_{signal}}{h_{noise\_max}} = \frac{H_{signal}}{h_{noise\_peak\_peak}/2}$$ chemistry

Gaussian noise: $PSNR_{max} \approx PSNR_{rms} / 3.3$

"In the NMR literature the RMS noise is usually multiplied by 2 for reasons that can be attributed only to tradition." → $PSNR_{rms}/2$

M. E. Lacey *et al.*, *Chem. Rev.* 99, 3133–3152 (1999).

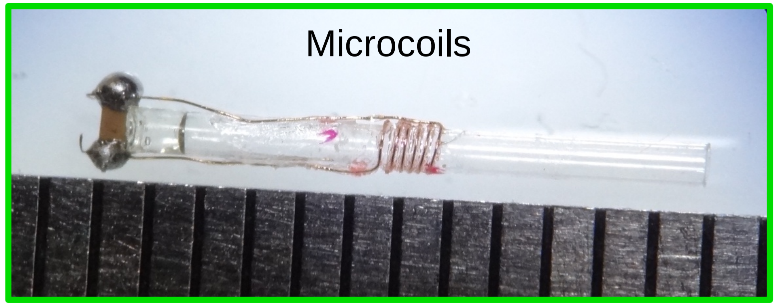


G. Laurent *et al.*, *Appl. Spectrosc. Rev.* 54, 602–630 (2019).

L_q: $PSNR_{max}$ = 3.0, quantification level
L_d: $PSNR_{max}$ = 1.0, detection level at unexpected position
L_c: $PSNR_{max}$ = 0.5, critical level, yes / no at expected position

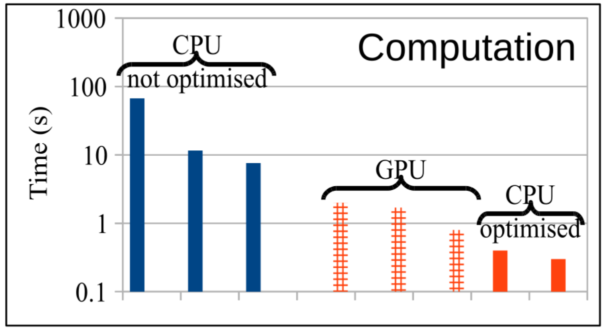
L. A. Currie, *Anal. Chem.* 40, 586–593 (1968).

Outline

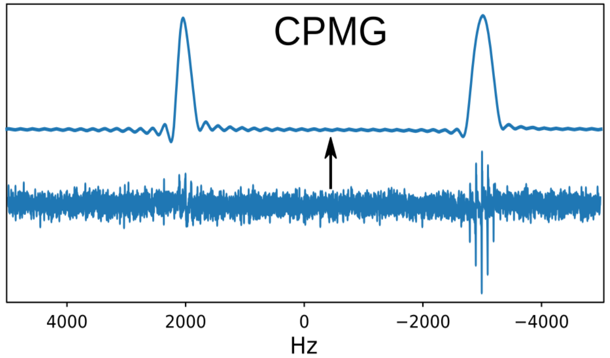


G. Laurent, Instrumenter et innover en chimie physique pour préparer l'avenir, Paris, France (2015).

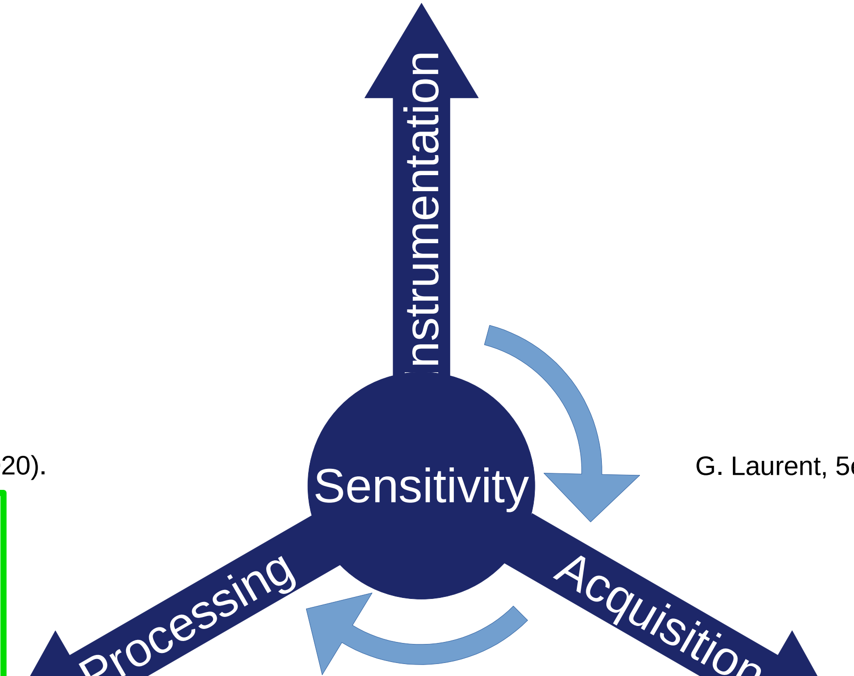
G. Laurent, XXXIème Congres du GERM, Saint Pierre d'Oléron, France (2019).

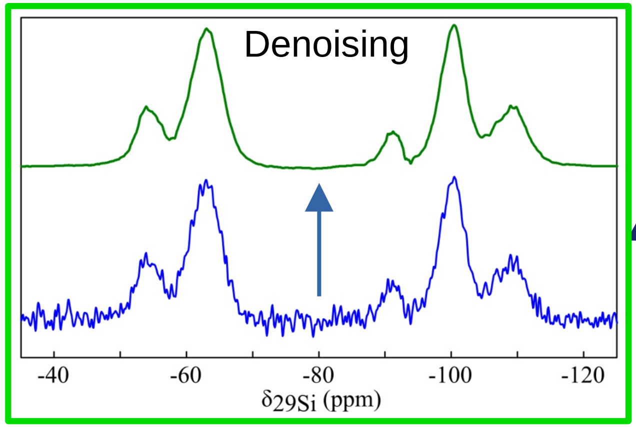


G. Laurent *et al.*, *Appl. Spectrosc. Rev.*, 55, 173-196 (2020).



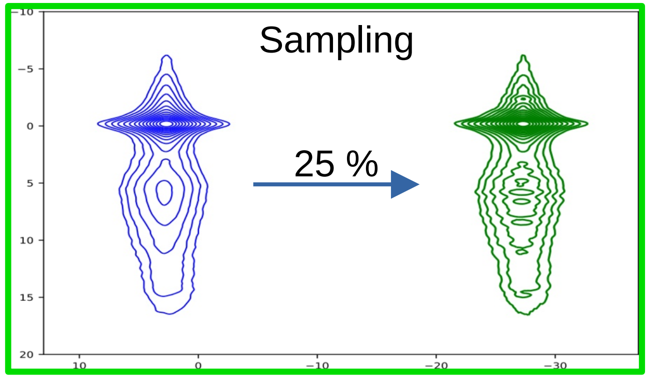
G. Laurent, 5èmes Journées nationales du développement, Rennes, France (2020).





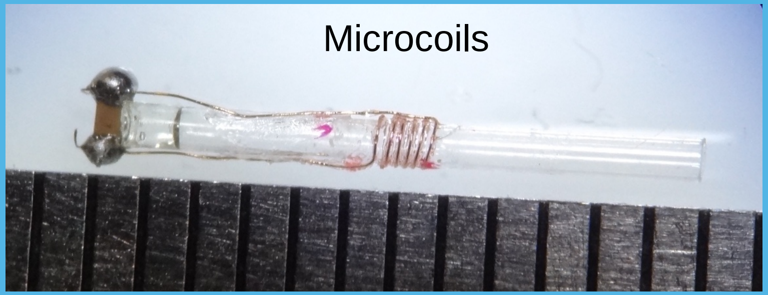
G. Laurent *et al.*, *Appl. Spectrosc. Rev.*, 54, 602–630 (2019).

Increasing NMR sensitivity without DNP



G. Laurent, RMN structurale dans le bassin parisien, Orléans, France (2018).

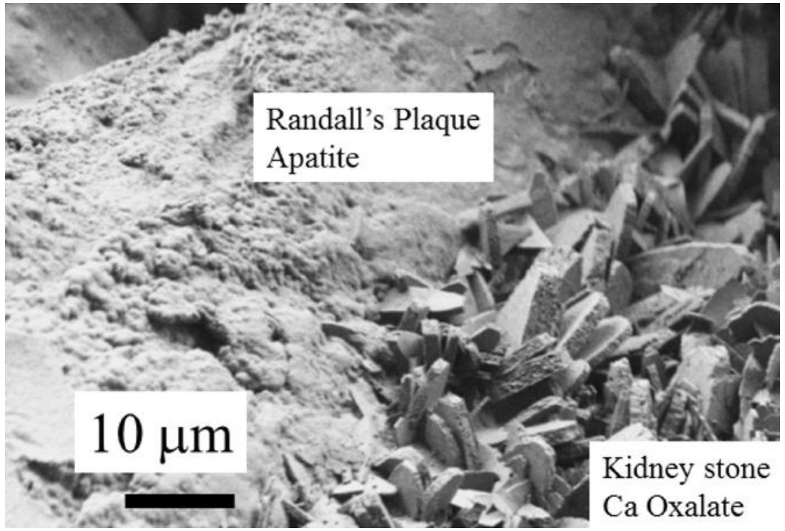
Instrumentation



Microquantities

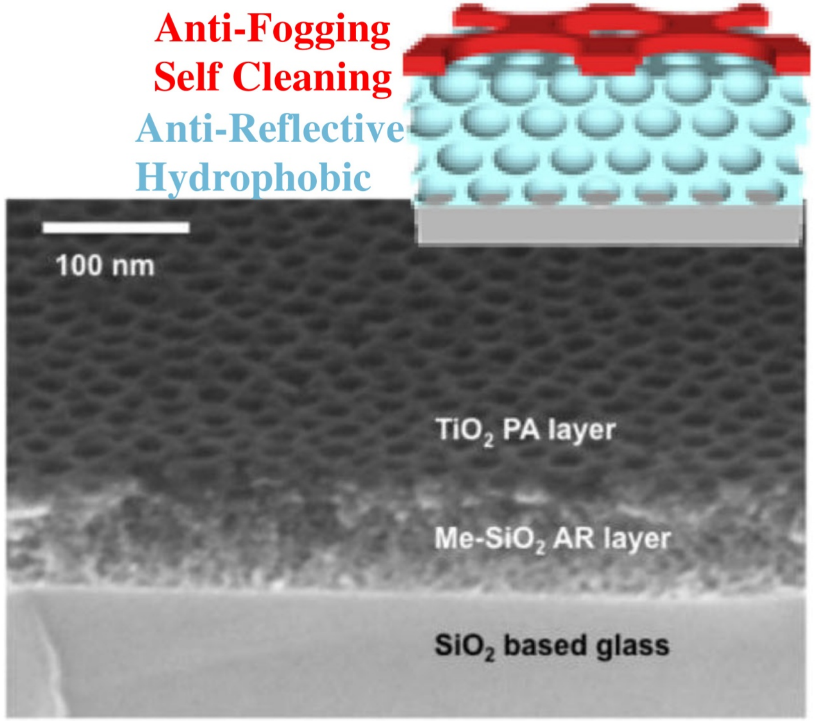
Usually in solid-state NMR,
m = 1-100 mg

Kidney stone, hydroxyapatite, m < 100 µg
Collab. with Tenon Hospital



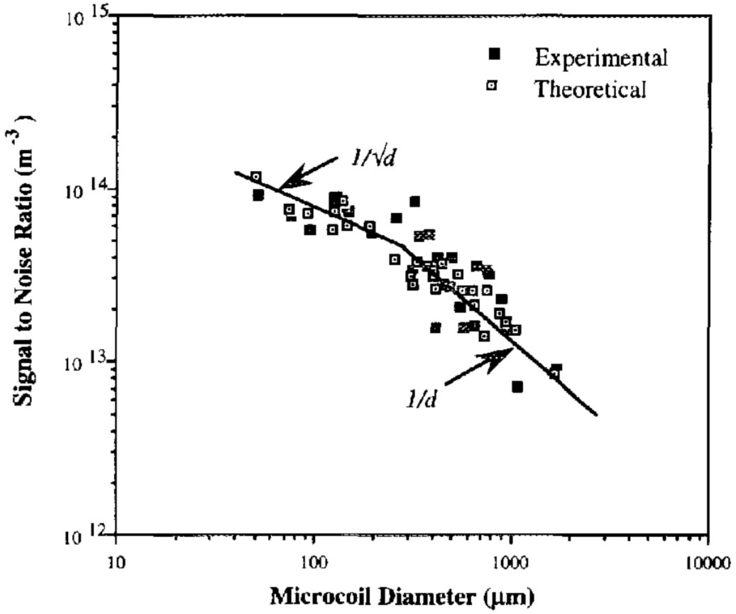
D. Bazin, M. Daudon
J. Phys. D: Appl. Phys.. 45, 383001, 1-10 (2012).

Sol gel film
S = 2 cm², h = 300 nm, m ~ 100 µg



M. Faustini *et al.*
J Sol-Gel Sci Technol. 70, 216–226 (2014).

Decrease coil size
Increase filling factor



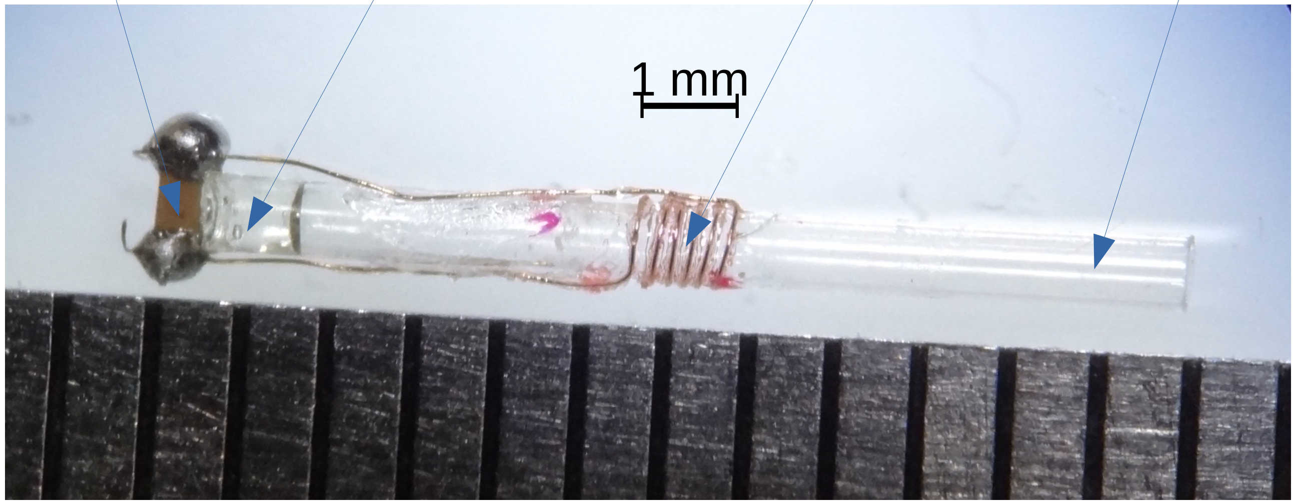
T. L. Peck *et al.*
J. Magn. Reson. Ser. B. 108, 114–124 (1995).

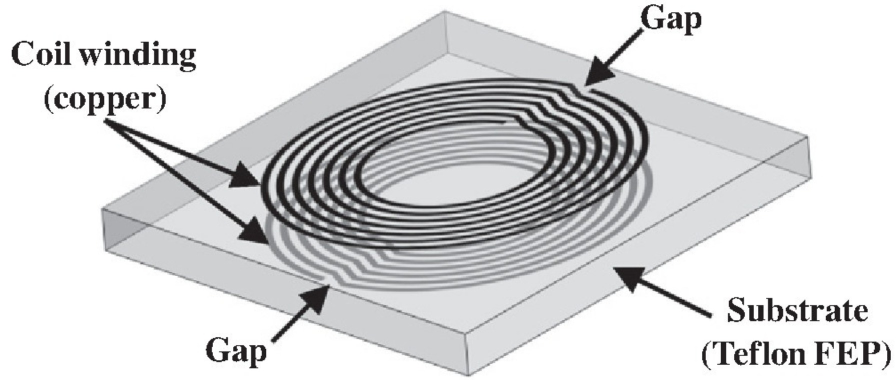
Solenoid and TLR coils

D. Sakellariou,
J. Lehmann-Horn, W.-C. Teh

capacitor epoxy resin coil + cyanoacrylate capillary

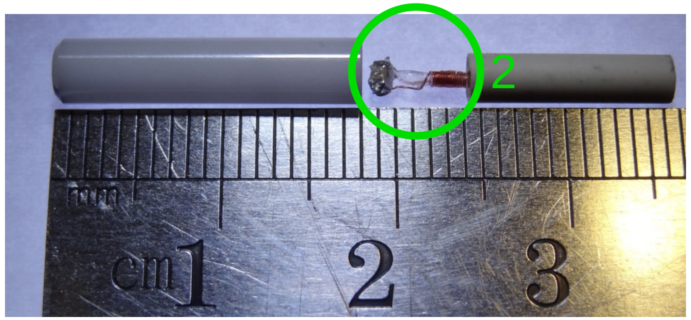
Solenoid

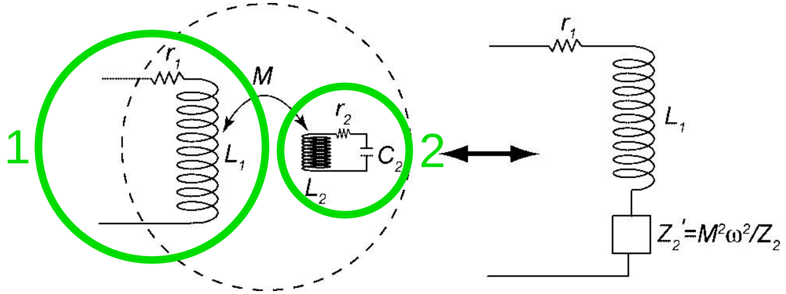




Transmission Line Resonator (**TLR**)

J.-C. Ginefri *et al.*, *J. Magn. Reson.* 224, 61–70 (2012).





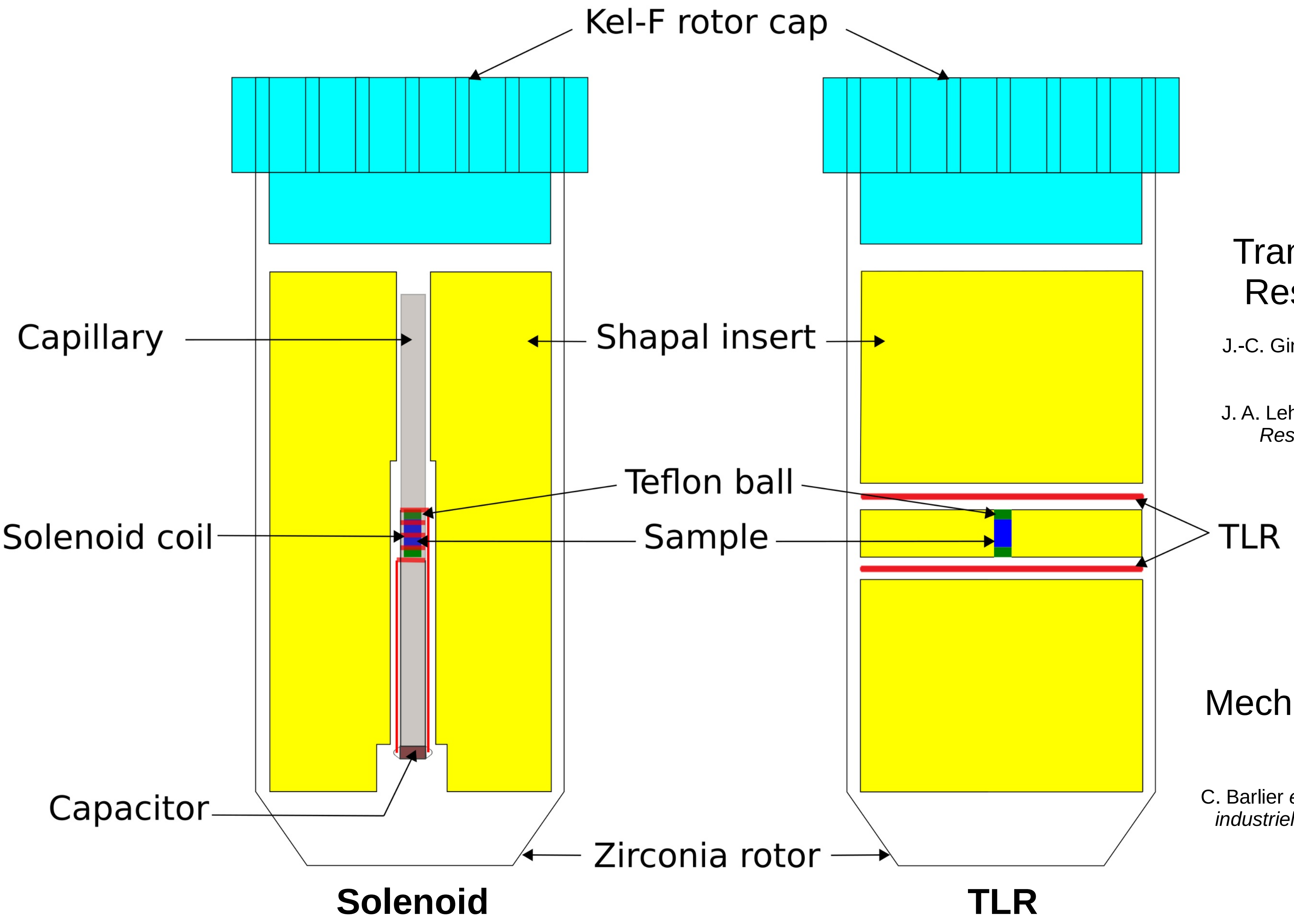
D. Sakellariou *et al.*, *Nature*. 447, 694–697 (2007).
J.-F. Jacquinot, D. Sakellariou, *Concept. Magn. Reson. A.* 38A, 33–51 (2011).

Inserts

Magic Angle Coil Spinning (**MACS**)

D. Sakellariou, J.-F. Jacquinot. WO2007020537, A3 (2007).

D. Sakellariou *et al.*, *Nature*. 447, 694–697 (2007).



Transmission Line Resonator (TLR)

J.-C. Ginefri *et al.*, *J. Magn. Reson.* 224, 61–70 (2012).

J. A. Lehmann-Horn *et al.*, *J. Magn. Reson.* 271, 46–51 (2016).

Mechanical tolerance: ~ 20 µm

C. Barlier *et al.*, *Construction mécanique industrielle* (Foucher, 1997), Data Sti.

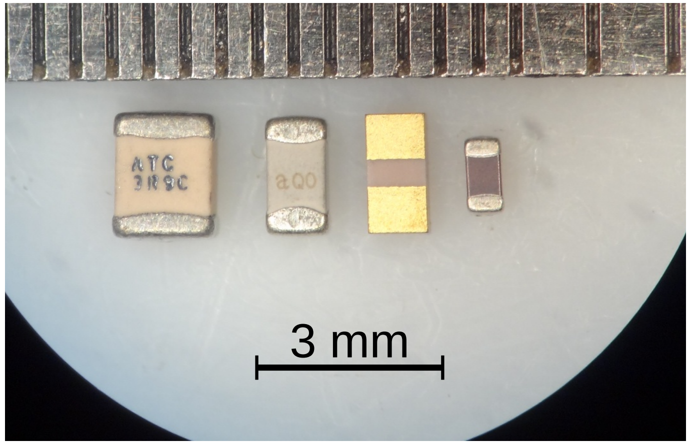
Coil parameters

Serial RLC

$$\nu = \frac{1}{2\pi\sqrt{LC}}$$

- ν → Frequency (Hz)
- C → Capacitance (F)
- L → Inductance (H)

Capacitors



Solenoid

LibreOffice calculation sheet

$$L = \frac{4\pi^2 N_{turns}^2 r_{coil}^2}{l_{coil}} k_L - 0.004\pi r_{coil} N_{turns} (k_S + k_M)$$

- N_{turns} → Number of turns
- r_{coil} → Coil radius (m)
- l_{coil} → Coil length (m)
- k_L → Nagaoka coefficient = f (d_{coil}/l_{coil})
- k_S → Self inductance = f (p_{pitch} / r_{wire})
- k_M → Mutual inductance = f (N_{turns})

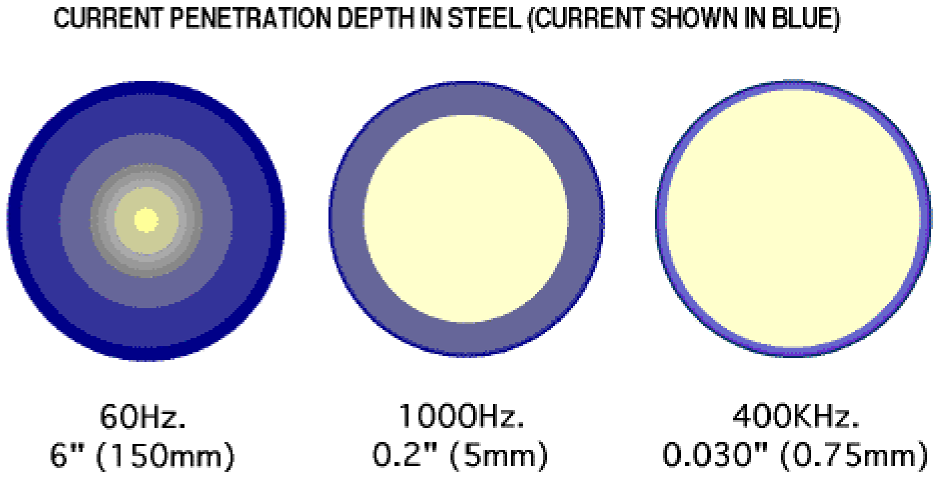
TLR
Matlab + Fasthenry software
FEKO electromagnetics simulations

R. Weaver, http://electronbunker.ca/eb/CalcMethods2a.html (2016).

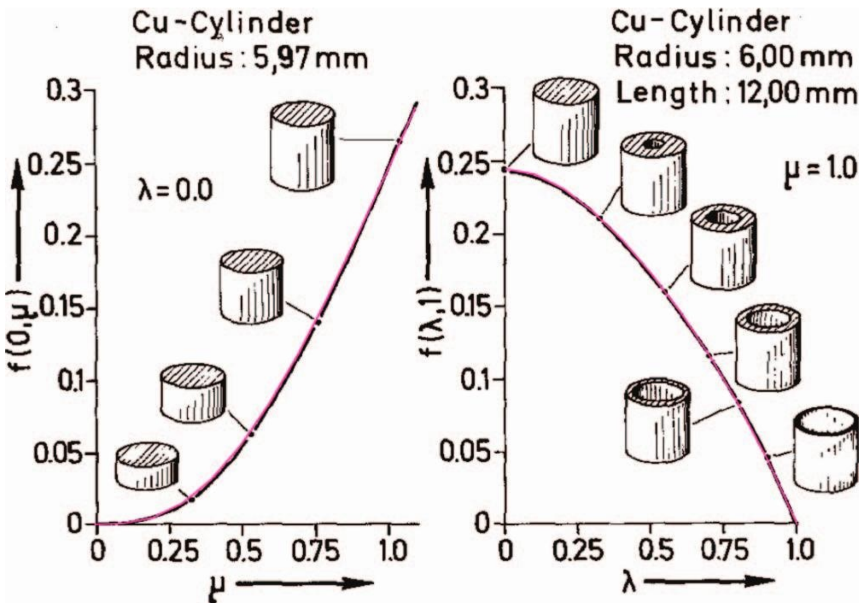
H. Nagaoka, *The Journal of the College of Science*, Imperial University of Tokyo, Japan. 27, 1–33 (1909).

E. B. Rosa, F. W. Grover, *Bulletin of the Bureau of Standards.* 8, 1–237 (1916).

Coil wire



http://tymkrs.tumblr.com



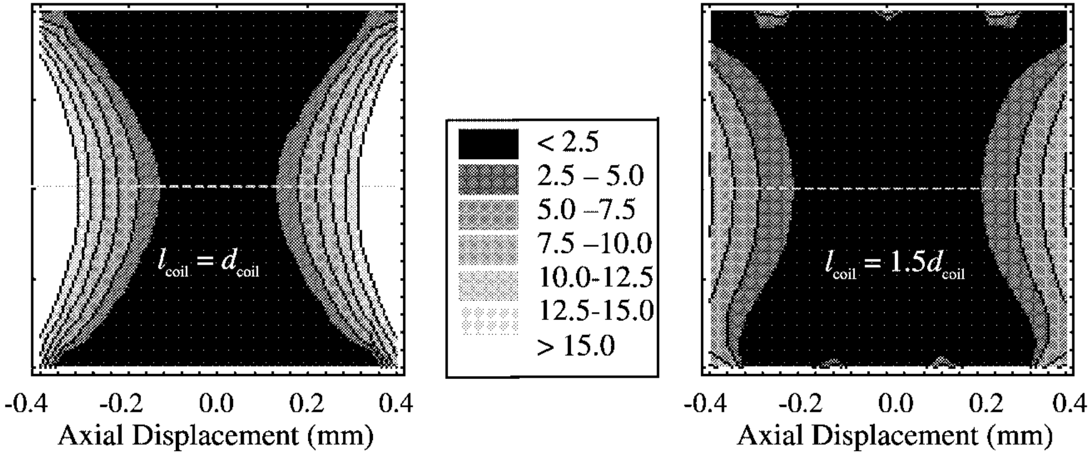
Power = f(h_{wire}, w_{wire})

G. Aubert *et al.*, *J. Chem. Phys.* 137, 154201-154201–14 (2012).

$$\delta = \sqrt{\frac{\rho}{\pi \mu_0 \nu}}$$

- ρ → Resistivity (Ω.m)
- ν → RF Frequency (Hz)
- μ_0 → Magnetic Permeability (H.m^{-1})

Wire diameter > 5x skin depth



Best RF homogeneity with elongated coil

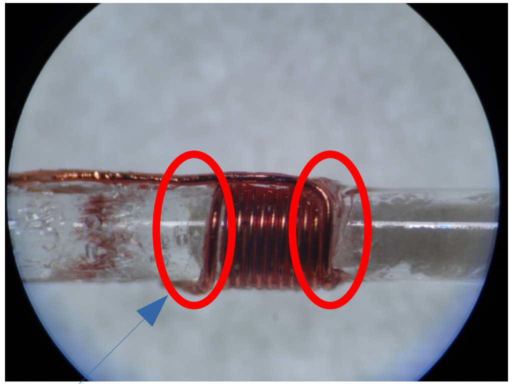
$l_{sample} : d_{coil} : l_{coil} = 0.5 : 1 : 1.2$

K. R. Minard, R. A. Wind, *Concepts Magnetic Res.* 13, 128–142 (2001).

Compromise between Eddy currents and RF homogeneity

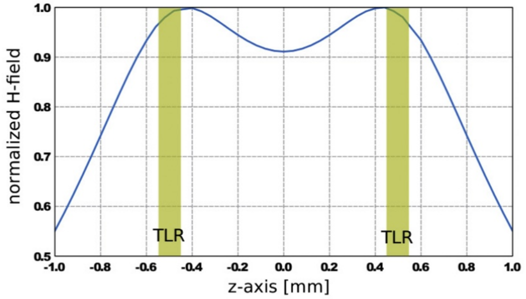
RF homogeneity

W.-C. Teh, J. Lehmann-Horn

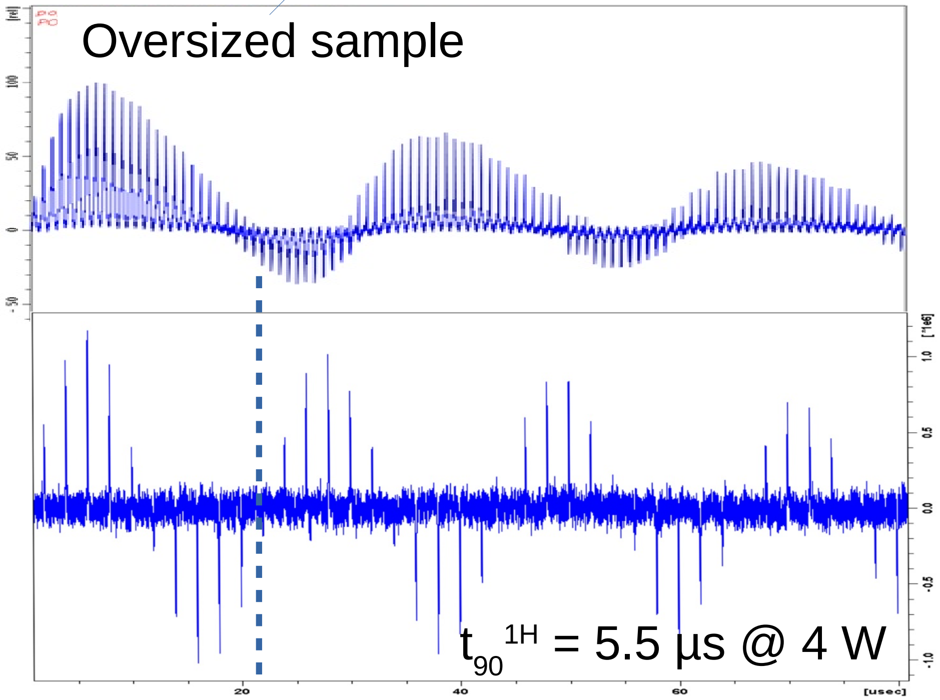


Solenoid

TLR

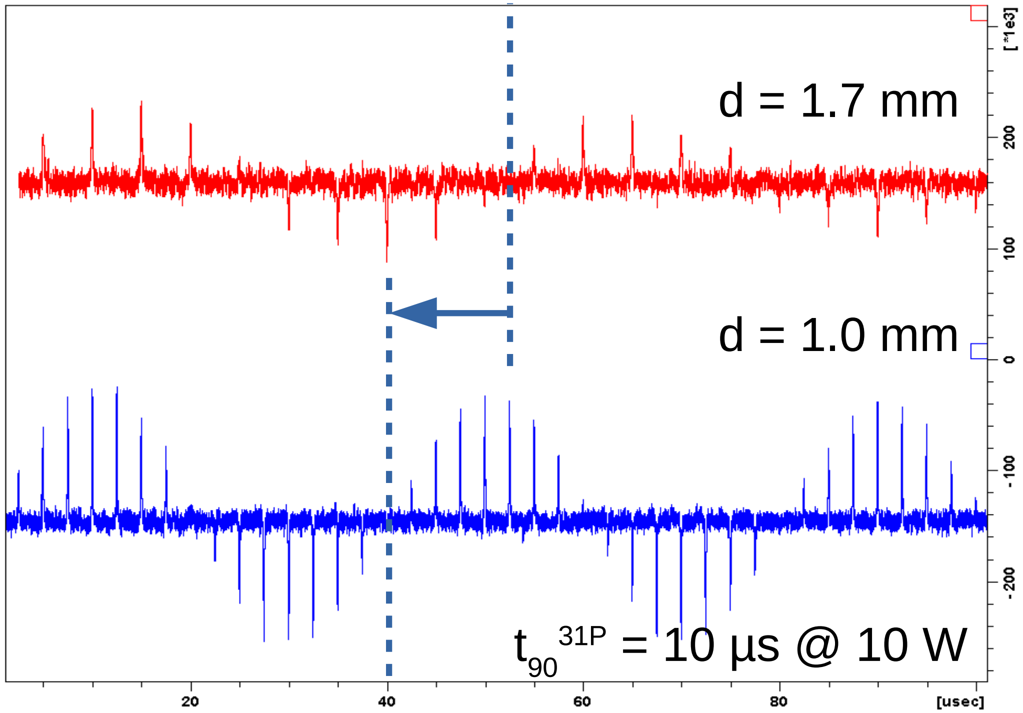


J. A. Lehmann-Horn *et al.*, *J. Magn. Reson.* 271, 46–51 (2016).



Nutation curve

$$PSNR_{max} \propto B_1 / \sqrt{P}$$



Strong influence of sample position

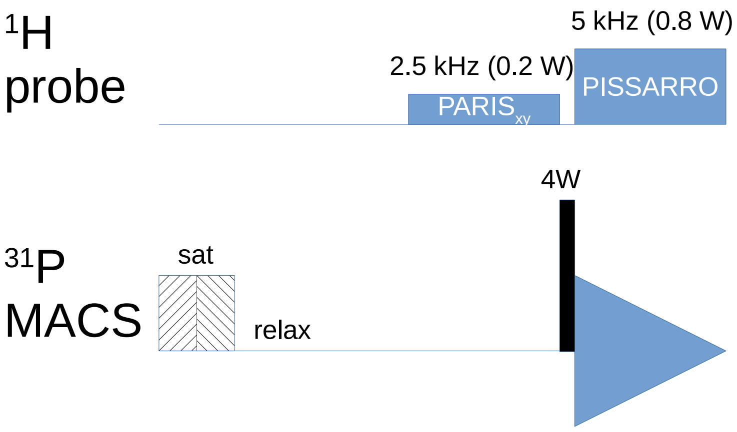
Strong influence of inter-coil distance

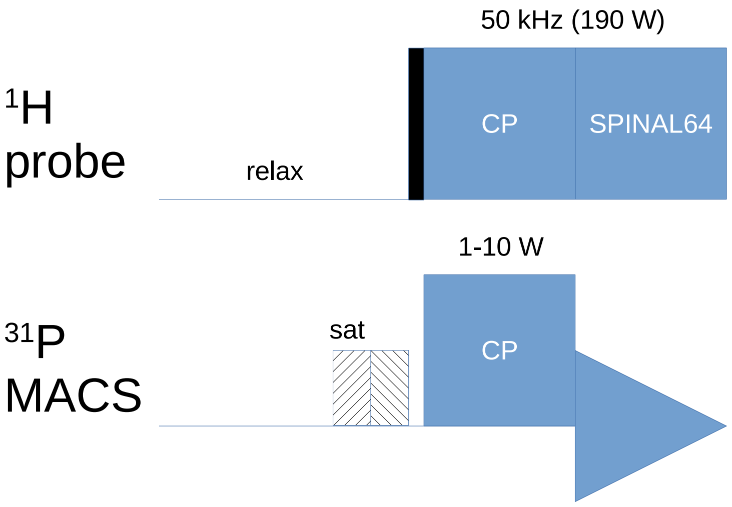
RF power

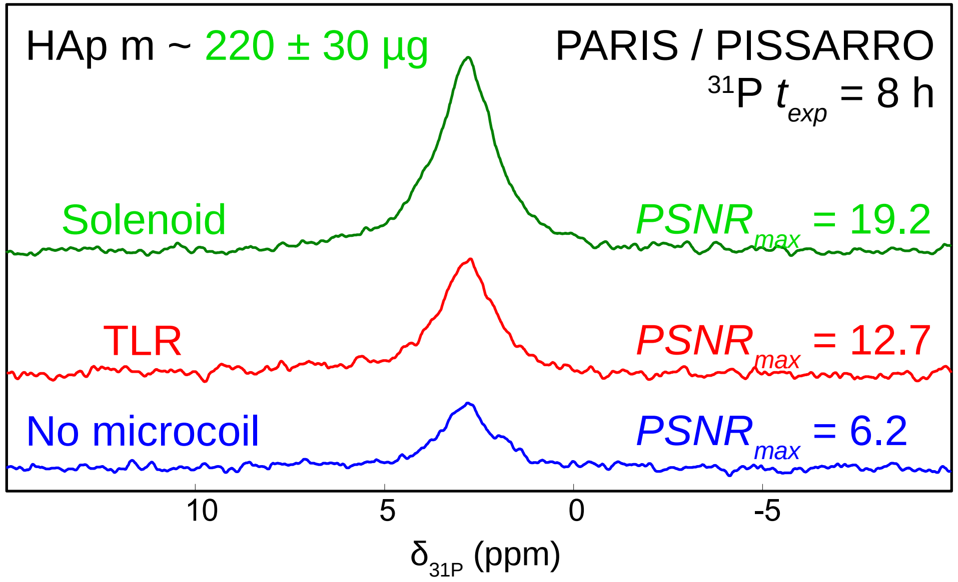
W.-C. Teh, J. Lehmann-Horn

M. Weingarth *et al.*, *Chem. Phys. Lett.* 466, 247–251 (2008).

M. Weingarth *et al.*, *Chem. Phys. Lett.* 488, 10–16 (2010).

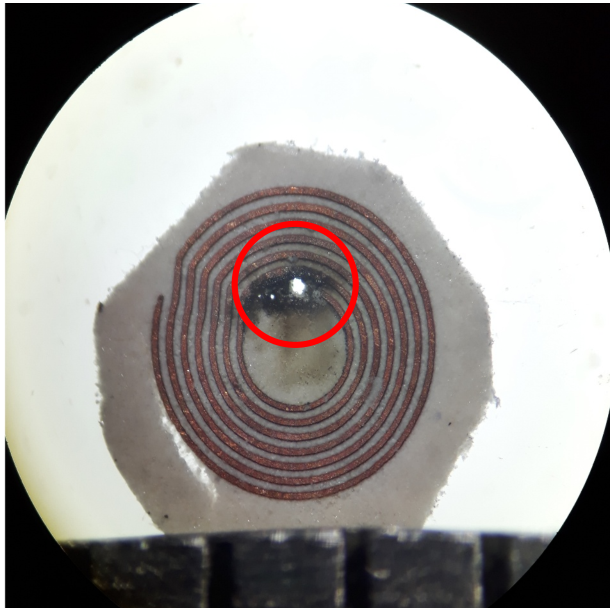






$$PSNR_{max}/\sqrt{time} \times 2.0\ \text{(TLR) or } 3.1\ \text{(solenoid)}$$

Time gain = 4.2 (TLR) or 9.6 (solenoid)



Coil burned (^{1}H electric field)

Max 50 W on both channels

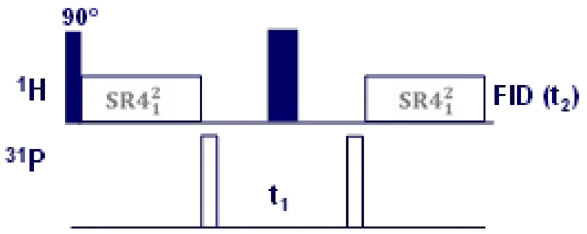
MAS rate 5-15 kHz

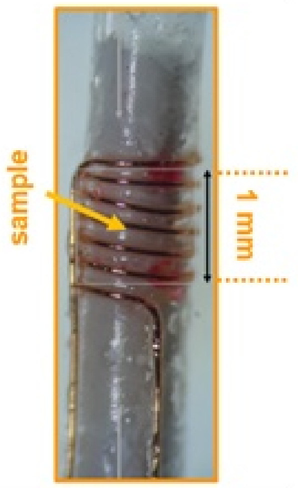
MACS summary

Characteristics	Solenoid coil	TLR coil
Design	🙂	☹
Manipulation	😐	🙂
Mechanical tolerance	😐	😐
Ease of spin	☹	🙂
RF homogeneity	🙂	😐
RF power	🙂	😐
Leakage point	Wire soldering	Substrate
Time gain	9.6	4.2

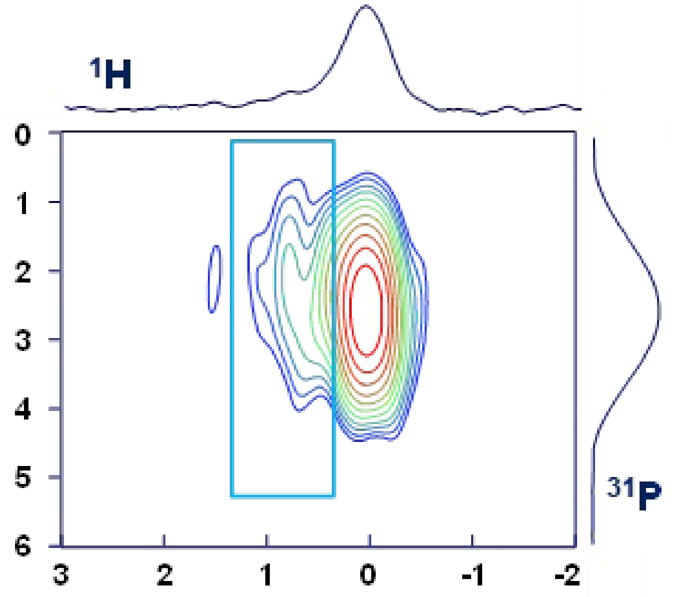
MACS outlook

Collab. Marie Poirier-Quinot

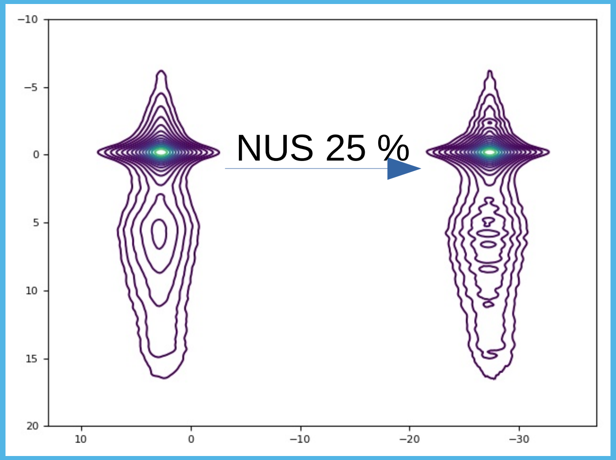




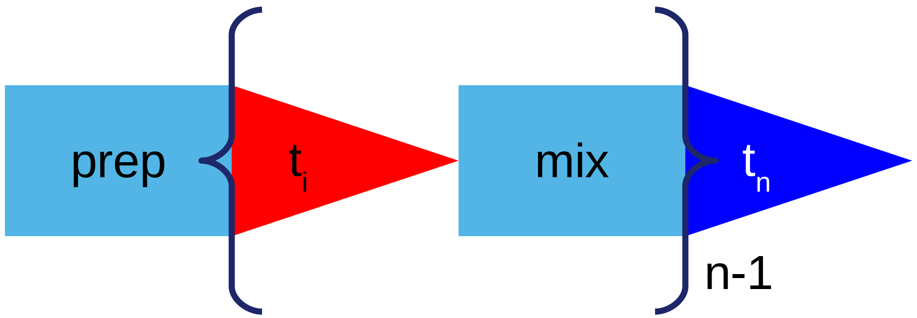
D-HMQC ^{1}H-^{31}P
7 T, 4 mm, t_{exp} = 4 h



Fast acquisitions



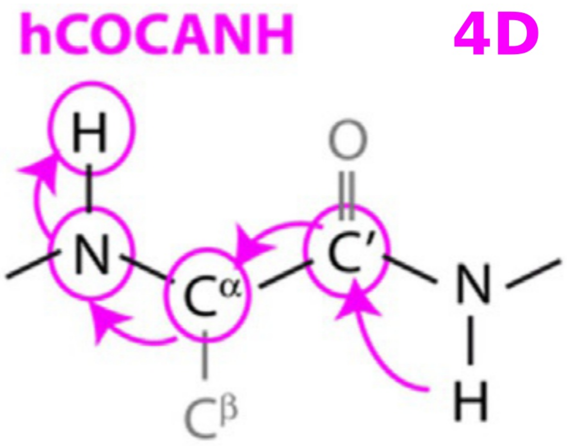
Multi dimensions



Relaxation & excitation

Indirect dimensions
- Point by point acquisition
- Sequential real & imaginary
- Apply NUS

Direct dimension
- One-shot acquisition
- Simultaneous real & imaginary
- Will be neglected

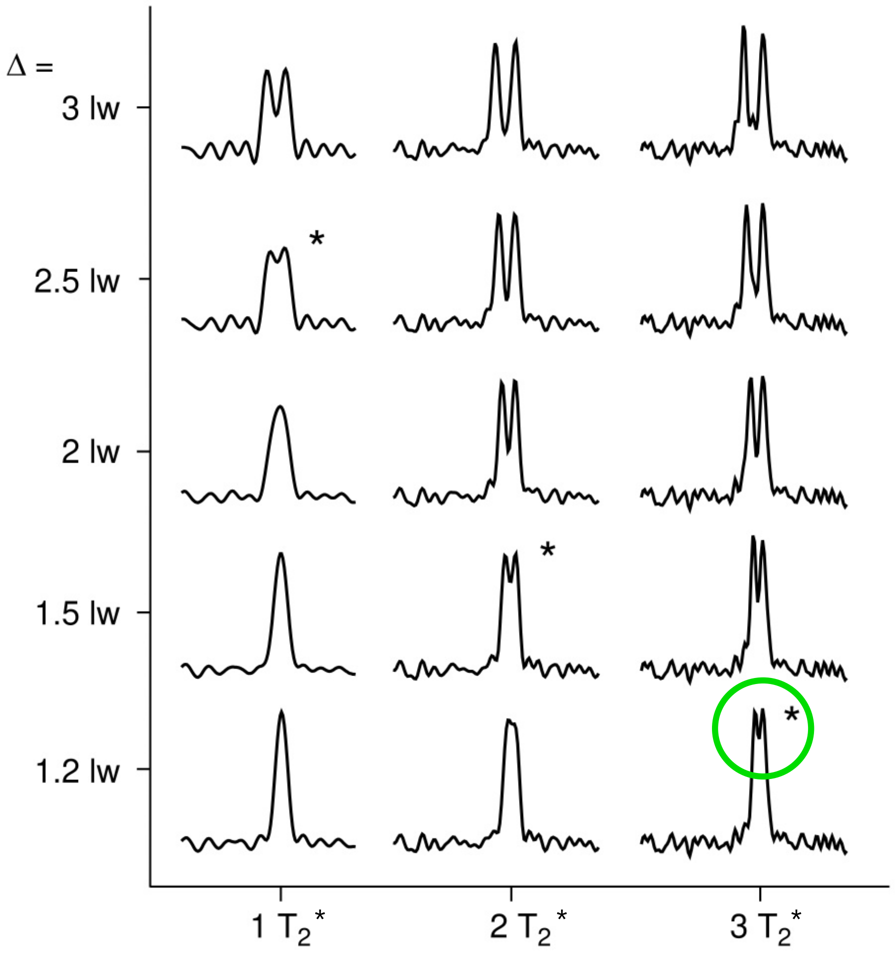


H. Fraga *et al.*, *ChemPhysChem*, 18, 19, 2697–2703 (2017).

How to decrease nD duration ?

Dims	Direct points	Indirect increments			Phase quad	Total FID	Time	Disk space
		#1	#2	#3				
1D	512	-	-	-	2 (sim)	2 (sim)	5 s	4.0 ko
2D	512	128	-	-	4	512	21 min	1.0 Mo
3D	512	128	128	-	8	1.3e5	3,8 d	268 Mo
4D	512	128	128	128	16	3.4e7	2,7 y	69 Go

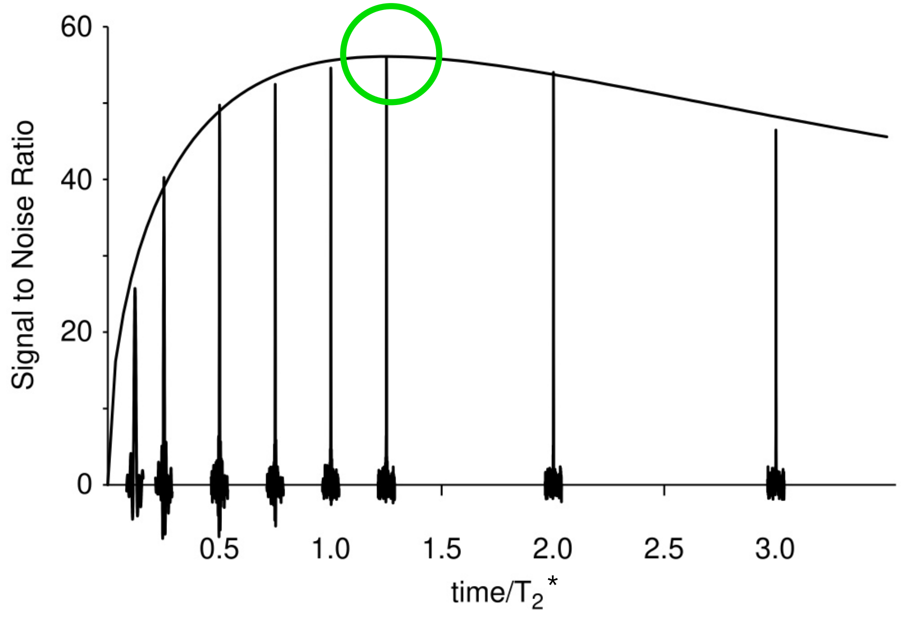
Truncation?



Max resolution at 3 T_2^*

D. Rovnyak *et al.*, *Magn. Reson. Chem.*, 49, 8, 483–491 (2011).

$$SNR(t_{max}) \propto \frac{T_2^*\left(1-e^{\frac{-t_{max}}{T_2^*}}\right)}{\sqrt{t_{max}}}$$



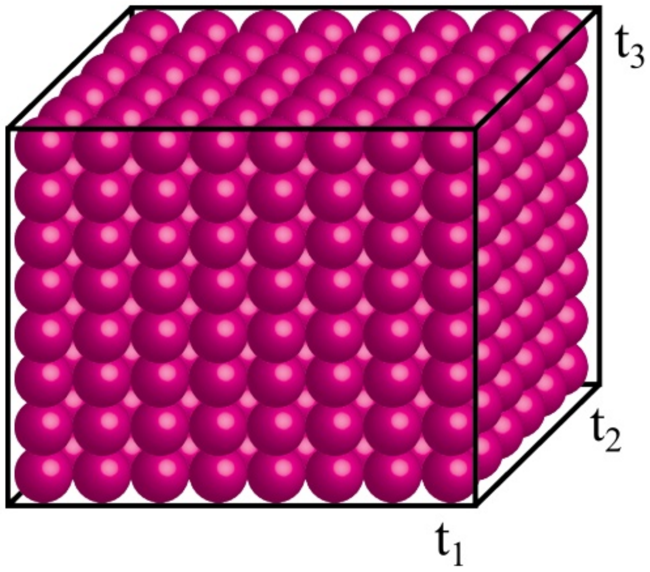
Max sensitivity at 1.26 T_2^*

😐 Limited duration decrease

☹ Resolution decrease

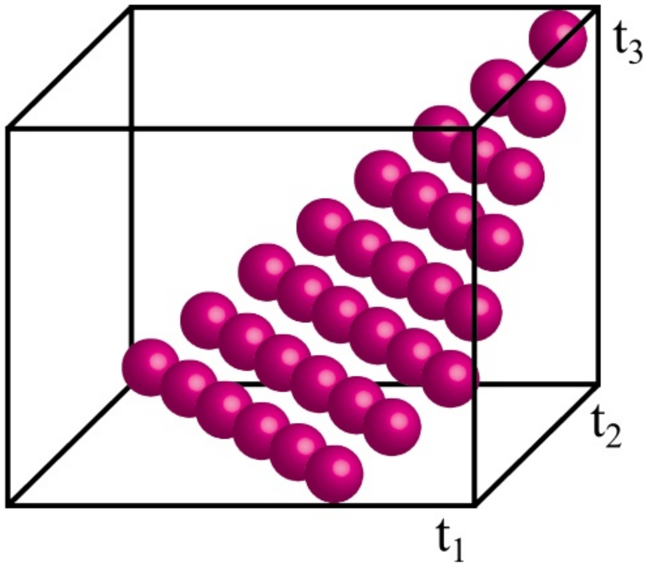
☺ Sensitivity increase

Radial / Non-Uniform Sampling



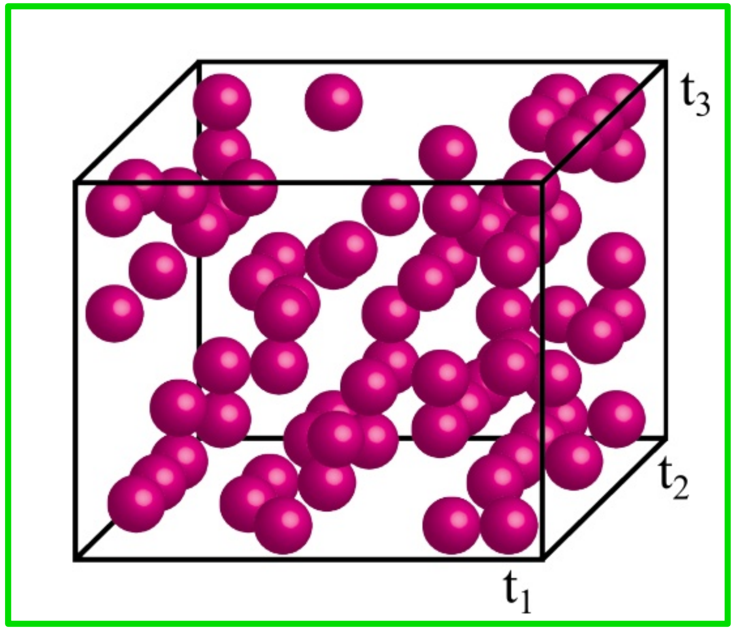
full sampling

V. Orekhov, Biomolecular NMR : modern tools for data processing and interpretation dynamics, Gothenburg, Sweden (2017).



radial sampling

G. Bodenhausen and R. R. Ernst, *J. Magn. Reson.* (1969), 45, 2, 367–373 (1981).



non-uniform sampling

J. C. J. Barna *et al*., *J. Magn. Reson.* (1969), 73, 1, 69–77 (1987).

☺ strong duration decrease
☺ full resolution
☺ sensitivity increase
☹ processing complexity

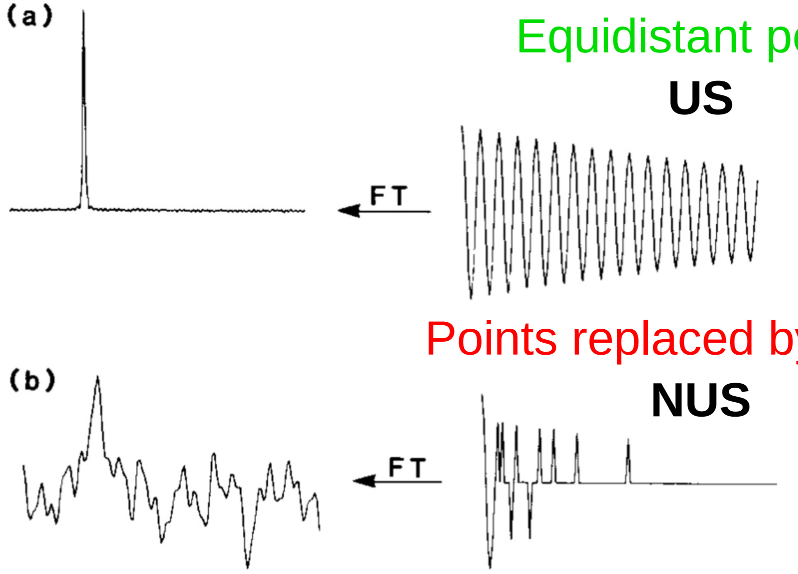
Non-uniform sampling

Equidistant points

US

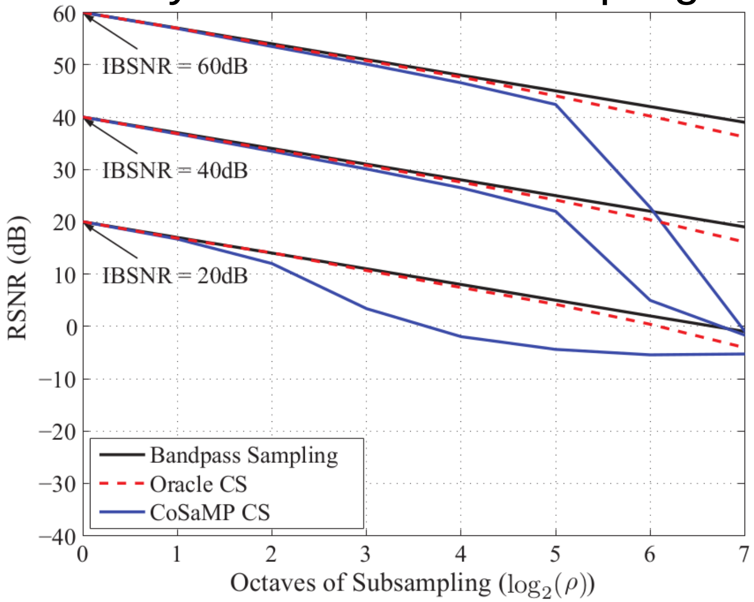
Points replaced by zeroes

NUS

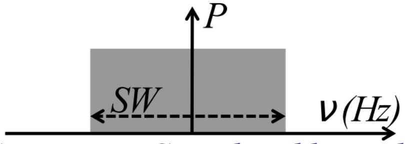


J. C. J. Barna *et al.*, *J. Magn. Reson. (1969)*, 73, 1, 69–77 (1987).

SNR / sqrt(2)
by factor 2 of subsampling



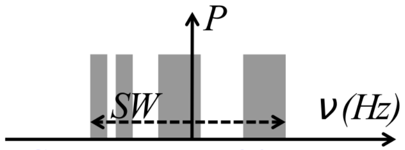
M. A. Davenport *et al.*, *IEEE T. Signal Proces.*, 60, 9, 4628–4642 (2012).



Spectrum is SW – band limited

Nyquist/Shannon theorem

$N_{NS} = 1 / SW$



Spectrum is K % sparse

Candes, Romberg & Tao

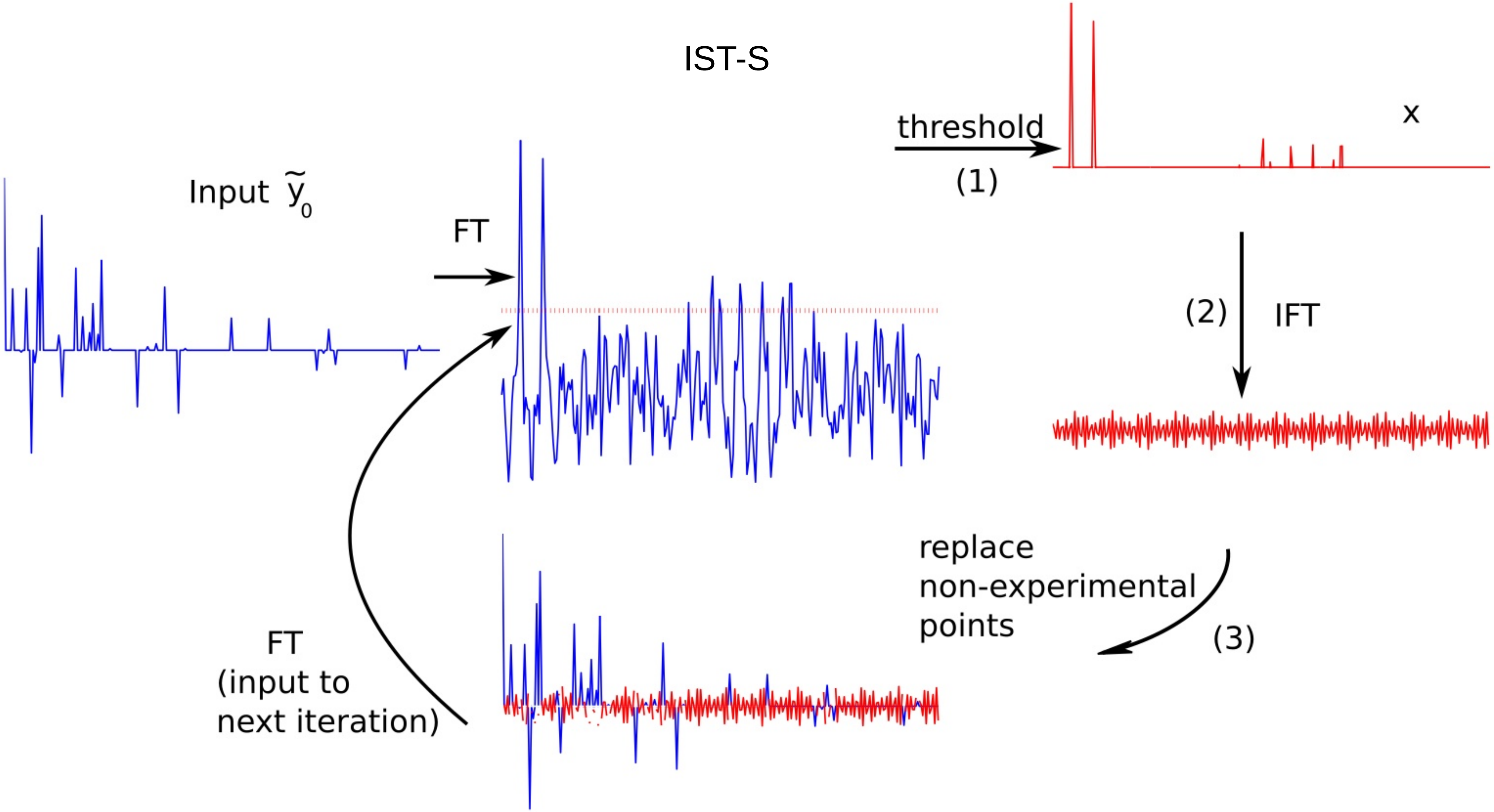
$N_{CS} = K \log (N_{NS}/K)$

Fourier Transform (FT) Compressed Sensing (CS)

V. Orekhov, Workshop on novel reconstruction strategies in NMR and MRI, Goettingen, Germany (2010).

Compressed sensing

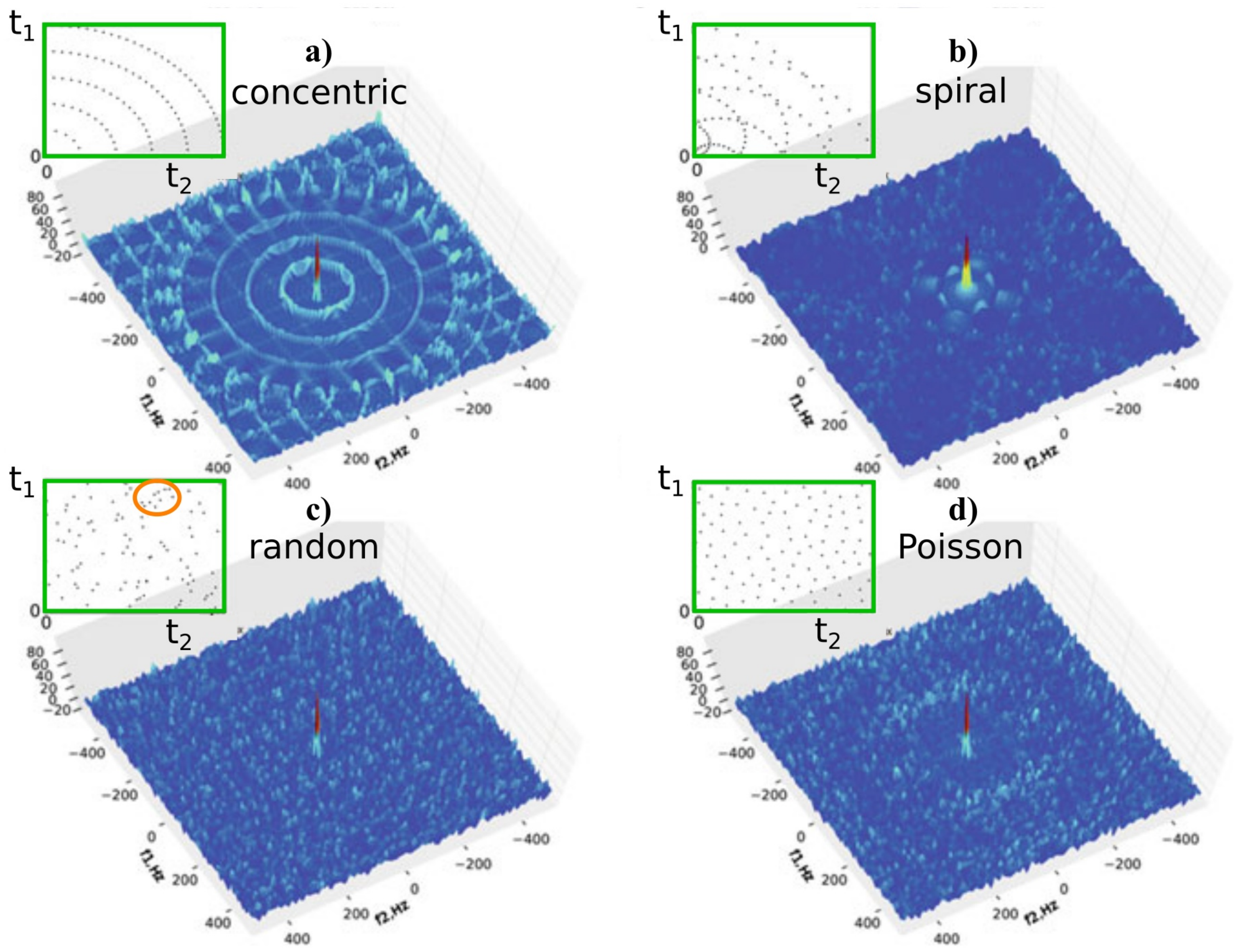
IST-S



A. Shchukina *et al.*, *J Biomol NMR*, 68, 2, 79–98 (2017).

2D artifacts

Point Spread Function

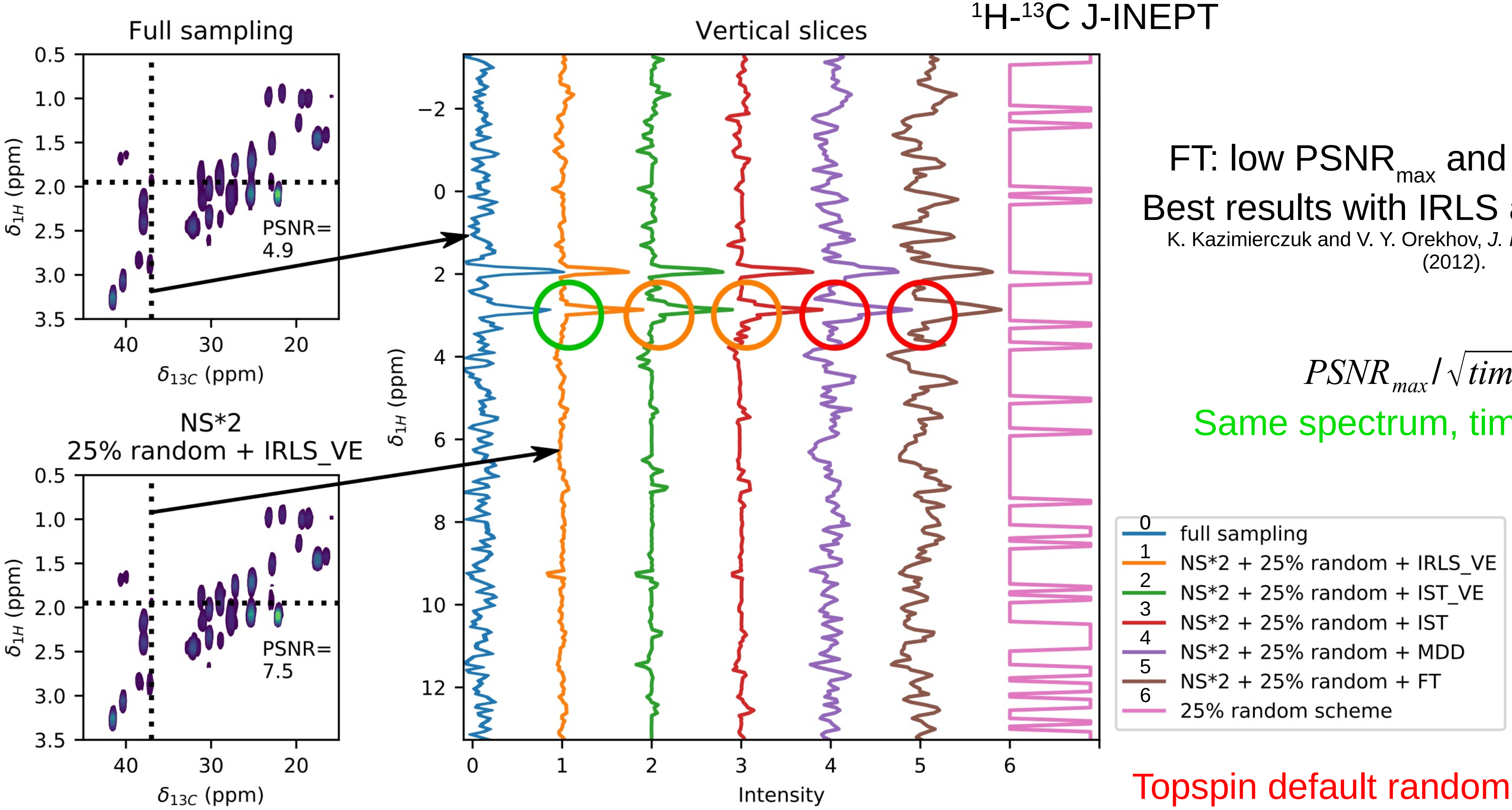


K. Kazimierczuk *et al.* in Novel sampling approaches in higher dimensional NMR, (Springer, 2012), 79–124.

Mobile sample

Gelatin: denatured collagen
Main protein of cornea and bone
F. Portier

^{1}H-^{13}C J-INEPT



FT: low $PSNR_{max}$ and low resolution

Best results with IRLS and virtual echo

K. Kazimierczuk and V. Y. Orekhov, *J. Magn. Reson.*, *223*, 1–10 (2012).

$$PSNR_{max} / \sqrt{time} \times 2.2$$

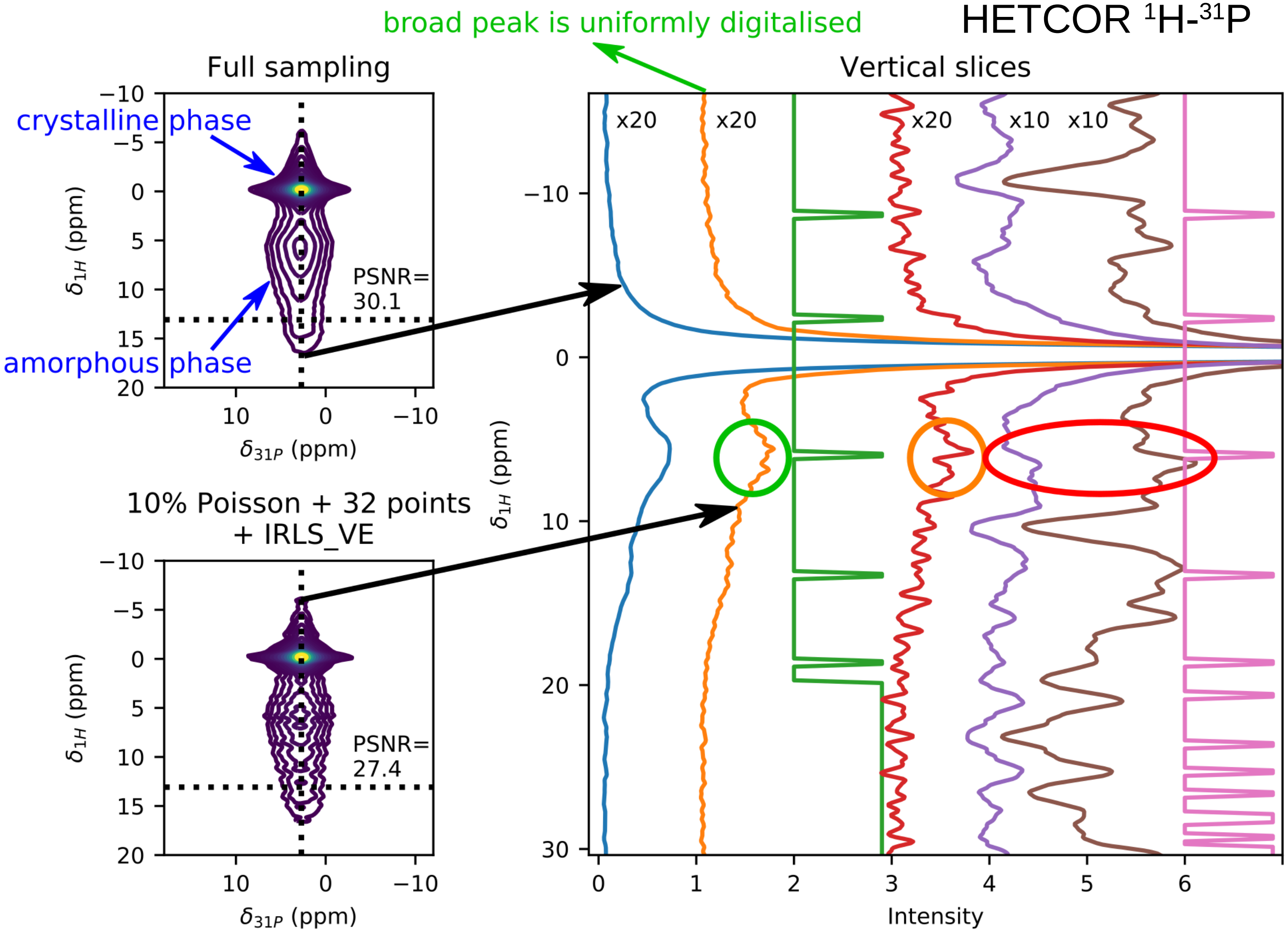
Same spectrum, time gain = 4.7

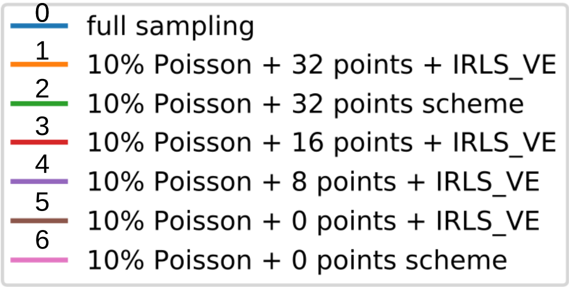
Topspin default random seed 54321

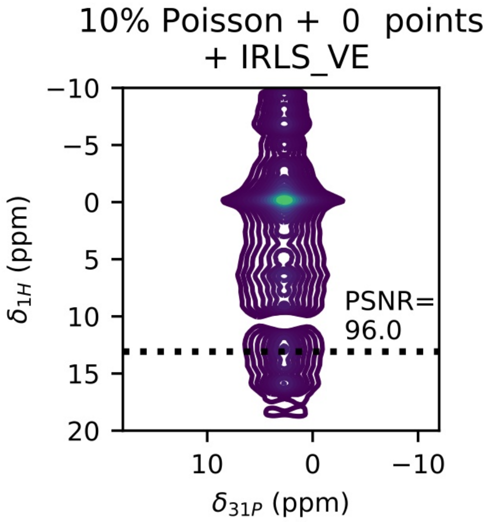
Hybrid sampling

Hydroxyapatite
S. Von Euw

HETCOR ^{1}H-^{31}P







Needs a discrete signal

E. J. Candes and M. B. Wakin, *IEEE Signal Proc. Mag.*, 25, 2, 21–30 (2008).

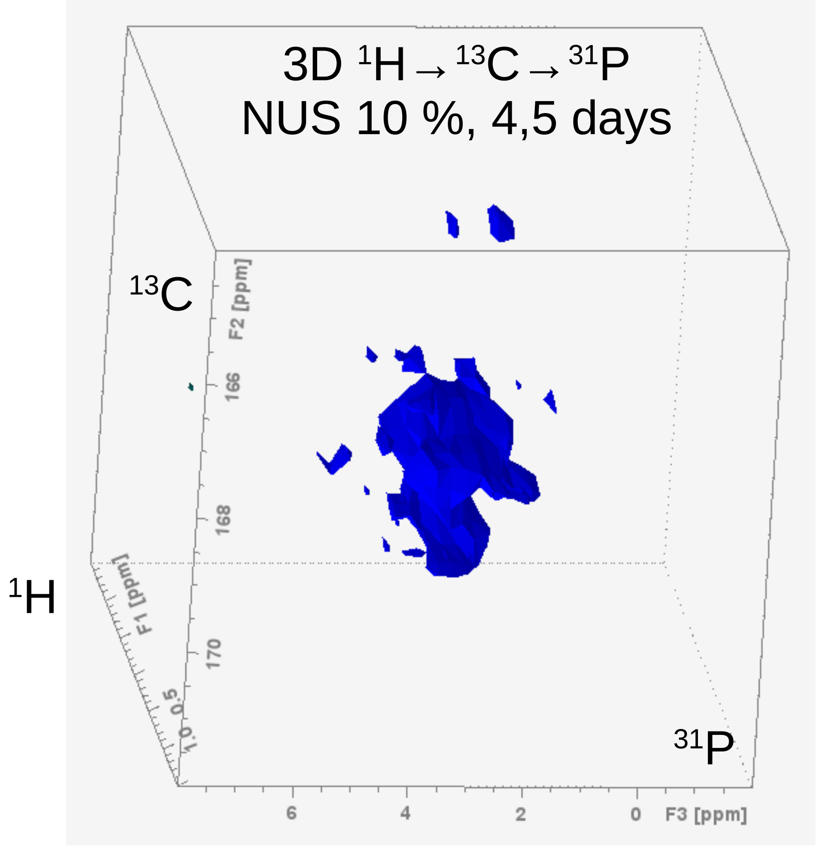
$$PSNR_{max} / \sqrt{time} \times 1.8$$

Time gain = 3.1

NUS summary

Characteristics	US	NUS
High dimension	😐	🙂
Sensitivity	☹	🙂
Resolution	☹	🙂
Sampling	🙂	😐
Reconstruction	🙂	☹
Topspin	🙂	😐
External	🙂	🙂
Time gain	NA	~3-5

NUS outlook



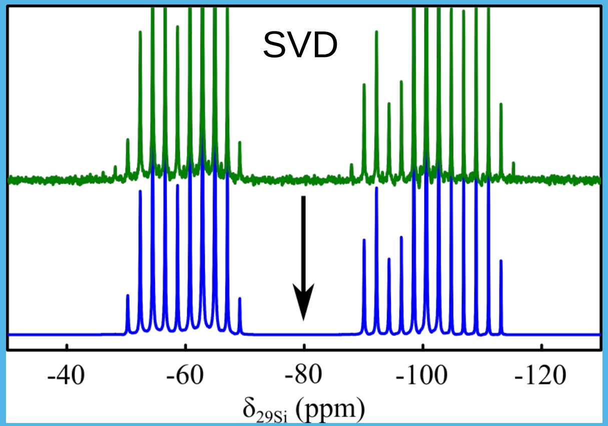
MddNMR

K. Kazimierczuk, V. Y. Orekhov, *Angew. Chem. Int. Ed.* 50, 5556–5559 (2011).

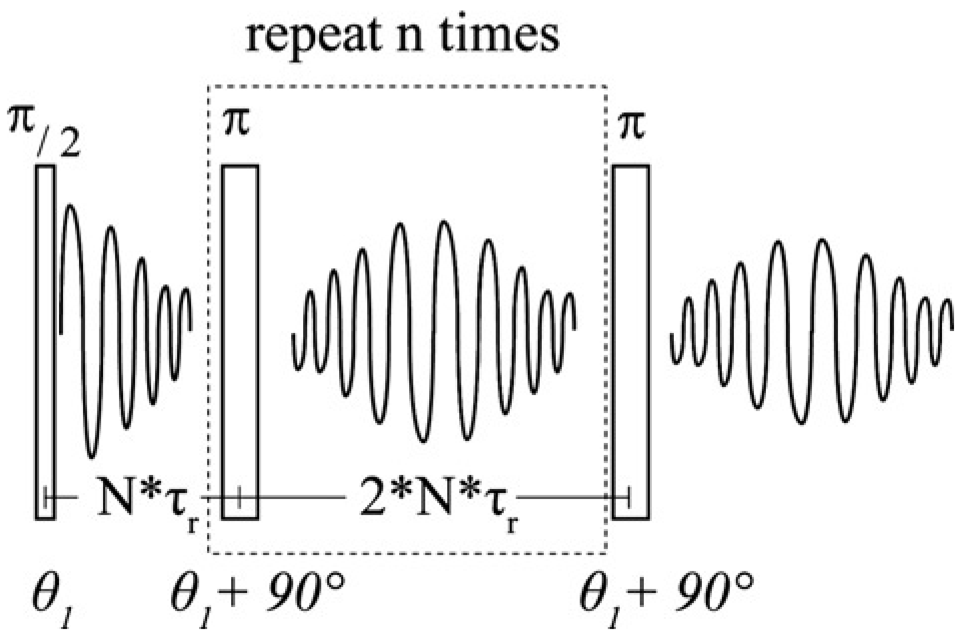
NMRbox.org

M. W. Maciejewski *et al.*, *Biophys. J.*, 112, 8, 1529–1534 (2017).

Signal processing



CPMG echoes

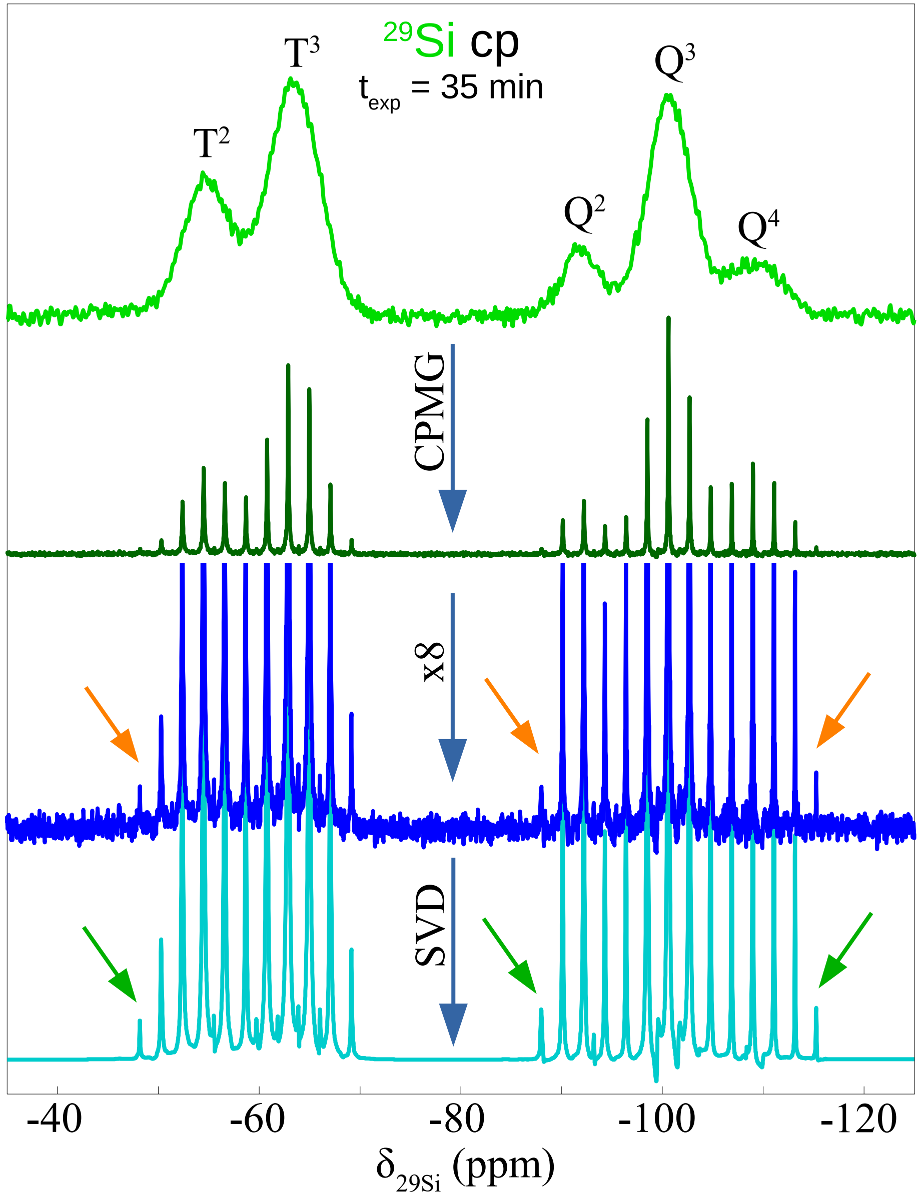


H. Y. Carr and E. M. Purcell, *Phys. Rev.*, 94, 3, 630–638 (1954).

S. Meiboom and D. Gill, *Rev. Sci. Instrum.*, 29, 8, 688–691 (1958).

W. J. Malfait and W. E. Halter, *J. of Non-Cryst. Solids*, 354, 34, 4107–4114 (2008).

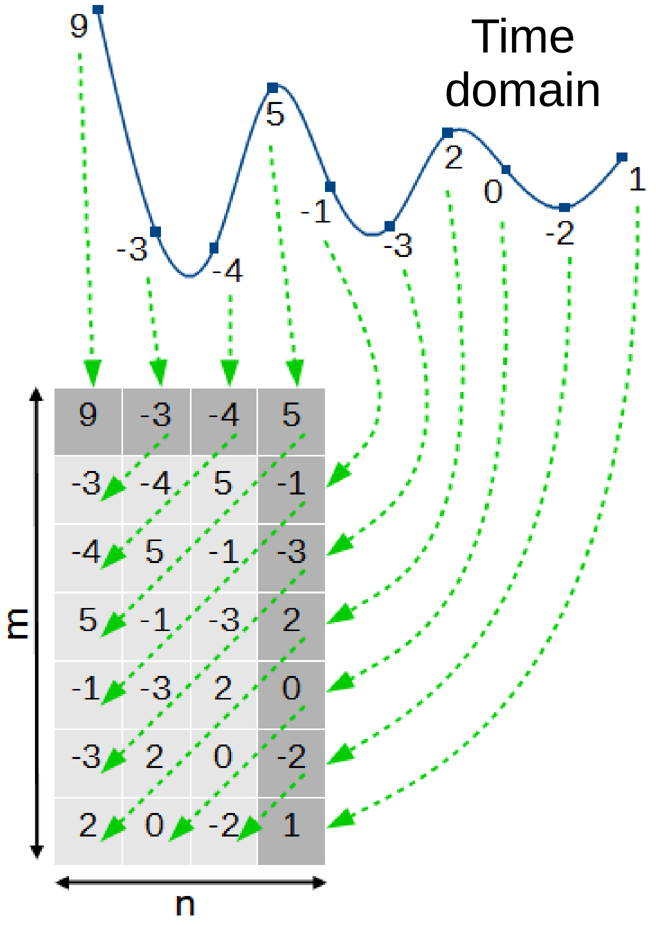
TEOS:MTEOS 1:1
V. Barret-Vivin



Discretize spectrum
Time gain ~3-100
Small spikelets necessary to reconstruct global shape
Limit of denoising ?

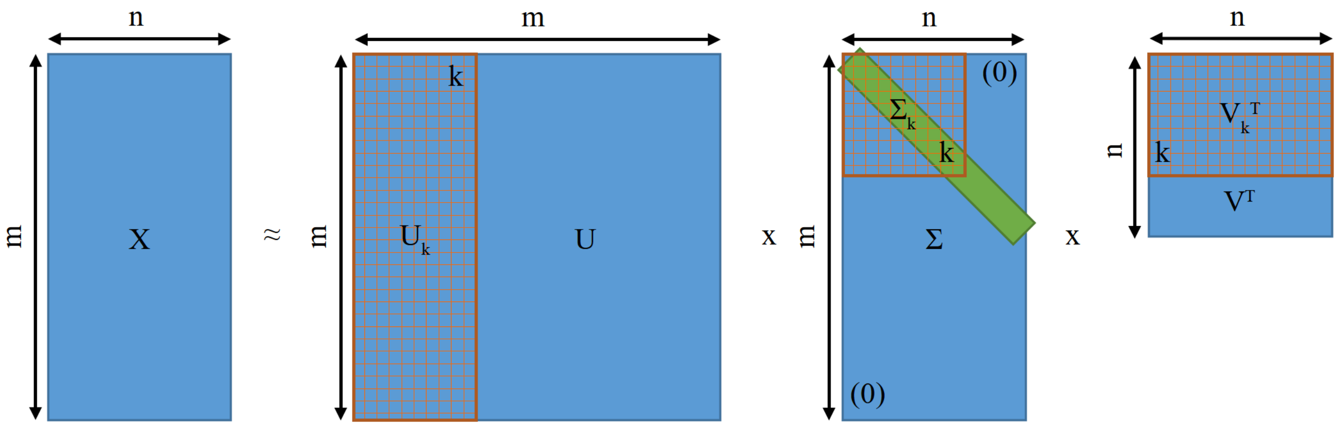
Chimie de la Matière Condensée de Paris

Singular Value Decomposition (SVD)



Hankel Matrix

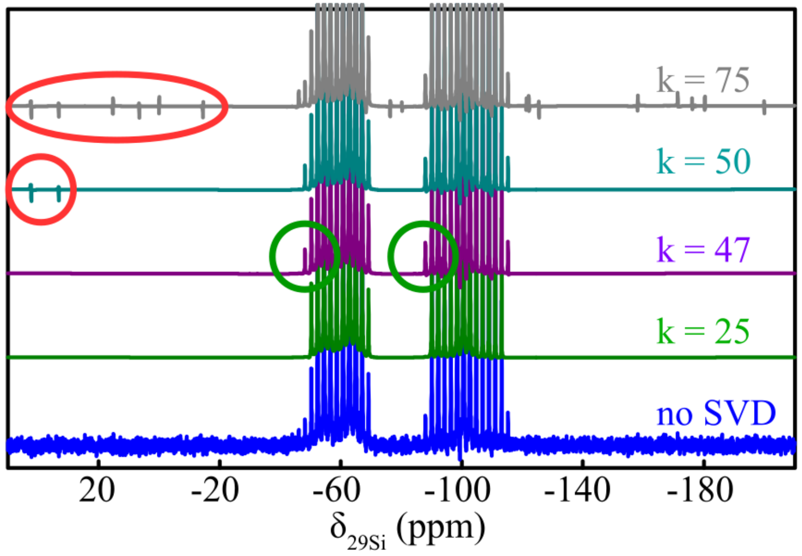
M. A. Arbib and E. G. Manes, *J. Comput. Syst. Sci.*, 20, 3, 330–378 (1980).



Low rank matrix approximation

D. W. Tufts *et al*, *P. IEEE*, 70, 6, 684–685 (1982).
J. A. Cadzow, *IEEE T. Acoust. Speech*, 36, 1, 49–62 (1988).

Frequency domain



G. Laurent *et al.*, *Appl. Spectrosc. Rev.*, 54, 602–630 (2019).

Automatic thresholding

E. R. Malinowski, *Factor analysis in chemistry* (Wiley, 3rd ed., 2002).

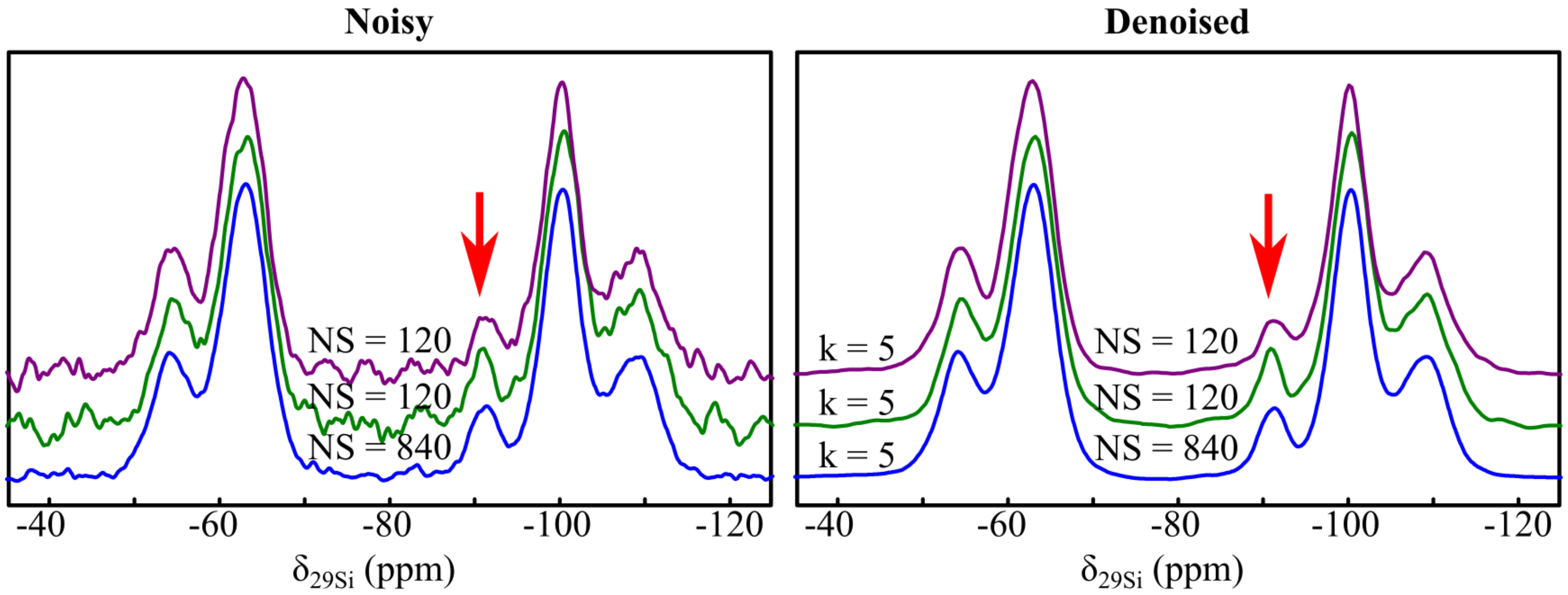
Image compression, data mining
(Principal Component Analysis, PCA)

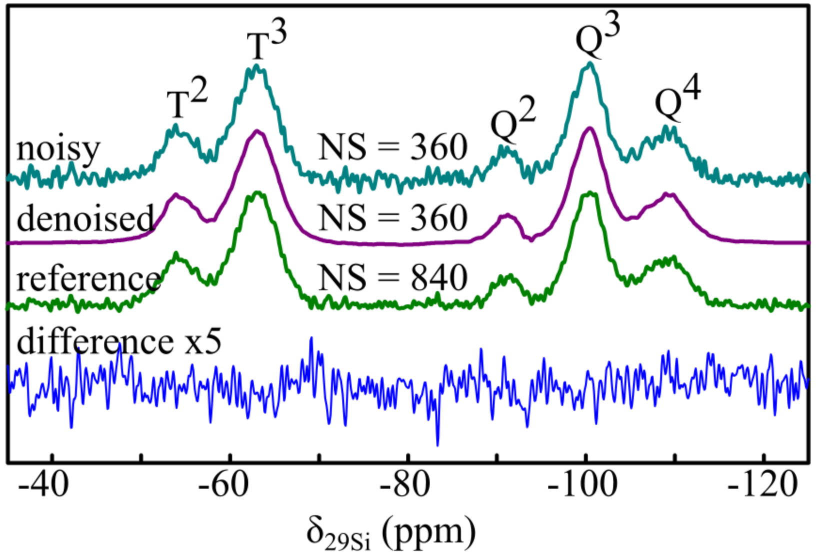
Sensitivity limit

TEOS:MTEOS

^{29}Si hpdec

t_{exp} = 2-14h





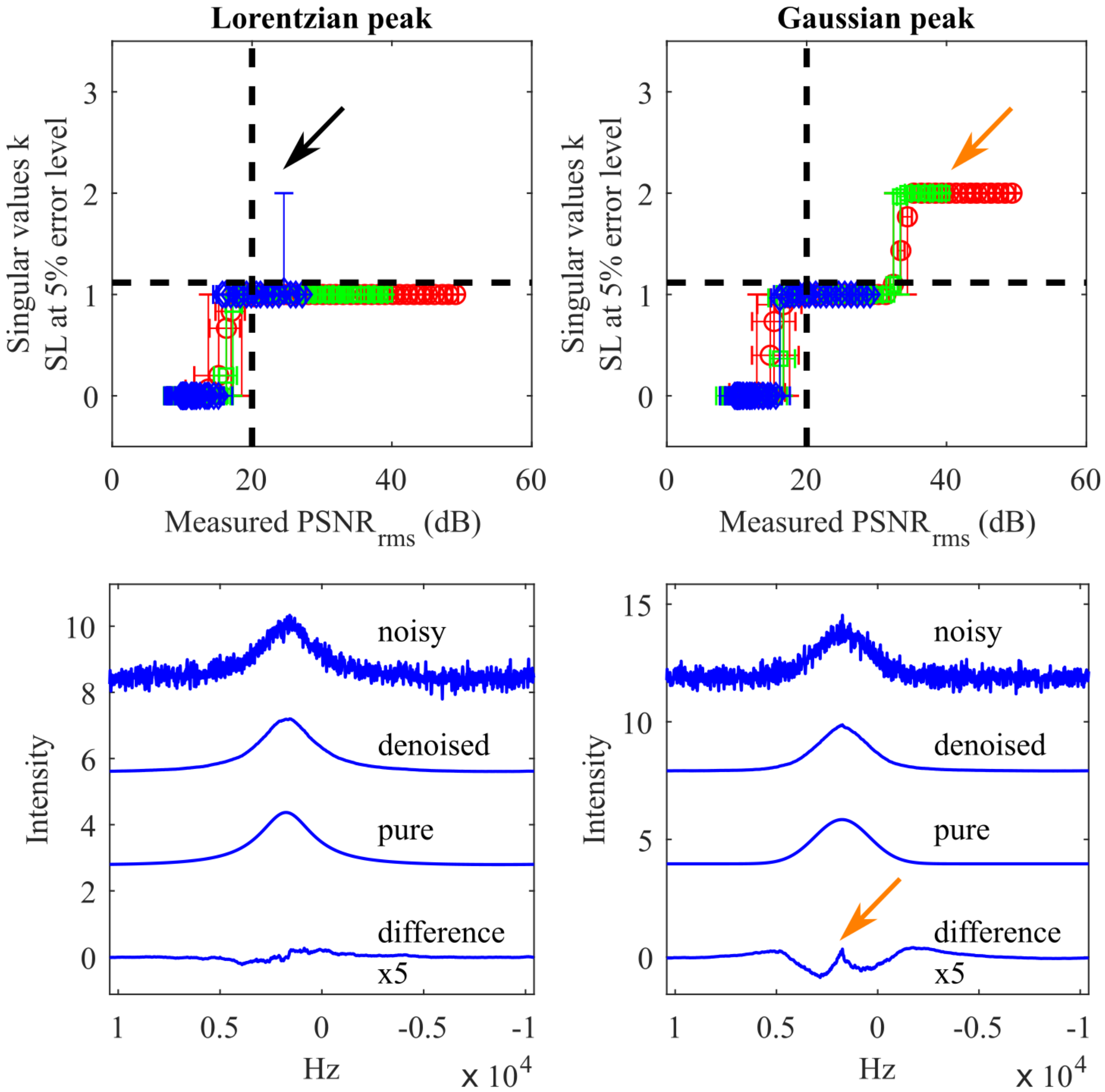
Real error: intensity corrupted by noise

Manual thresholding dangerous

$$PSNR_{max} / \sqrt{time} \times 1.5$$

Time gain = 2.3

Automatic thresholding



6*7380 **simulated spectra**

Malinowski's Significance Level (SL) at 5 %

E. R. Malinowski, *Factor analysis in chemistry* (Wiley, 3rd ed., 2002).

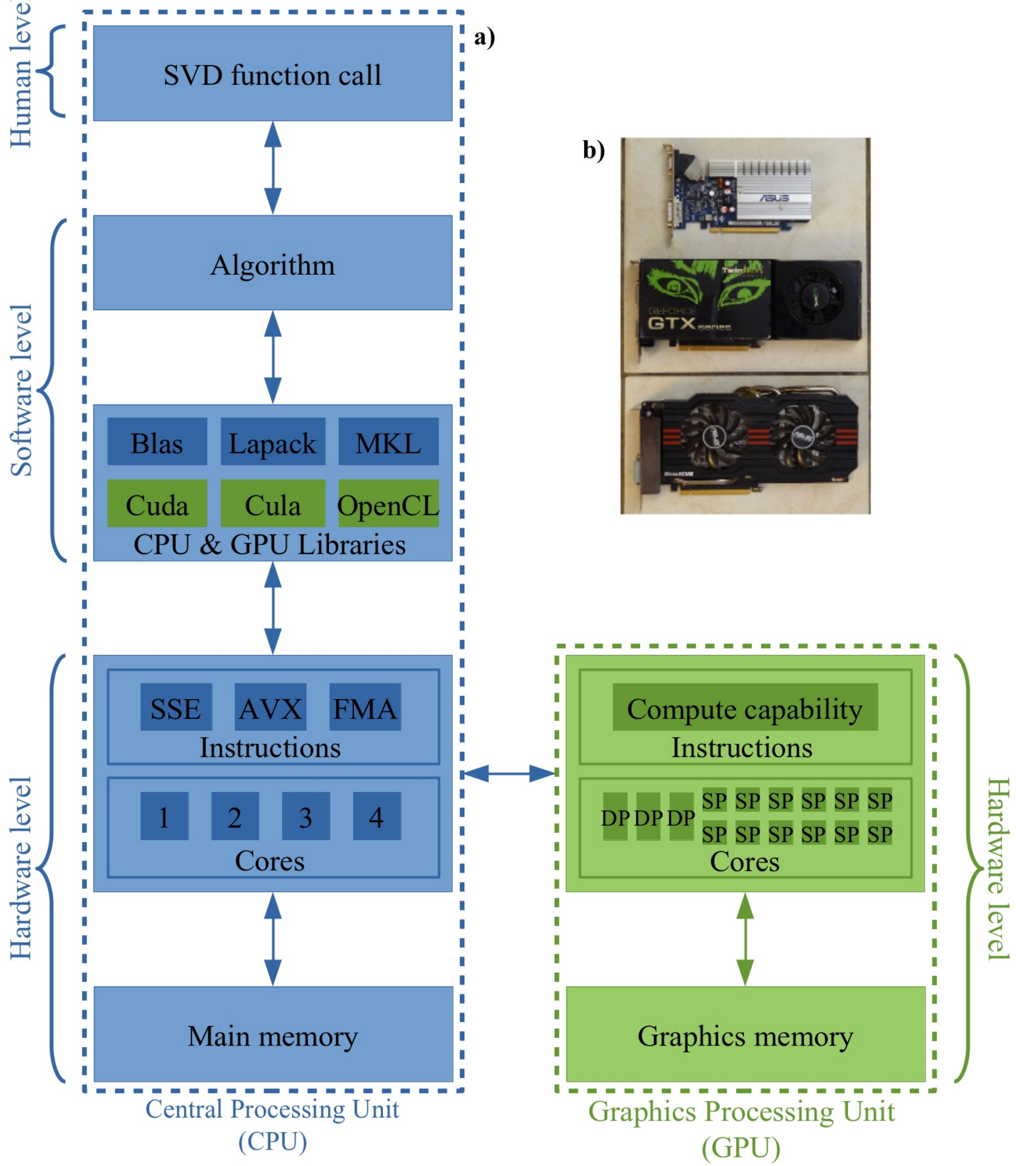
$PSNR_{max} = 2$

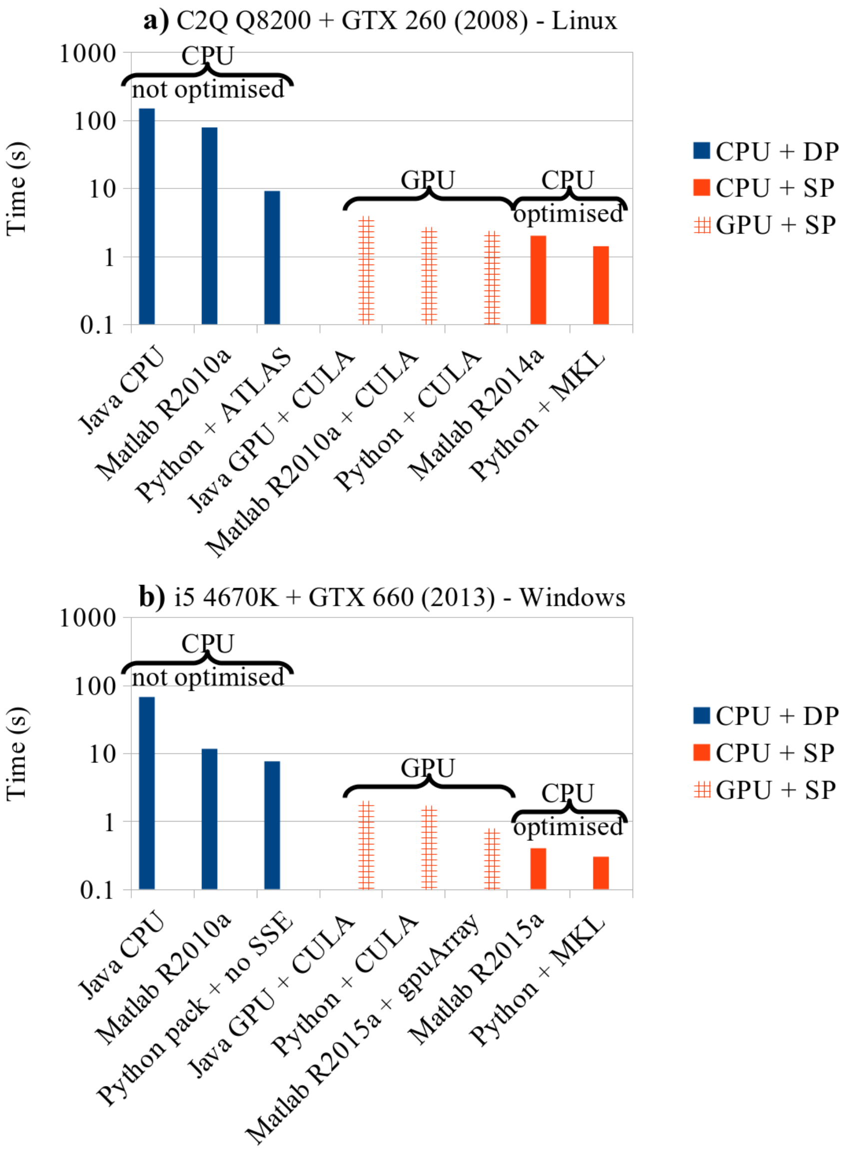
Gaussian peak: two components

Extracted error: overestimation by 20 %

Z. Dong *et al.*, *Am. J. Neuroradiol.* 30, 1096–1101 (2009).

SVD computation time





G. Laurent *et al.*, *Appl. Spectrosc. Rev.*, 55, 173–196 (2020).

SVD summary

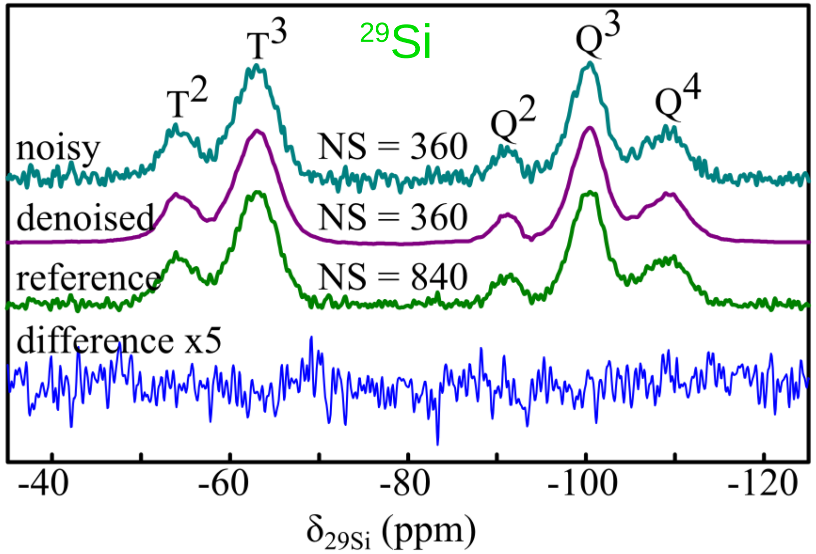
Useful to denoise spectra

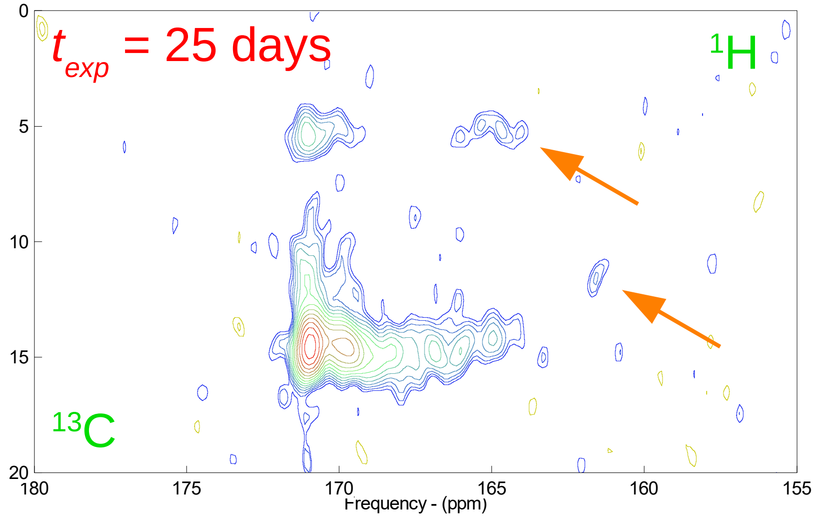
***$PSNR_{max}$* ~2**

Time gain ~2.3

Computation time gain ~100

~20 % overestimation of Gaussian peaks





Abalone shell – Biomineralization axis

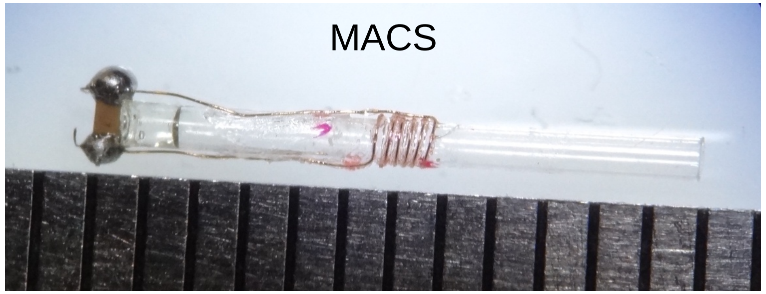
W. Ajili *et al.*, *J. Phys. Chem. C.* 124, 14118–14130 (2020).

SVD outlook

Improve 2D denoising

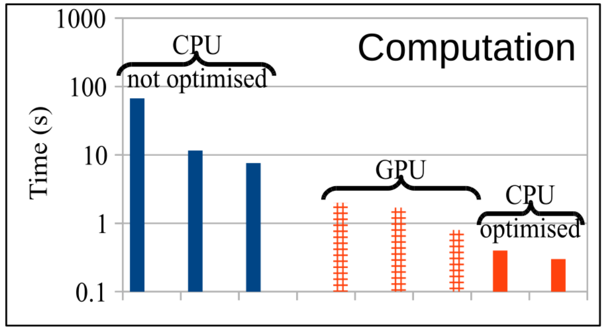
Conclusion

General conclusion

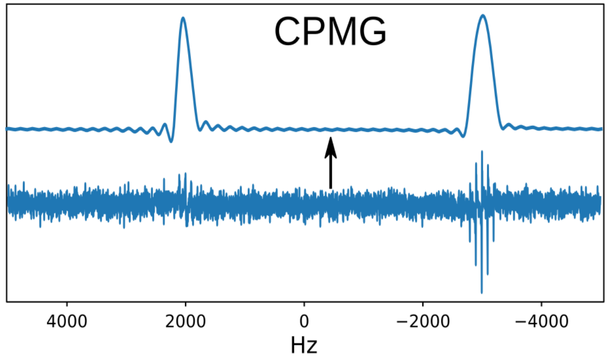


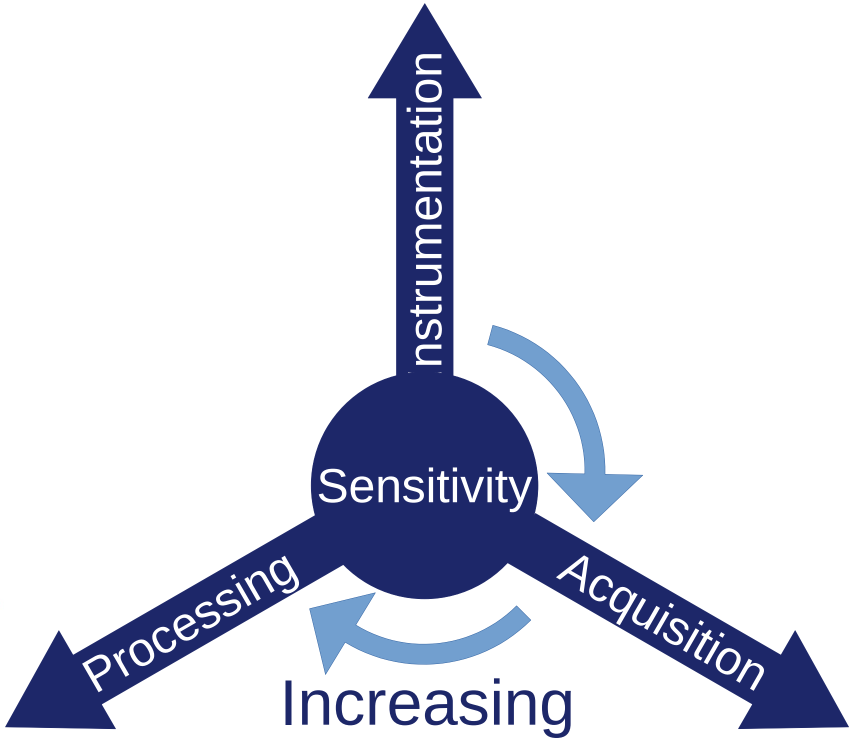
Time gain 4-10

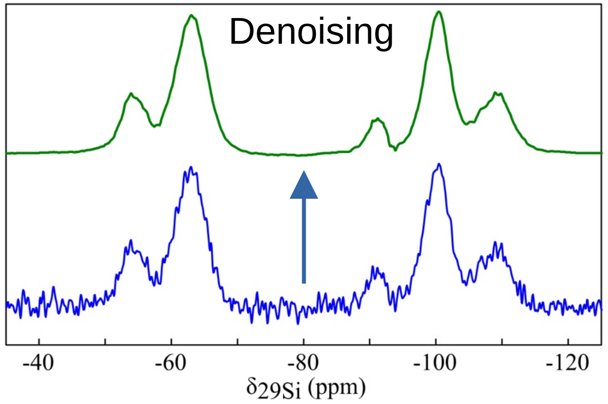
Time gain ~100

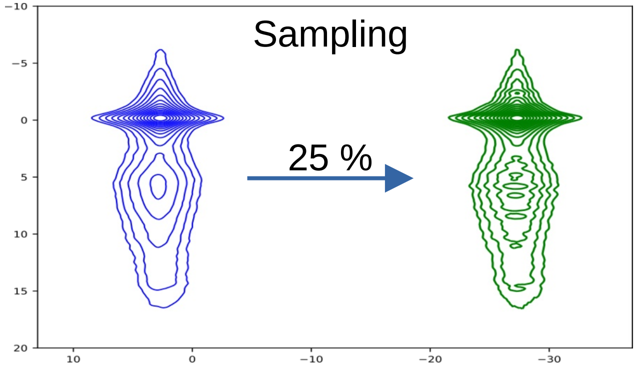


Time gain 3-100









Time gain 2-3

Increasing NMR sensitivity without DNP

Time gain 3-5

General conclusion

PSNR gain of 2→ time gain of 4

Potential decrease of acquisition time by > 500

More samples or more complex materials

Time consuming developments

Need of programming

General outlook

Combining techniques

Improving MACS dipolar recoupling

Process 3D NUS spectra

Improving SVD on 2D spectra

Chimie de la Matière Condensée de Paris CMCP

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cnrs


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- Andrew Rankin (2020-2021)


NMR staff

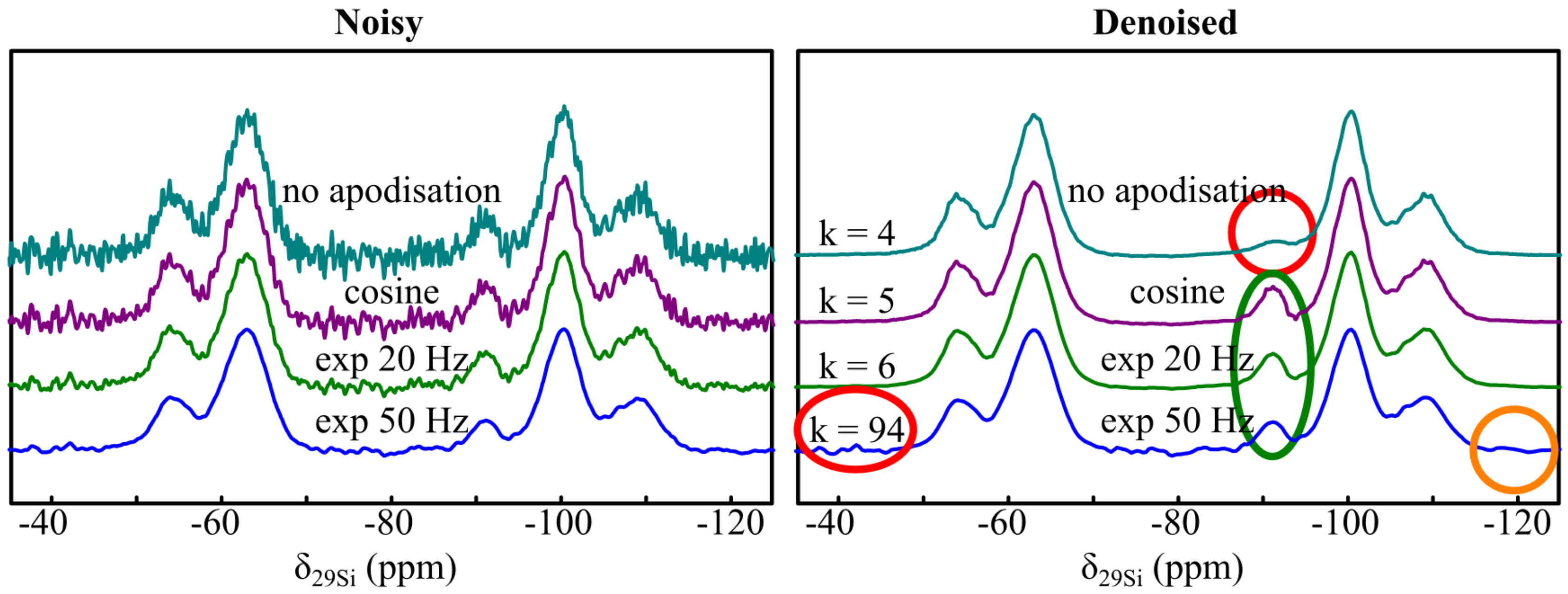

Photographers

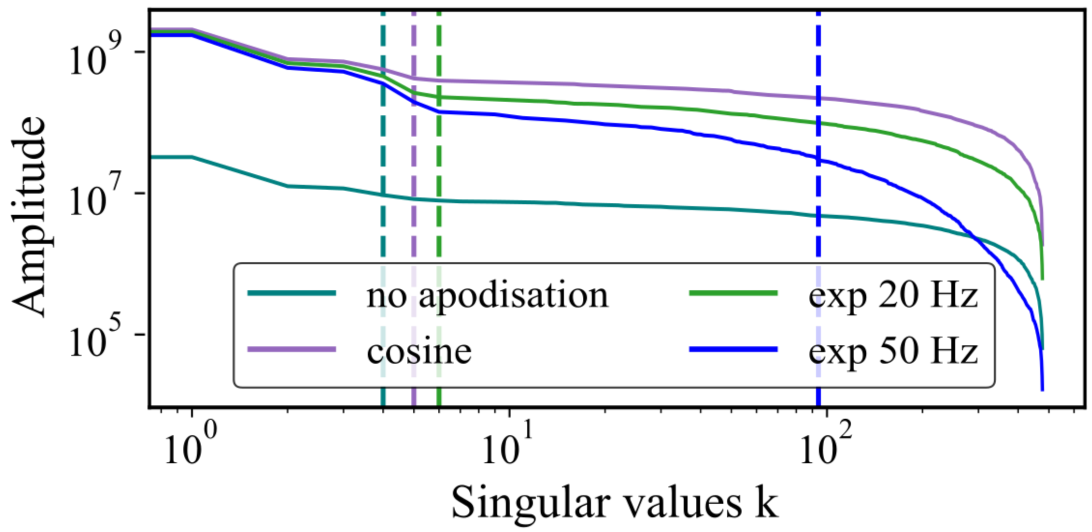

Thank you for your attention
GERM
GROUPEMENT D'ETUDES de
RESONANCE MAGNETIQUE

Supplementary materials

Apodisation

TEOS:MTEOS
^{29}Si hpdec
t_{exp} = 6h





Preprocessing step

Strong apodisation degrades automatic thresholding

Best results with cosine