Zangger-Sterk and band-selective methods

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NMR Methodology group

The University of Manchester

Workshop on Pure Shift NMR

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School of Chemistry, University of Manchester, Manchester, UK.

Outline

Introduction:

- Set the scene
- Shift selection
- Slice and shift selection

Pure shift methods:

- Zangger-Sterk (ZS)
- Band-selective (BS)

Practical implementation:

- Band-selective: selective pulses
- Zangger-Sterk: spatial encoding gradient and selective pulses

Applications

Summary

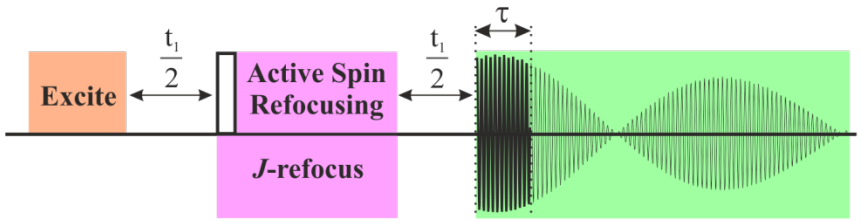
Outline

Introduction:

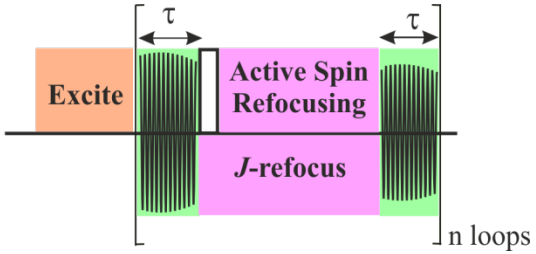
- Set the scene
- Shift selection
- Slice and shift selection

Acquisition mode

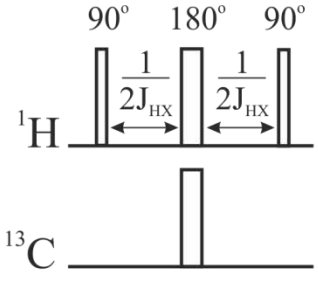
Interferogram



Real-time

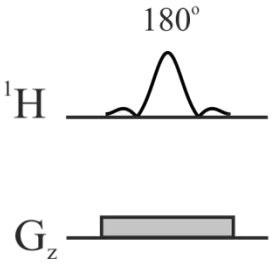


Active spin refocusing methods



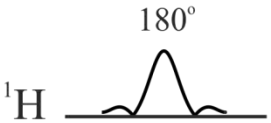
BIRD

BIlinear Rotation Decoupling



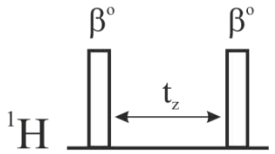
ZS

Zangger-Sterk



BS

Band-Selective HOBS/BASH/BASHD

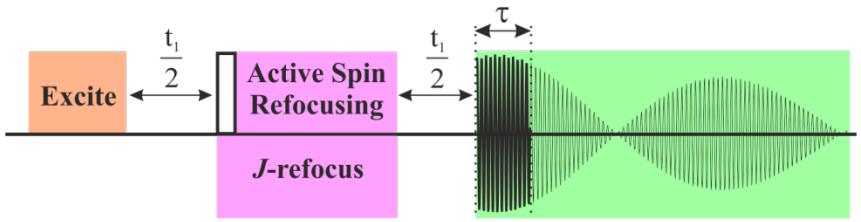


“double β”

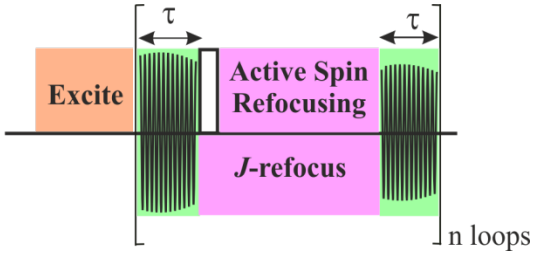
Anti-z-COSY PSYCHE

Acquisition mode

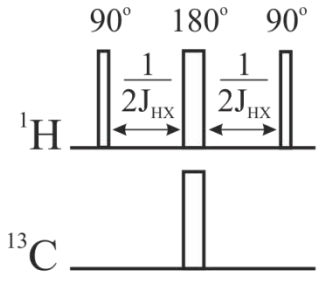
Interferogram



Real time

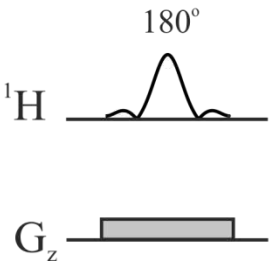


Active spin refocusing methods



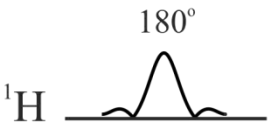
BIRD

BIlinear Rotation Decoupling



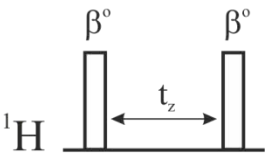
ZS

Zangger-Sterk
(Slice and shift selection)



BS

Band-Selective
(shift selection)

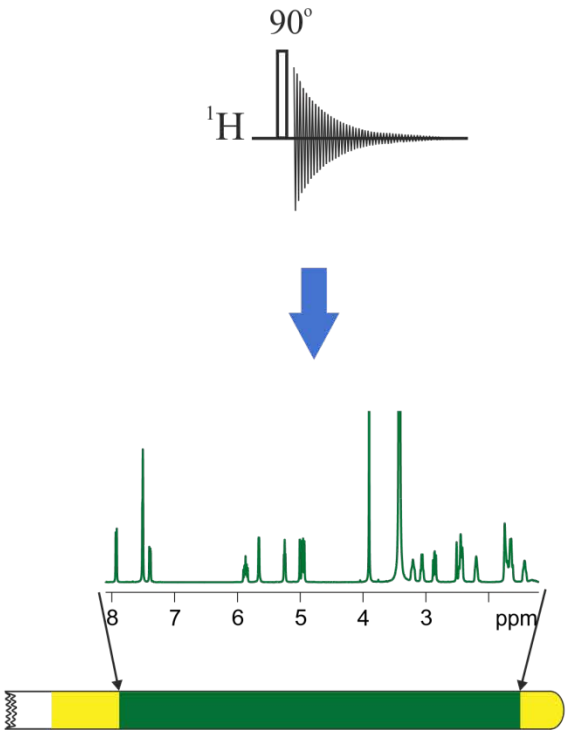


“double β”

Anti-z-COSY
PSYCHE

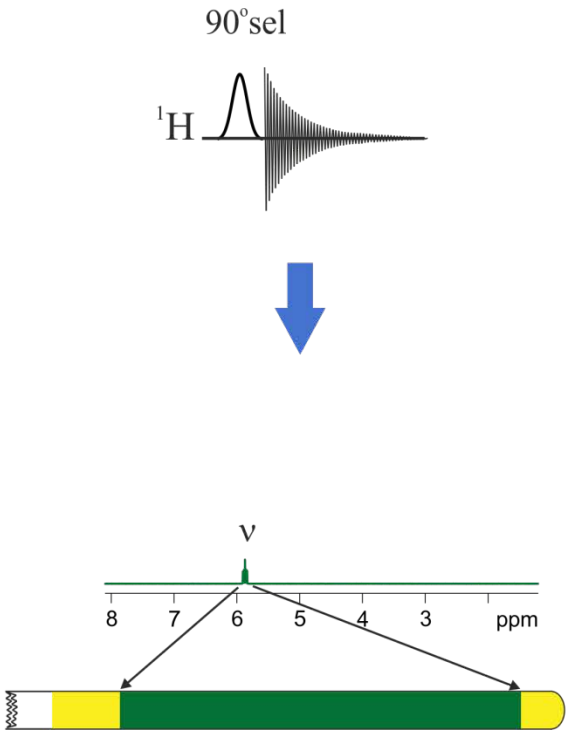
Inversion of active spins using selective pulses

Broadband



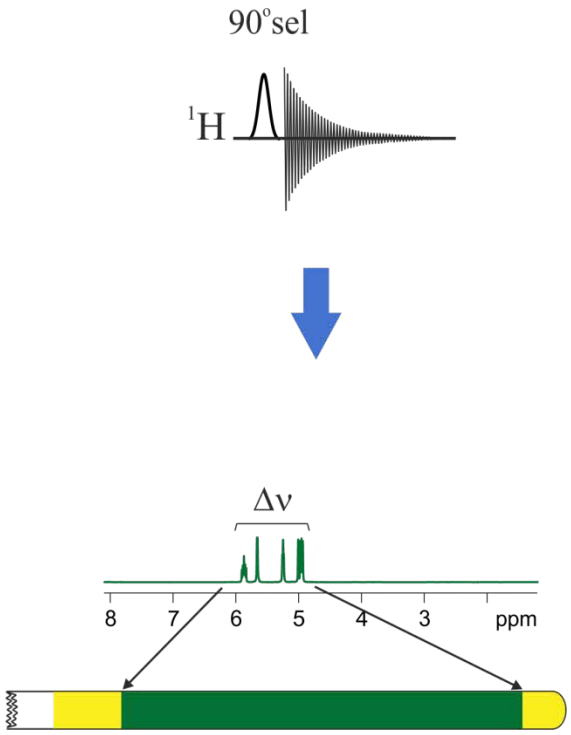
All frequencies are excited in the whole active volume

Frequency selection



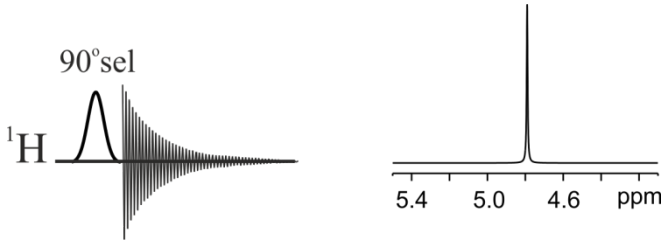
A narrow range of frequencies is excited in the whole active volume

Band selection

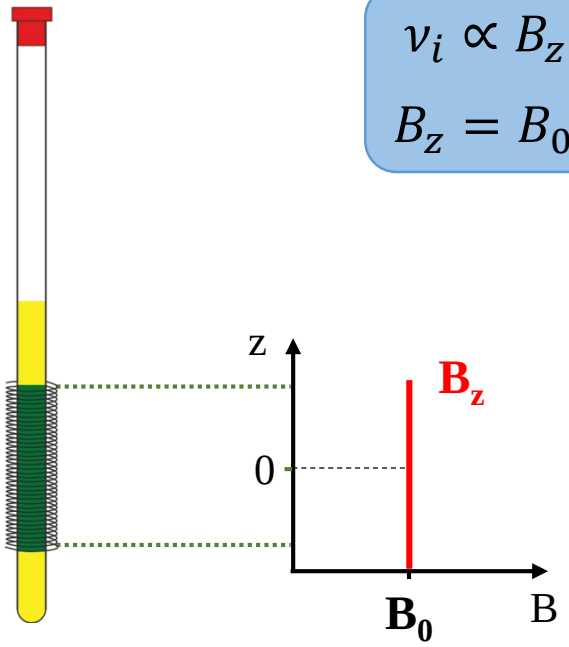


A wide range of frequencies is excited in the whole active volume

Shift selection

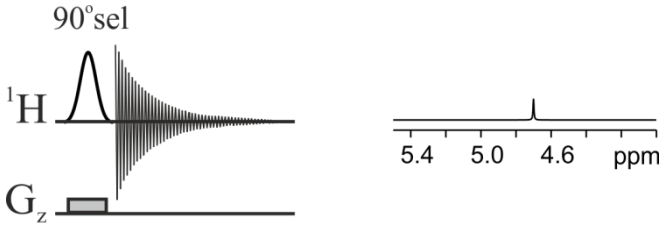


$$\nu_i \propto B_z$$
$$B_z = B_0$$

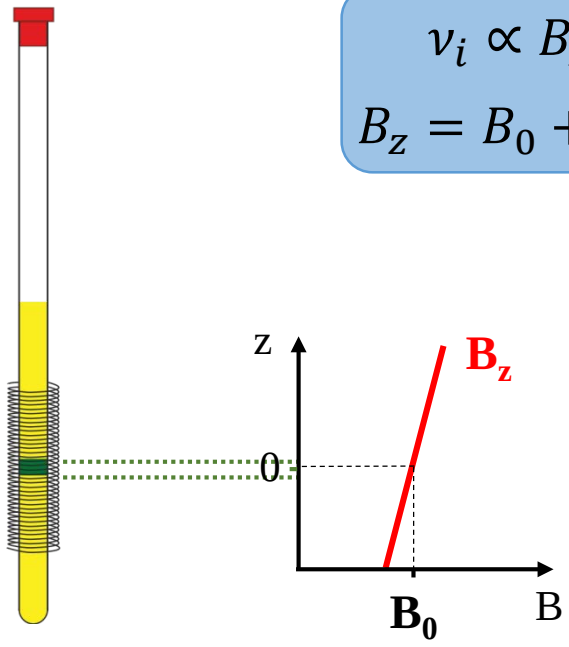


In absence of PFG B_z is constant along z-axis

Slice and shift selection

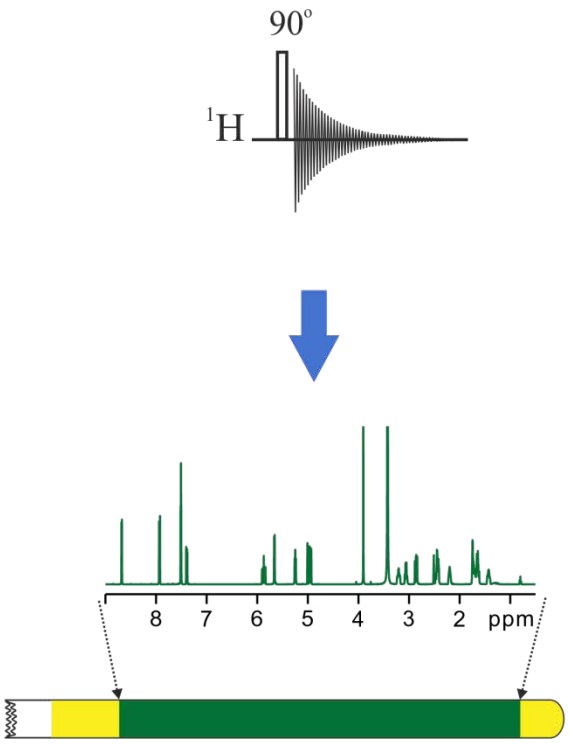


$$\nu_i \propto B_z$$
$$B_z = B_0 + zG$$



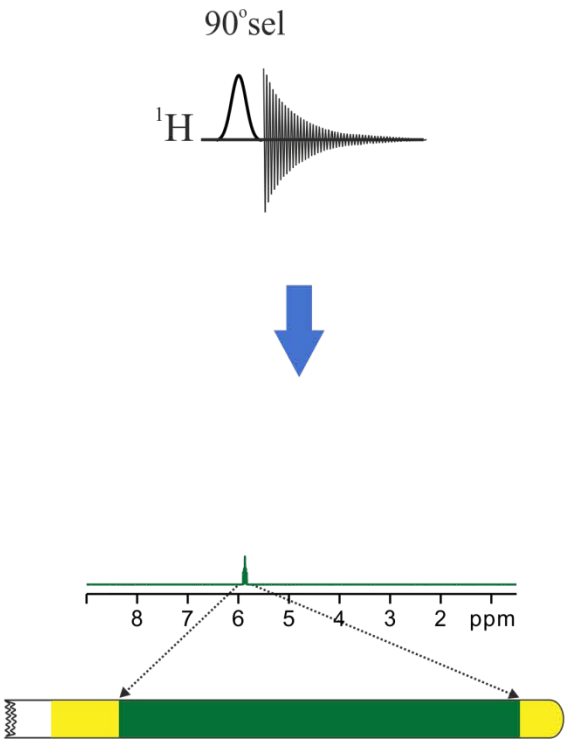
In presence of PFG B_z varies linearly along z-axis

Broadband



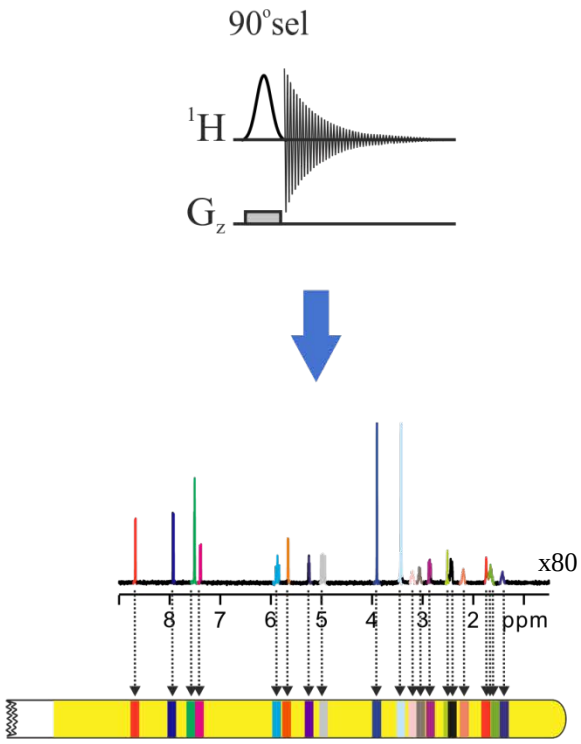
All frequencies are excited in the whole active volume

Shift selection



A range of frequencies are excited in the whole active volume

Slice and shift selection



Different frequencies are excited in different parts of the active volume

Sensitivity

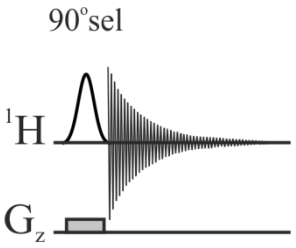
Typical experimental conditions

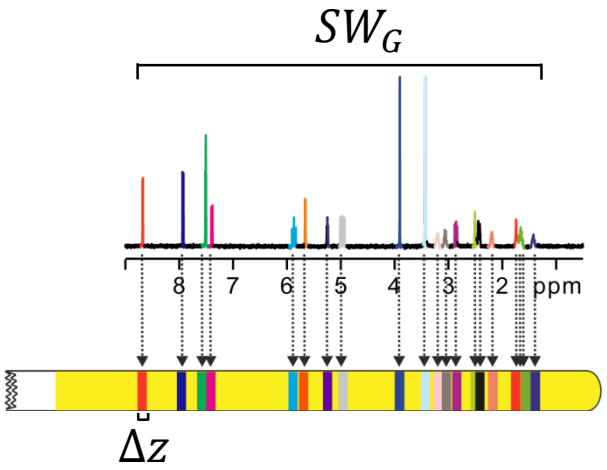
- Rsnob pulse ($\Delta\nu$ = 50 Hz)
- SW_G = 5000 Hz (10 ppm @ 500 MHz)
- L = 1.8 cm
- G = 0.65 G/cm

Δz = 0.018 cm

(≈ 100 slices)

Sensitivity ≈ 1%





Spectral window covered by the gradient:

$$SW_G = \frac{\gamma}{2\pi} LG$$

z-position:

$$z = (\Omega - \nu_i) / \frac{\gamma}{2\pi} G$$

Slice thickness:

$$\Delta z = \Delta\nu / \frac{\gamma}{2\pi} G$$

The selectivity and spectral range required will determine the sensitivity in each case

Selectivity ↔ $\Delta\nu$

SW_G ↔ G

→ Δz ↔ **SNR**

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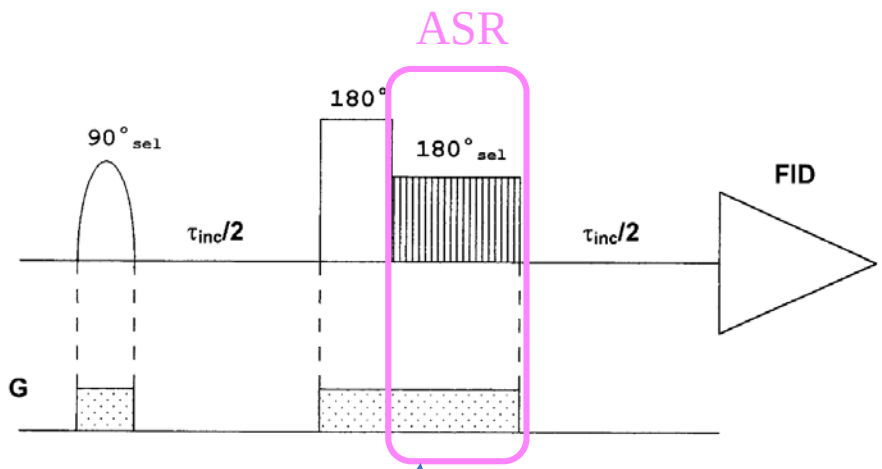
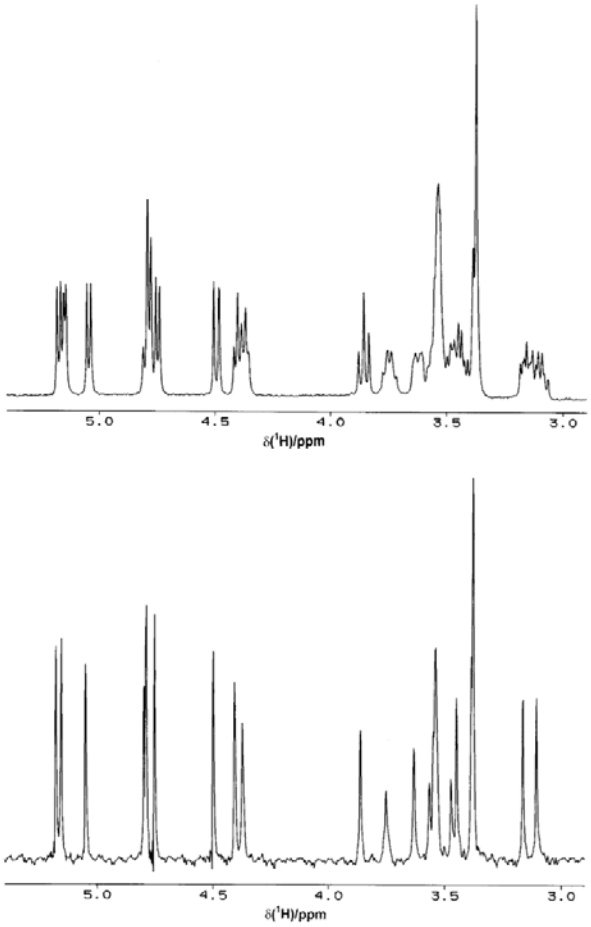
Homonuclear Broadband-Decoupled NMR Spectra

KLAUS ZANGGER AND HEINZ STERK*



Soft 180° pulses (DANTE) in the presence of a weak PFG



J. Magn. Reson. **124**, 486 (1997)

Homonuclear Broadband-Decoupled NMR Spectra

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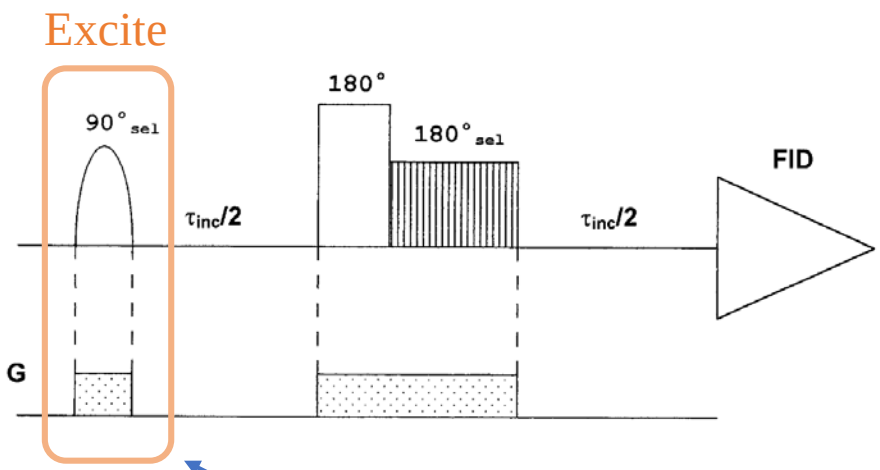
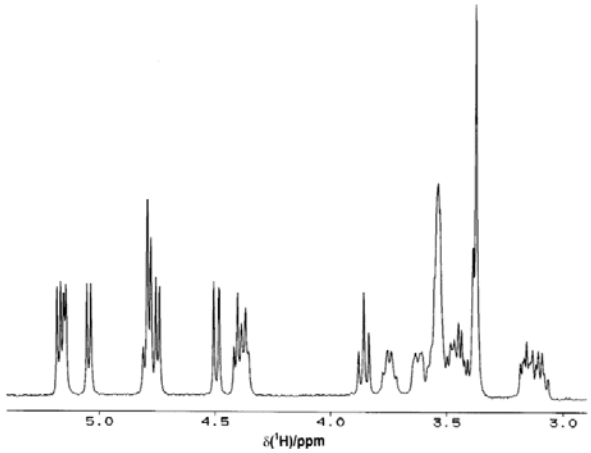
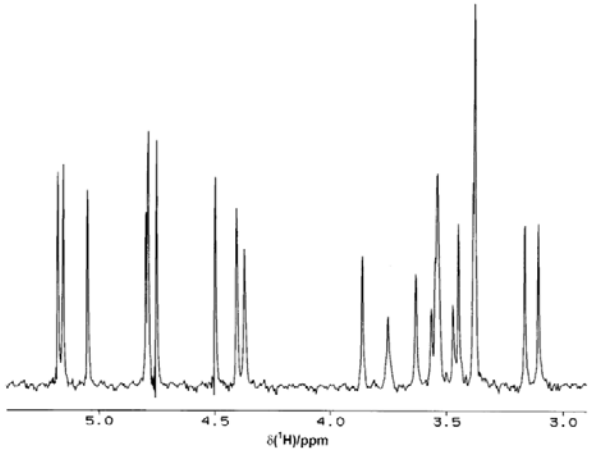


Initial slice and shift selective 90° pulse





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Homonuclear Broadband-Decoupled NMR Spectra

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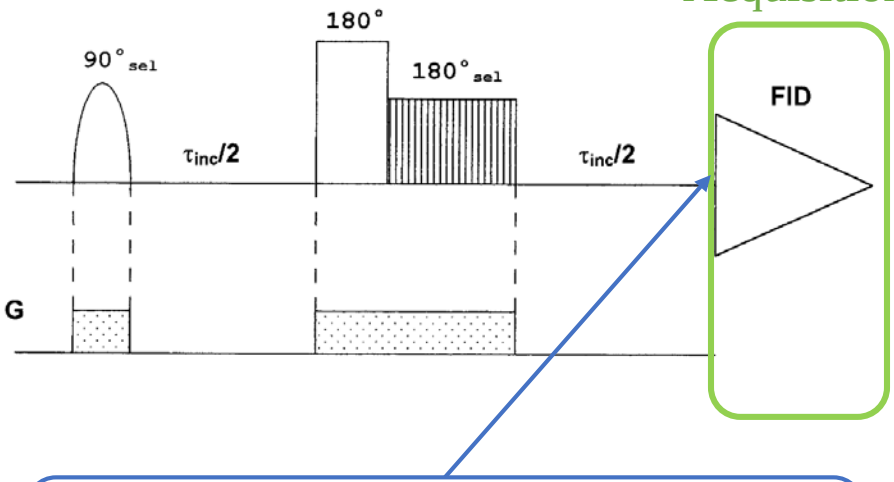
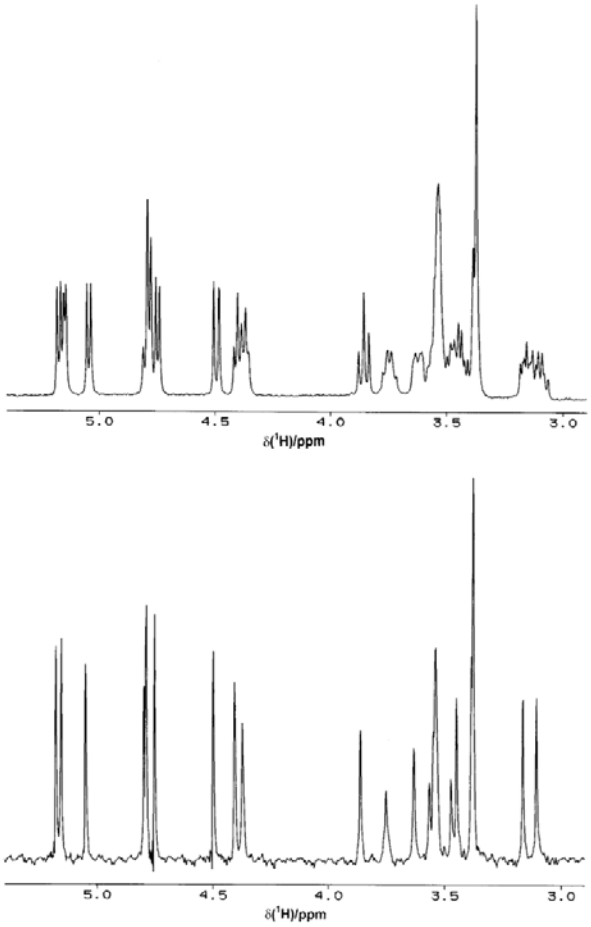




Interferogram acquisition. J_{HH} is refocused at the beginning of each chunk

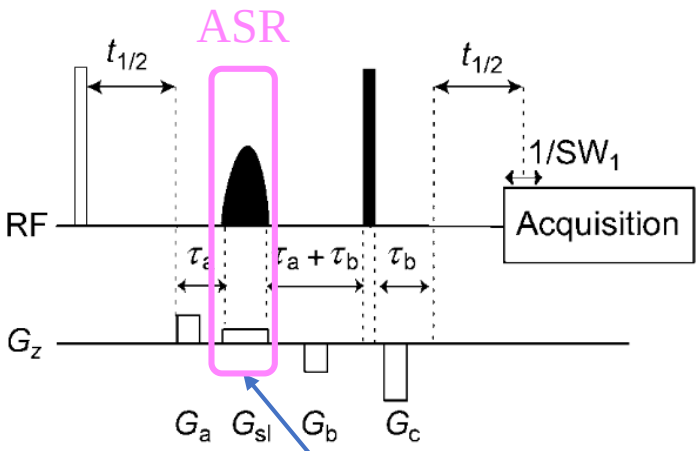
J. Magn. Reson. **124**, 486 (1997)

¹H NMR without Couplings

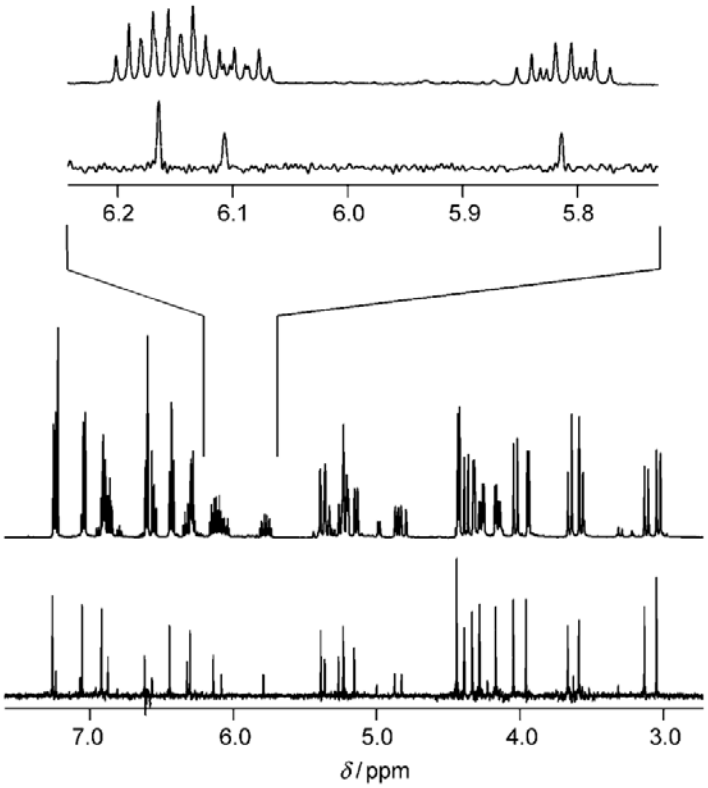
DOI: 10.1002/anie.201001107

Pure Shift ^{1}H NMR: A Resolution of the Resolution Problem?**

*Juan A. Aguilar, Stephen Faulkner, Mathias Nilsson, and Gareth A. Morris**



Slice and shift selective (Rsnob) 180° pulse



Angew. Chem. Int. Ed. **49**, 3901 (2010)

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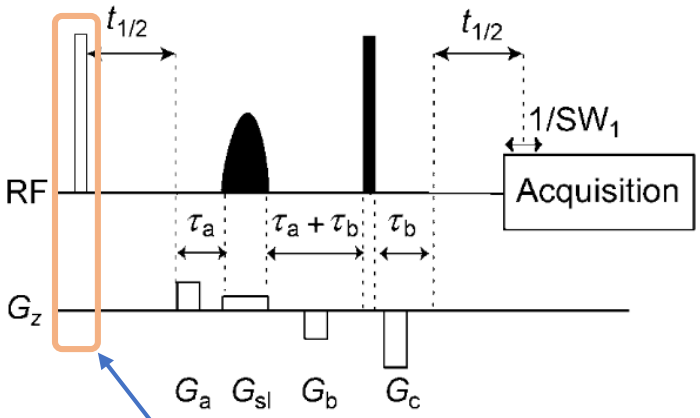
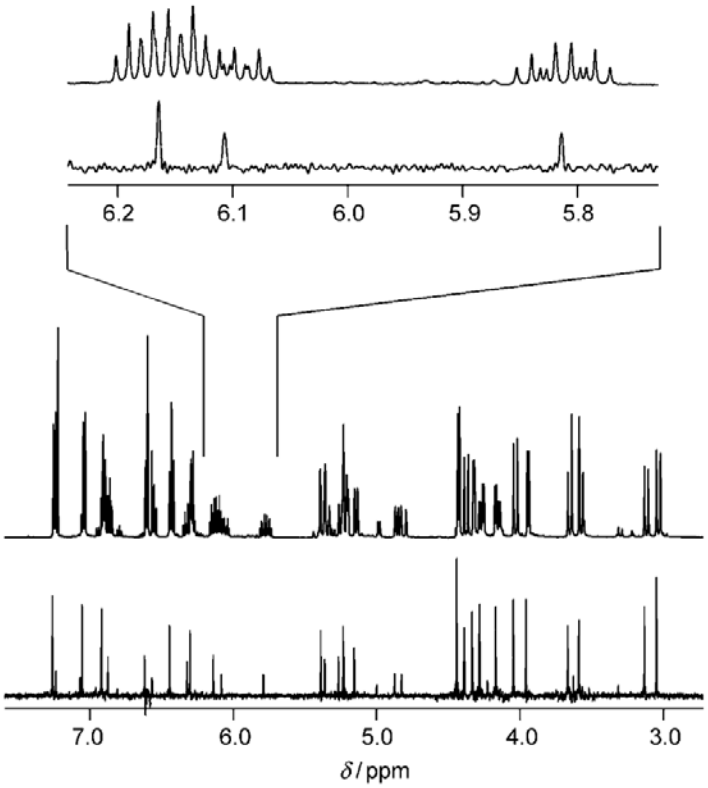
Excite



Initial hard 90° pulse
- Simplifies the experiment
- Improves sensitivity
- Slight increase in artefacts



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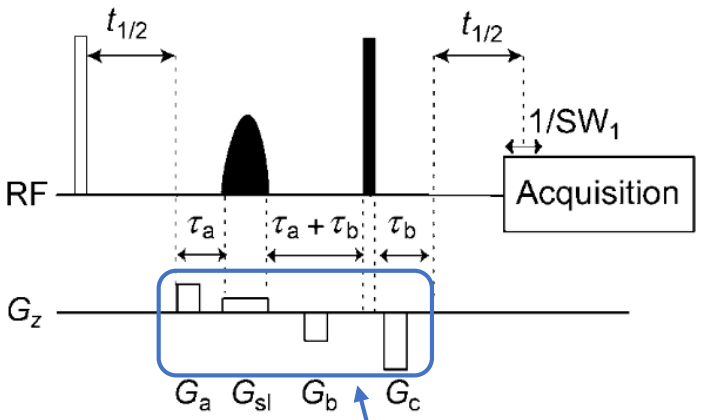
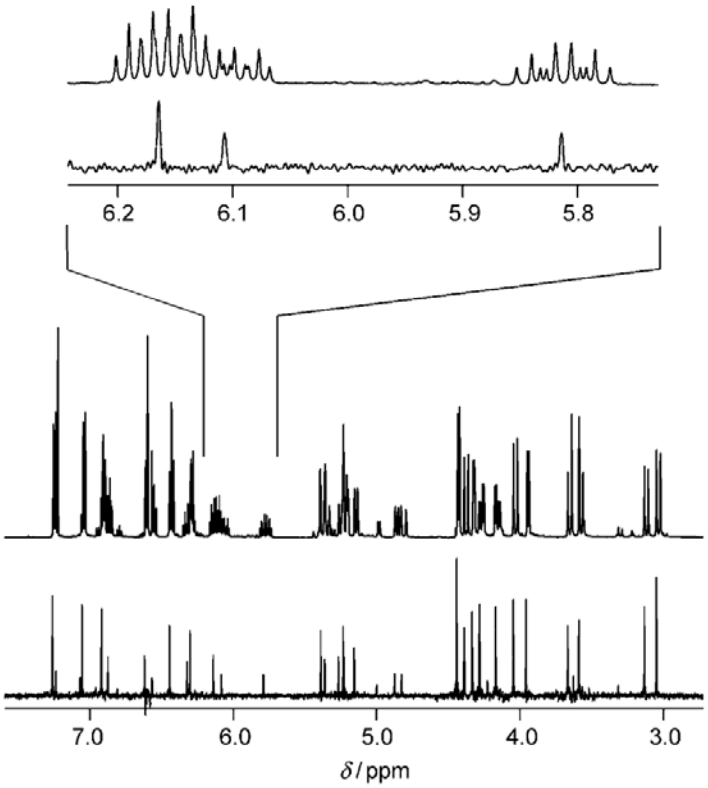


PFGs and phase cycling enforce the coherence transfer pathway



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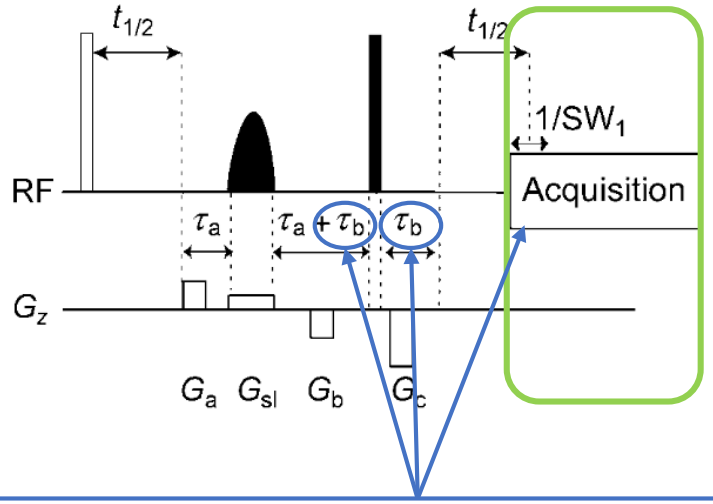
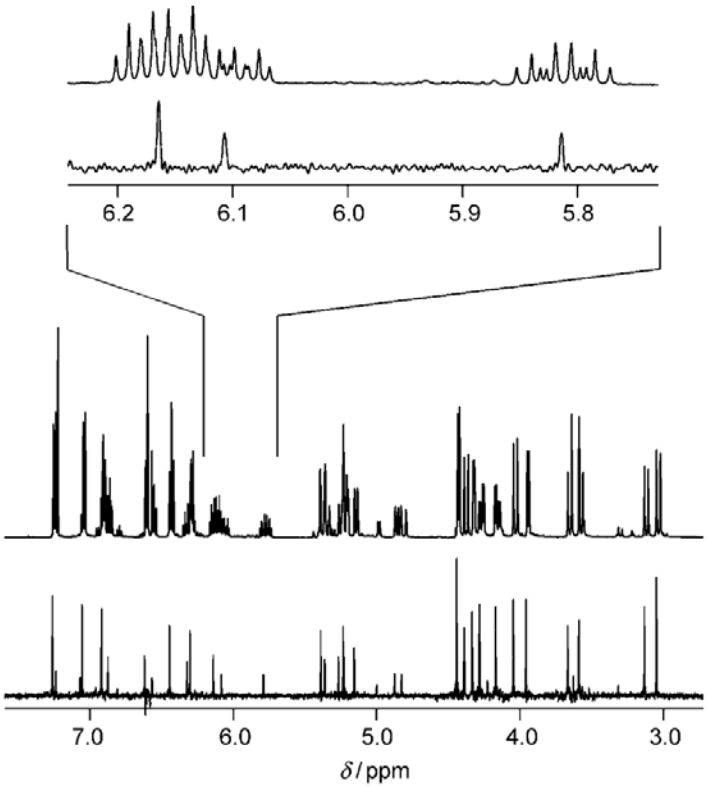
Acquisition



Timing to ensure that J_{HH} is refocused in the middle of the chunk (chunks twice as long)



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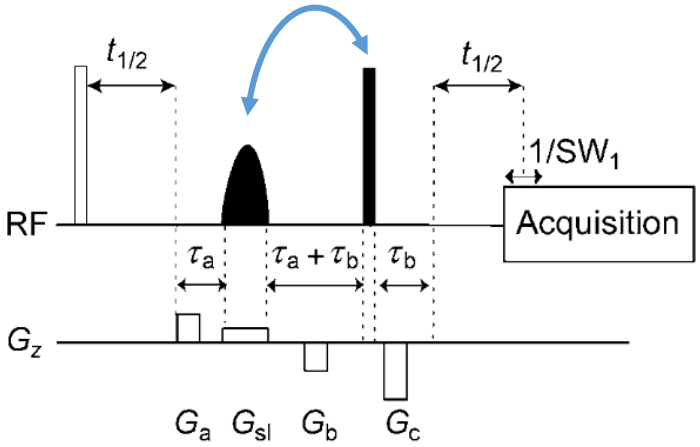
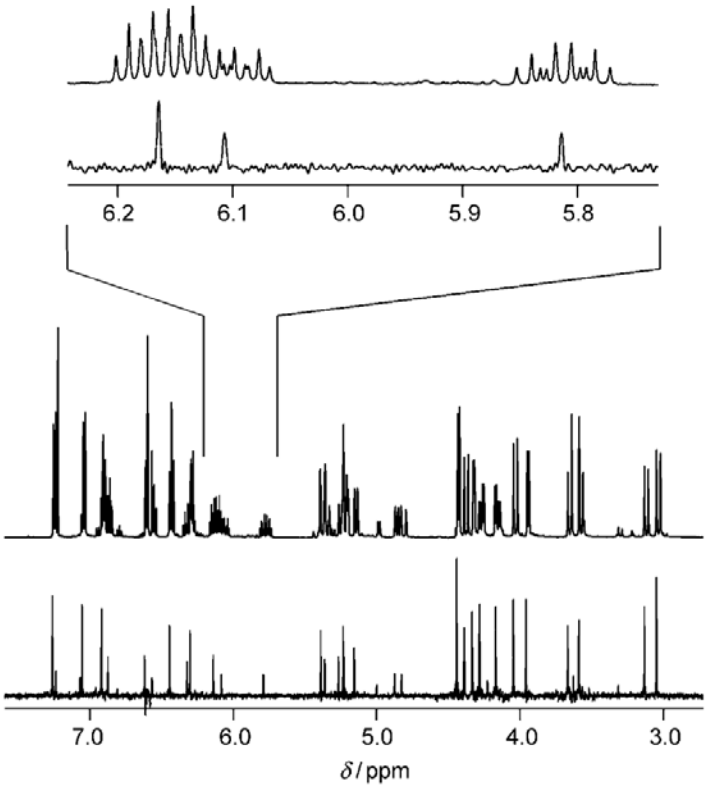




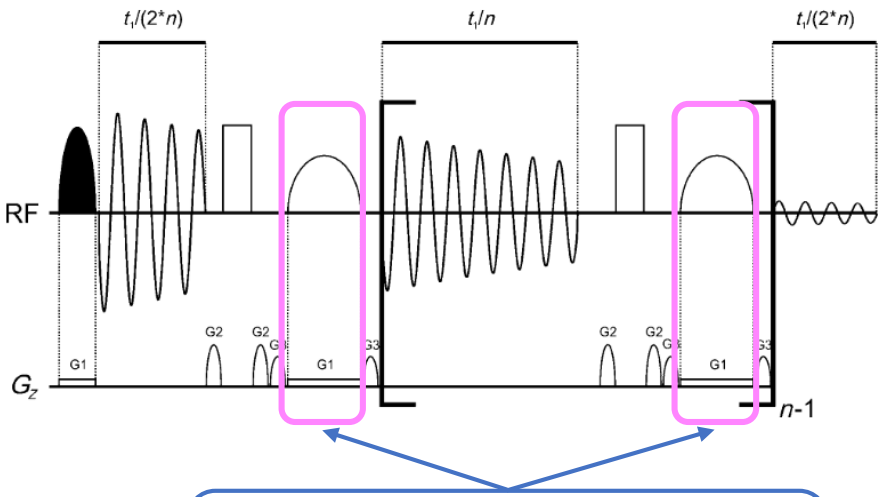
Angew. Chem. Int. Ed. **49**, 3901 (2010)

NMR Spectroscopy

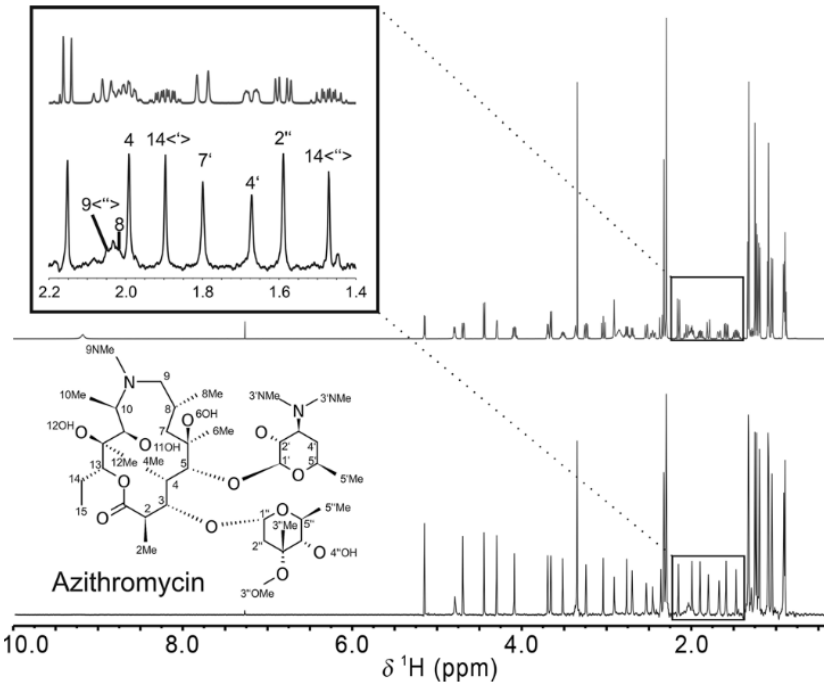
DOI: 10.1002/anie.201300129

Simplifying Proton NMR Spectra by Instant Homonuclear Broadband Decoupling**

*N. Helge Meyer and Klaus Zangger**

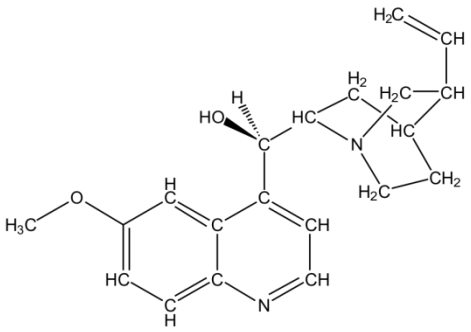


Slice and frequency selective (Gauss) 180° pulses



Angew. Chem. Int. Ed. **52**, 7143 (2013)

Slice and shift selective (Zangger-Sterk) pure shift NMR



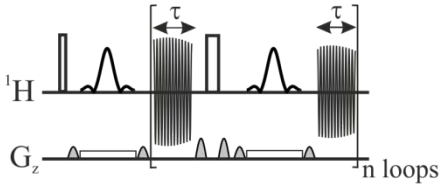
Sensitivity

^{1}H NMR

100 %

x1

Real-time



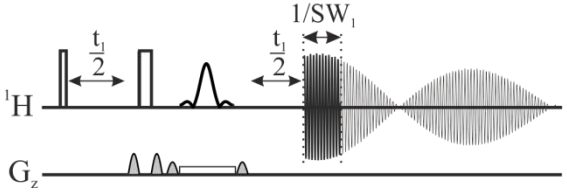
1.9 %

x64

Sensitivity

Spectral quality

Interferogram



0.4 %

x2048

Sensitivity

Spectral quality

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 ppm

How to increase the sensitivity in ZS experiments?

Using **multiple-frequency selective pulses** to simultaneously excite different slices in a single NMR experiment.

Equidistant

T. Parella et al, *Chem. Eur. J.* **19**, 15472 (2013)

Nonequidistant

D. Jeannerat et al, *Angew. Chem. Int. Ed.* **54**, 6016 (2015)

Using **multiple-frequency selective pulses** to excite different slices in successive scans, reducing the recycle delay (fast pulsing approach).

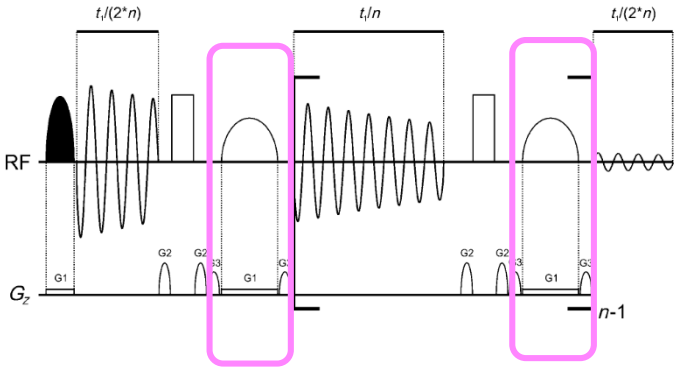
P. Sakhaii et al, *J. Magn. Reson.* **233**, 92 (2013)

Using polarization sharing to transfer polarization from unutilized protons (passive) to selectively excited (active) protons.

N. Suryaprakash et al, *Chem. Commun.* **50**, 8550 (2014)

Band-selective (BS) pure shift NMR

Zangger-Sterk

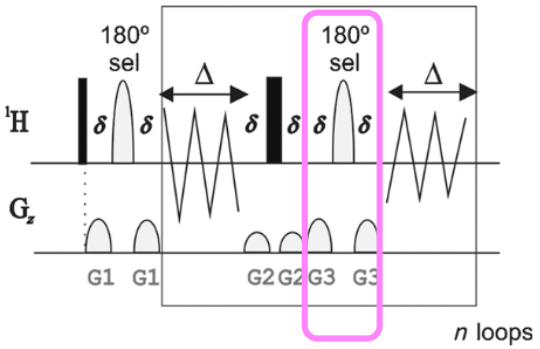


Selective pulse + encoding gradient

Low sensitivity

Broadband pure shift spectrum

Band-selective



Selective pulse

Excellent sensitivity

Band-selective pure shift spectrum

Band-selective (BS) pure shift NMR

Full Sensitivity and Enhanced Resolution in Homodecoupled Band-Selective NMR Experiments

Laura Castañar,[a, b] Pau Nolis,[a] Albert Virgili,[b] and Teodor Parella*[a]

HOBS (HOmonuclear Band-Selective)

Chem. Eur. J. **19**, 17283 (2013)

Homonuclear decoupling for enhancing resolution and sensitivity in NOE and RDC measurements of peptides and proteins

Jinfa Ying, Julien Roche, Ad Bax *

BASH (BAnd-Selective Homodecoupling)

J. Magn. Reson. **241**, 97 (2014)

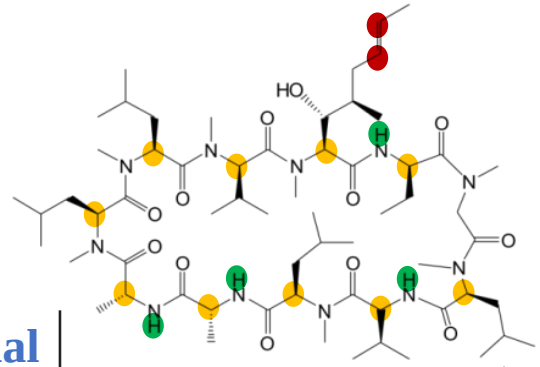
Diastereomeric ratio determination by high sensitivity band-selective pure shift NMR spectroscopy†

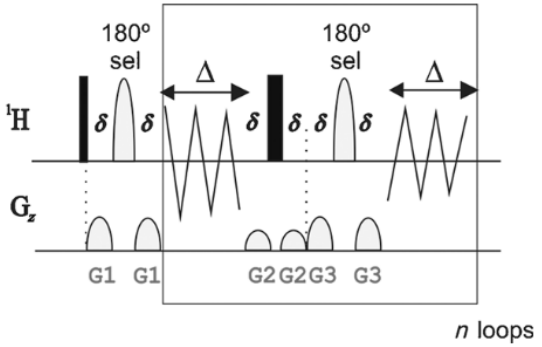
Ralph W. Adams,[a] Liam Byrne,[a] Péter Király,[ab] Mohammadali Foroozandeh,[a] Liladhar Paudel,[a] Mathias Nilsson,[ac] Jonathan Clayden[a] and Gareth A. Morris*[a]

BASHD (BAnd-Selective Homonuclear Decoupling)

Chem. Commun. **50**, 25127 (2014)

Band-selective pure shift NMR

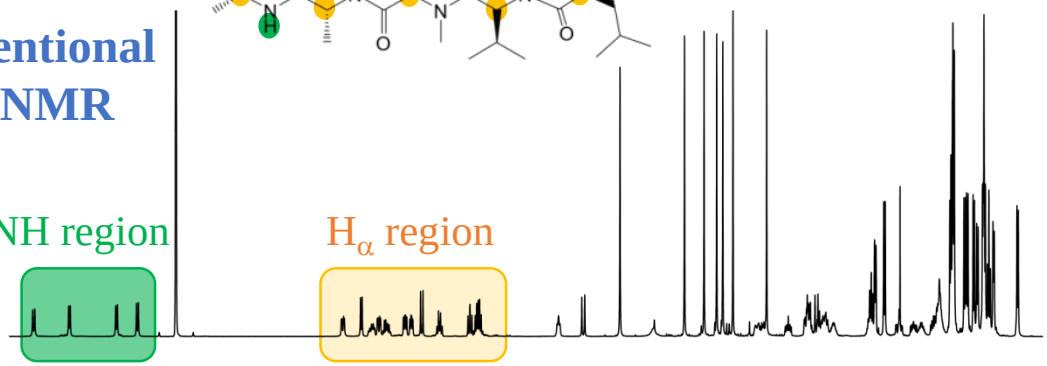




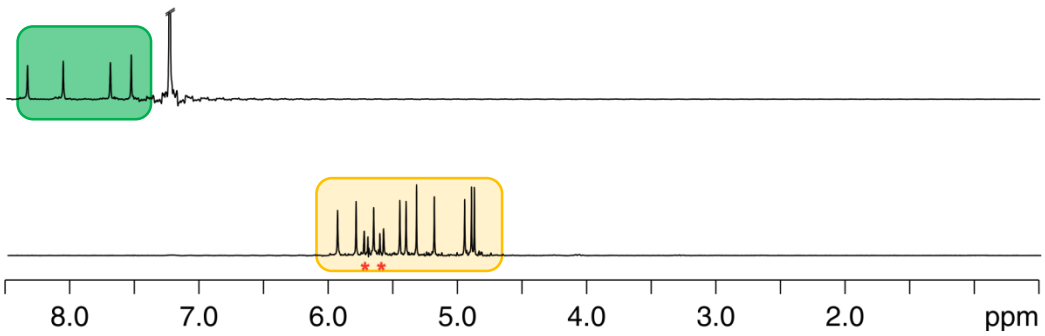
Conventional ^{1}H NMR

NH region

H_α region

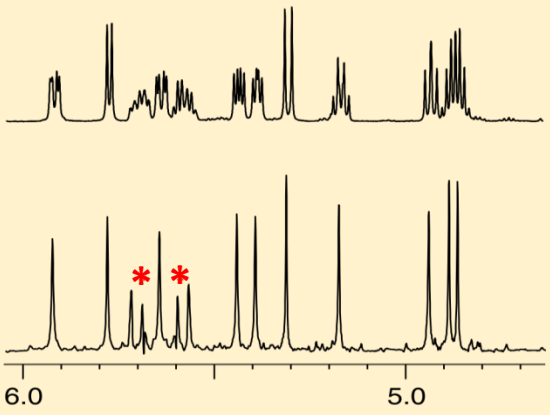


Band-selective

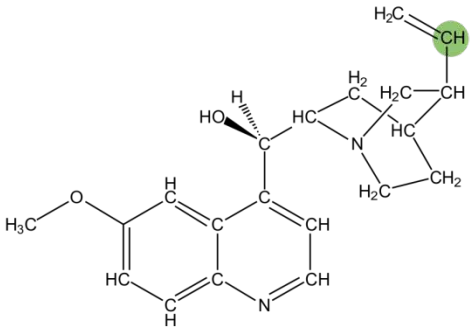


Main condition:
Avoid exciting coupled protons

Expanded H_α region



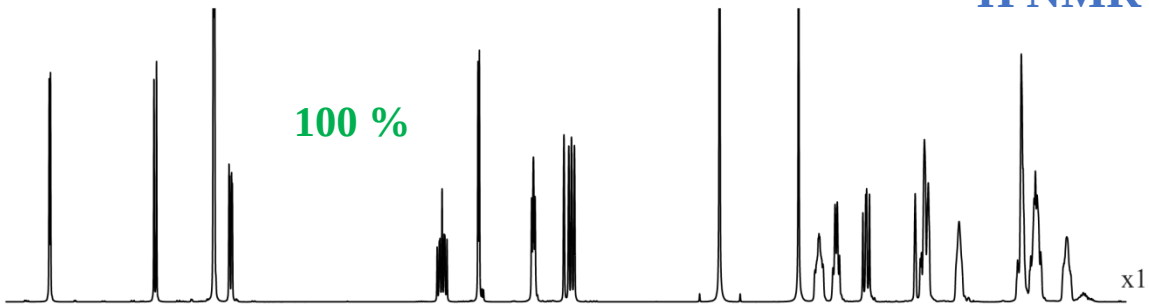
Frequency-selective pure shift NMR



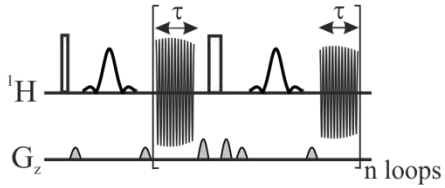
Sensitivity

^{1}H NMR

100 %

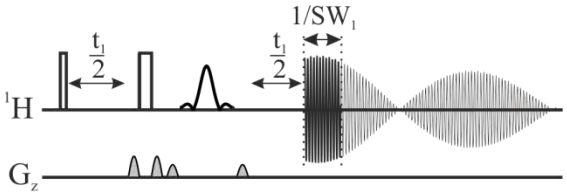


Real-time

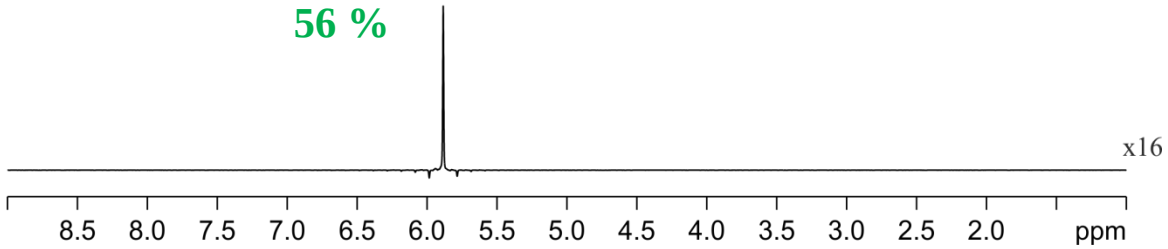


250 %

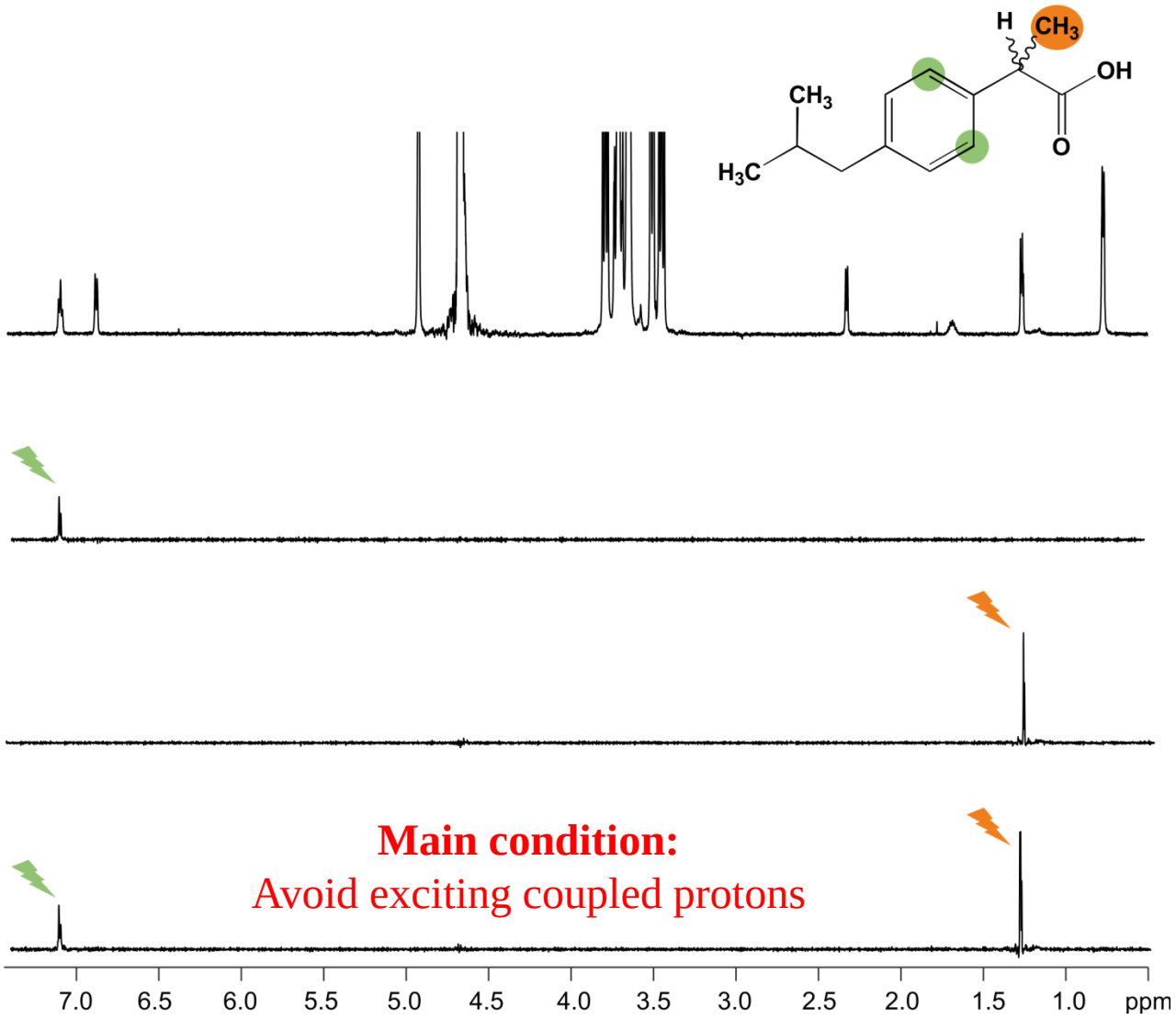
Interferogram



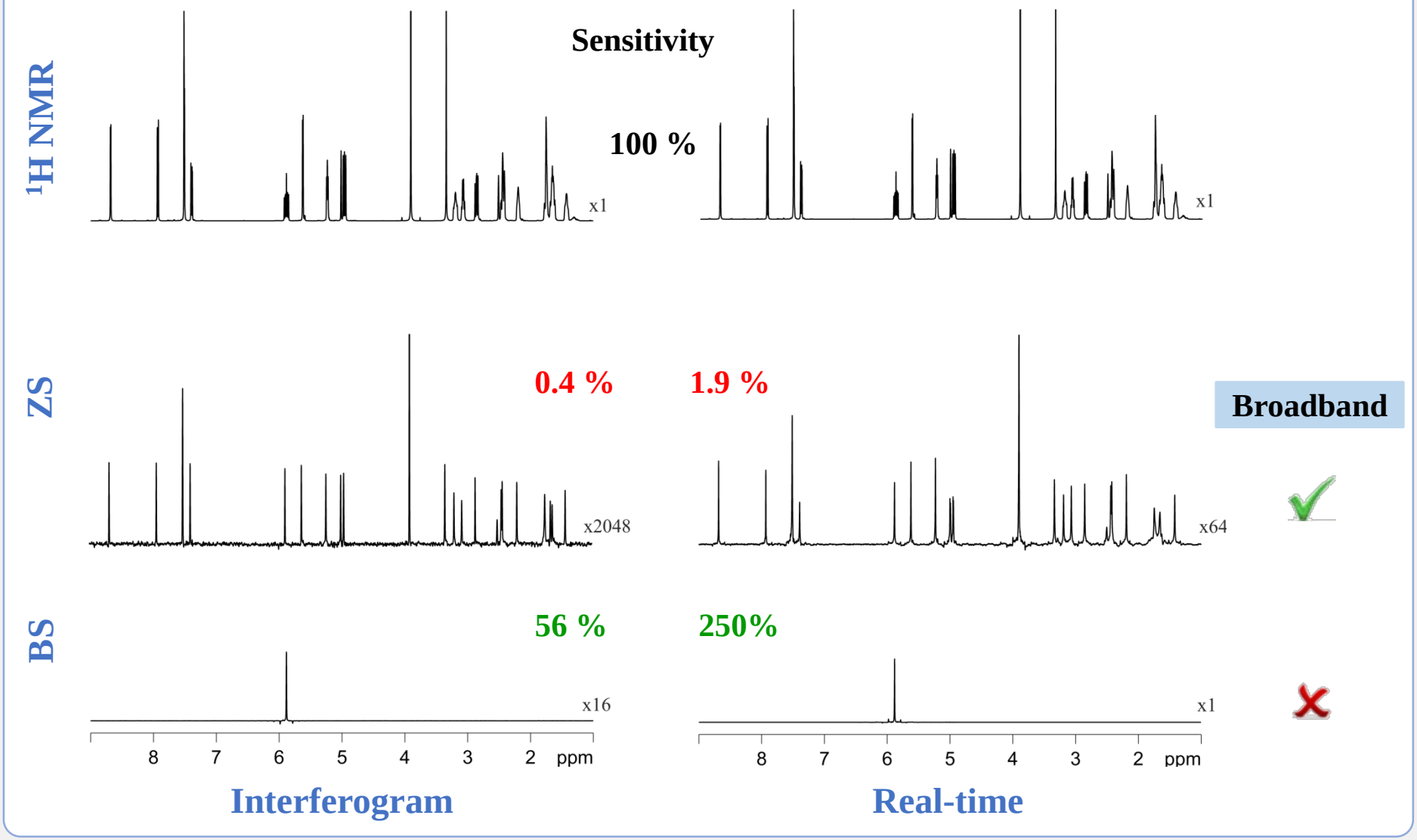
56 %



Multi-frequency-selective pure shift NMR



Comparison: BS vs ZS pure shift



Outline

Introduction:

- Set the scene
- Shift selection
- Slice and shift selection

Pure shift methods:

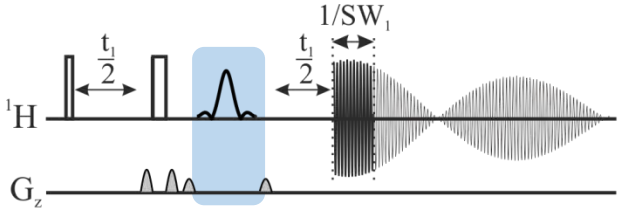
- Zangger-Sterk (ZS)
- Band-selective (BS)

Practical implementation:

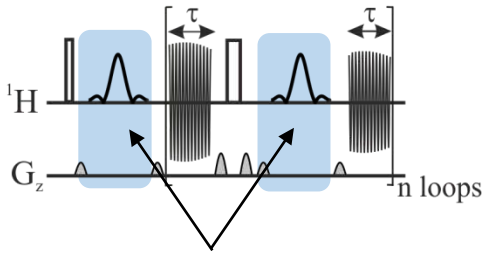
- Band-selective: selective pulses
- Zangger-Sterk: spatial encoding gradient and selective pulses

Setting up selective pulses

Interferogram

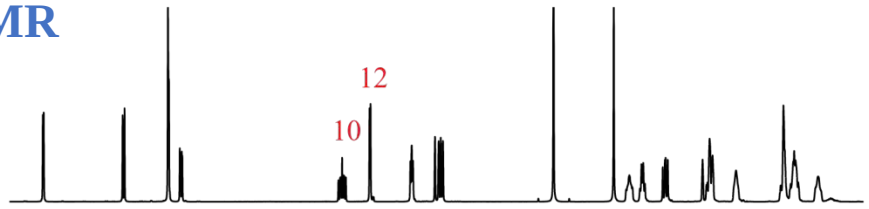


Real-time

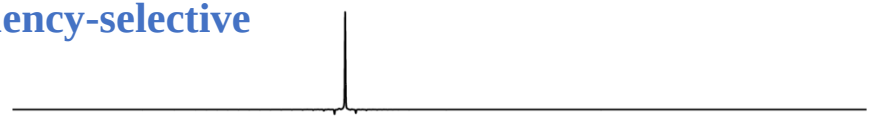


Same selective
180° refocusing pulse

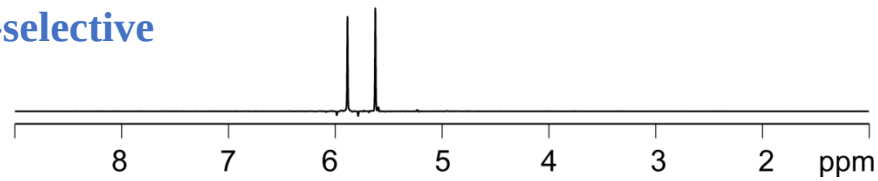
^{1}H NMR

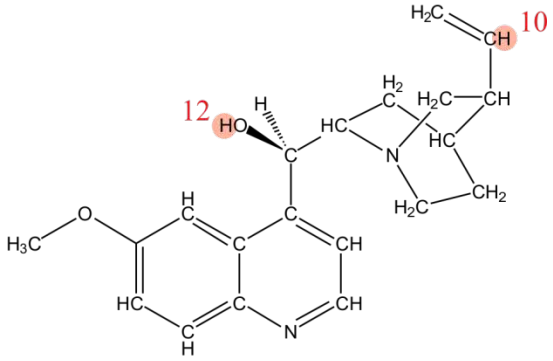


Frequency-selective

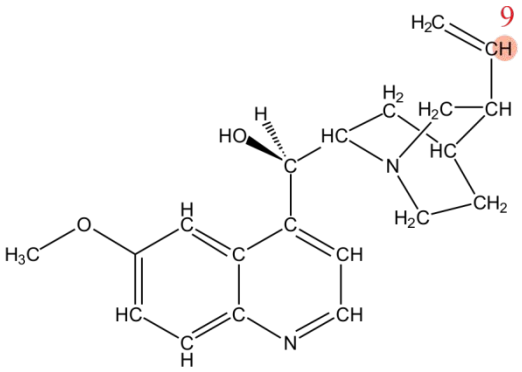


Band-selective

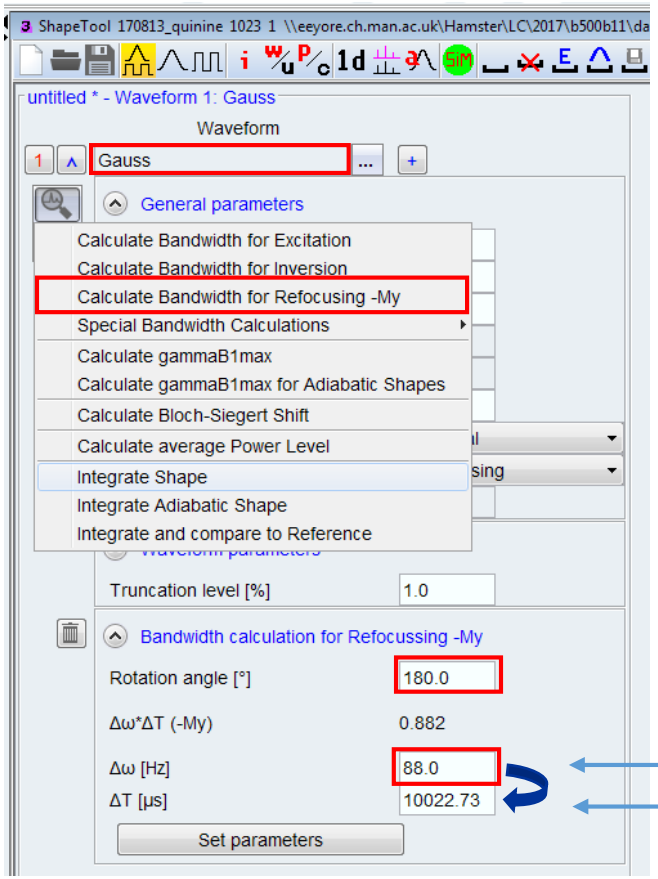




Setting up selective pulses: selectivity

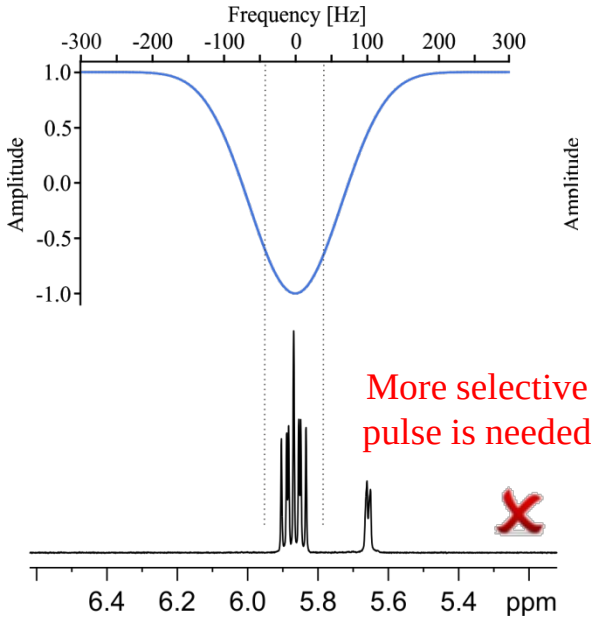


Selective 180° refocusing pulse ($\Delta\nu$ = 88 Hz)



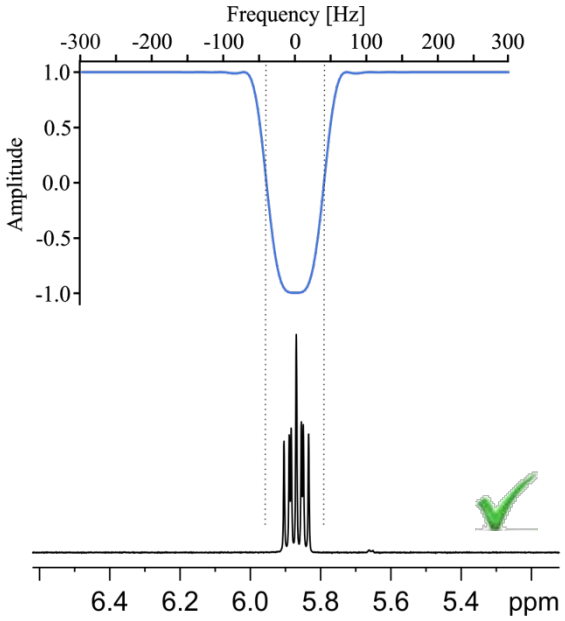
Setting up selective pulses: shape of the pulse

Gauss
$\Delta\nu$ = 88 Hz
Duration = 10 ms

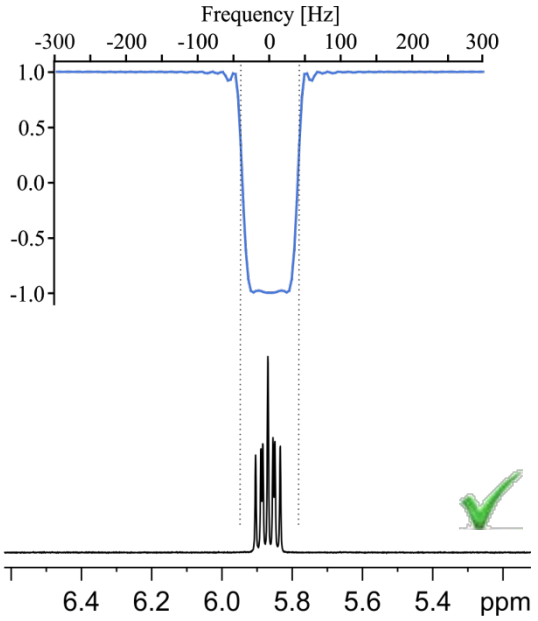


More selective pulse is needed

Rsnob
$\Delta\nu$ = 88 Hz
Duration = 30 ms

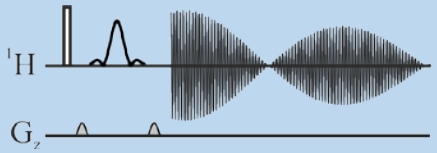


ReBurp
$\Delta\nu$ = 88 Hz
Duration = 70 ms



Very selective pulses can be used to deal with strong couplings

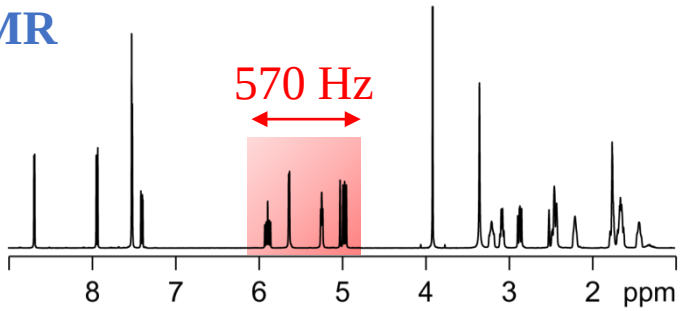
Pulse sequence used: selective spin echo



Bruker pp: selgpse

Setting up band-selective pulses

^{1}H NMR

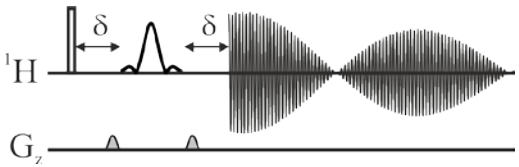


Rsnob
$\Delta\nu$ = 570 Hz
Duration = 4 ms

Selective spin echo

J_{HH} modulation

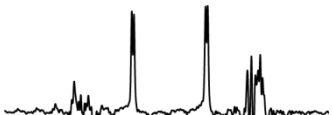
t_{exp}= 5 s



δ = 50 ms

Pure shift

Not homodecoupled

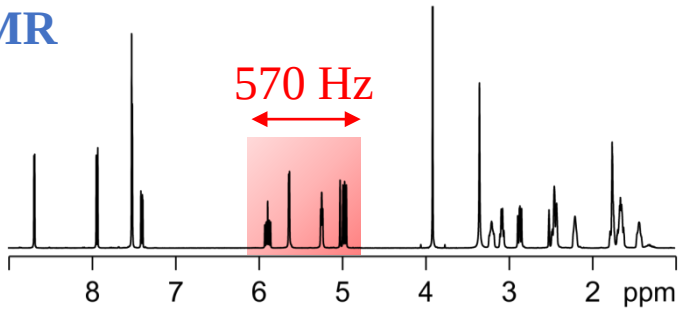


t_{exp}= 2 min 42 s

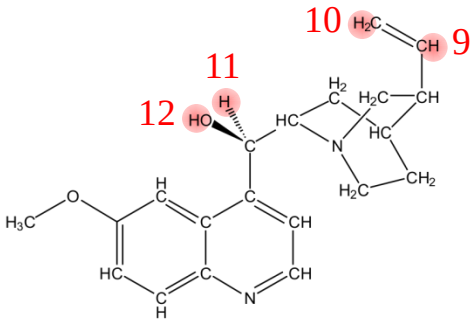
Coupled protons have been excited

Setting up band-selective pulses

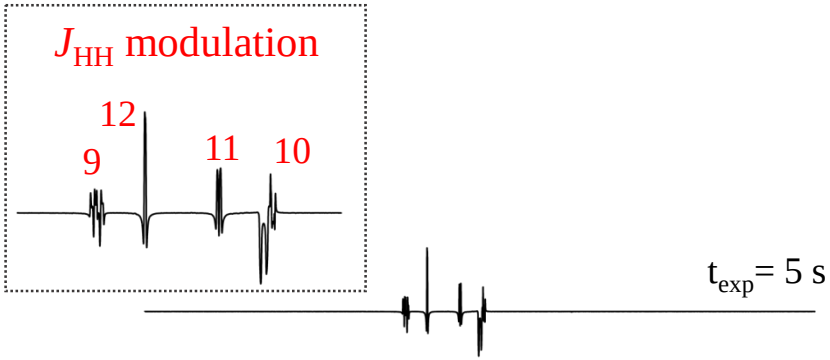
^{1}H NMR

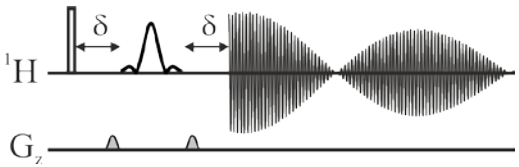


Rsnob
$\Delta\nu$ = 570 Hz
Duration = 4 ms



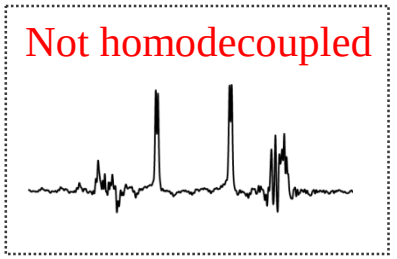
Selective spin echo





δ = 50 ms

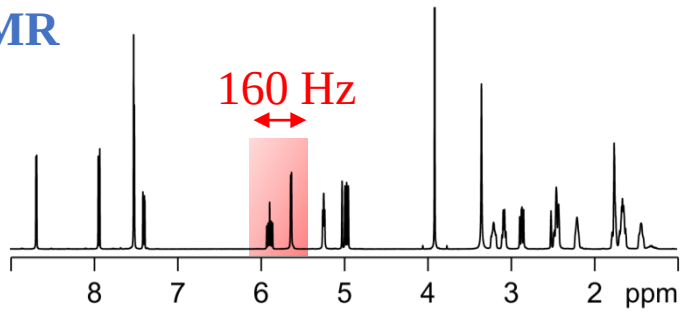
Pure shift



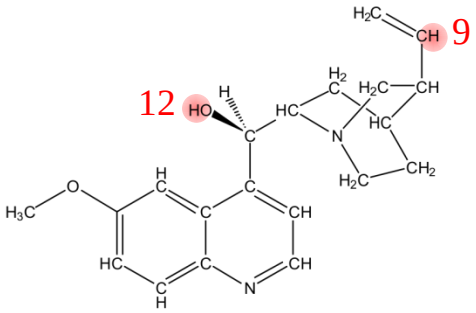
Coupled protons have been excited

Setting up band-selective pulses

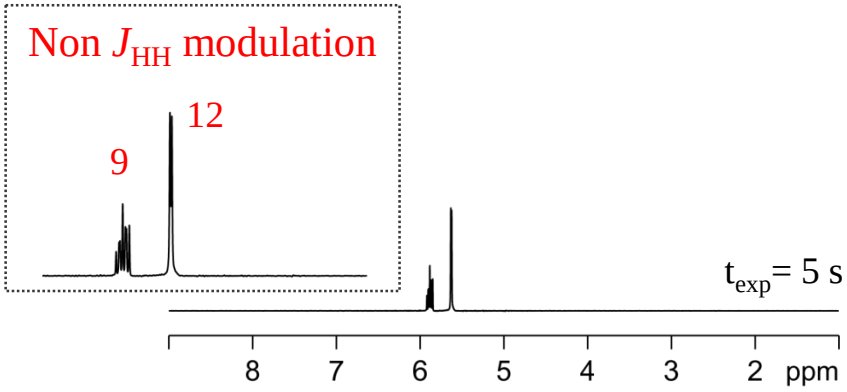
^{1}H NMR



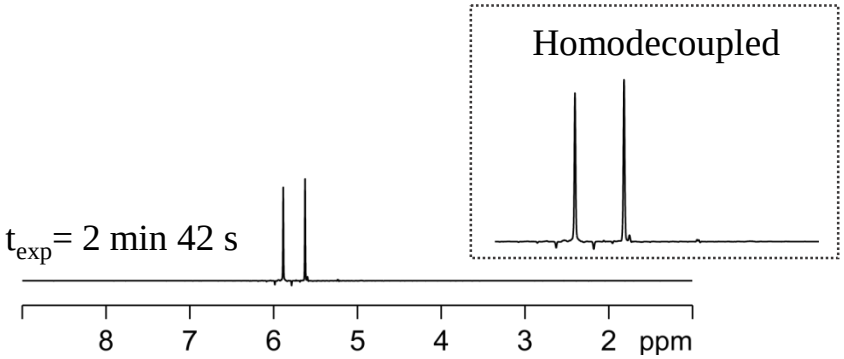
Rsnob
$\Delta\nu$ = 160 Hz
Duration = 15 ms



Selective spin echo



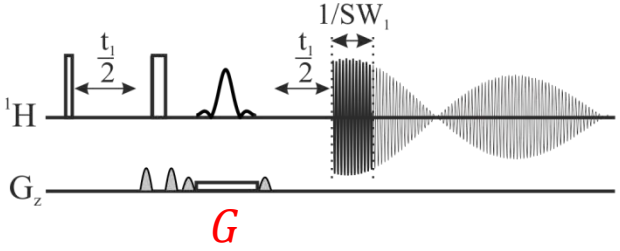
Pure shift



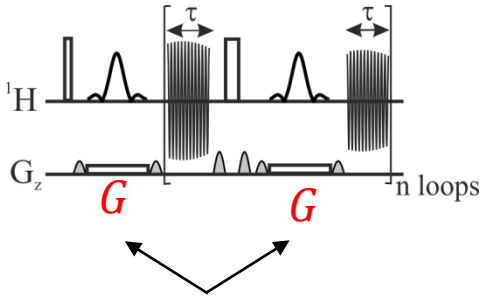
Main condition:
Avoid exciting coupled protons

Setting up encoding gradient and selective pulses

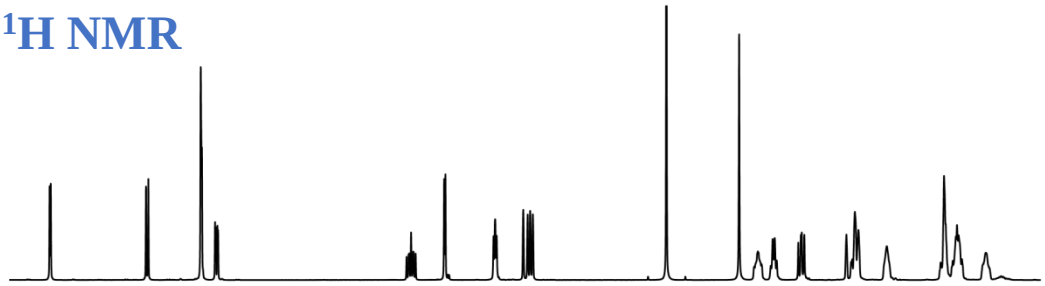
Interferogram



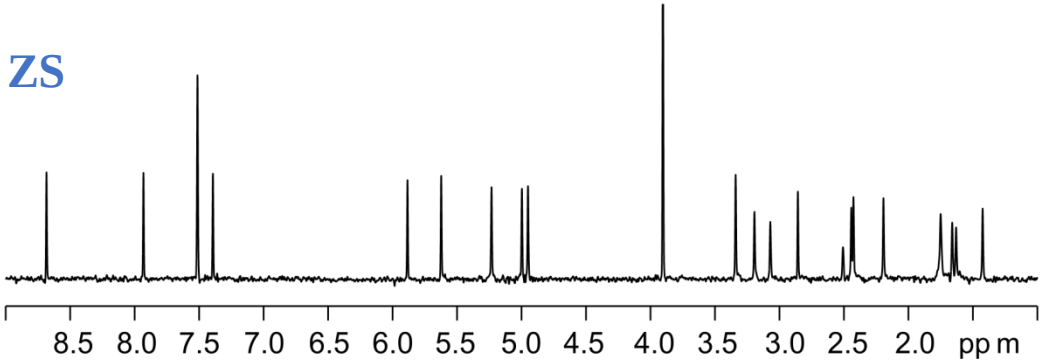
Real-time



^{1}H NMR



ZS

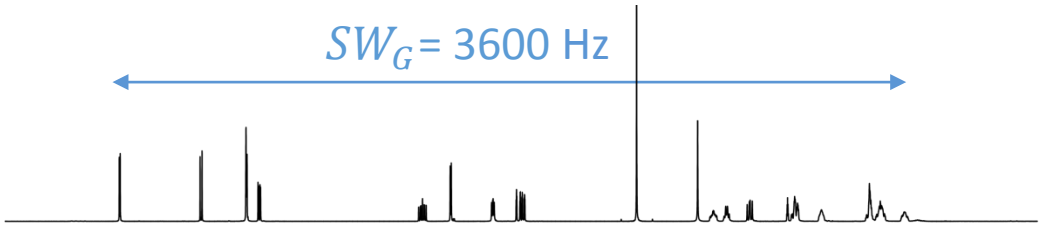


Same **selective 180°** pulse

"Same" **encoding gradient**

Setting up encoding gradients

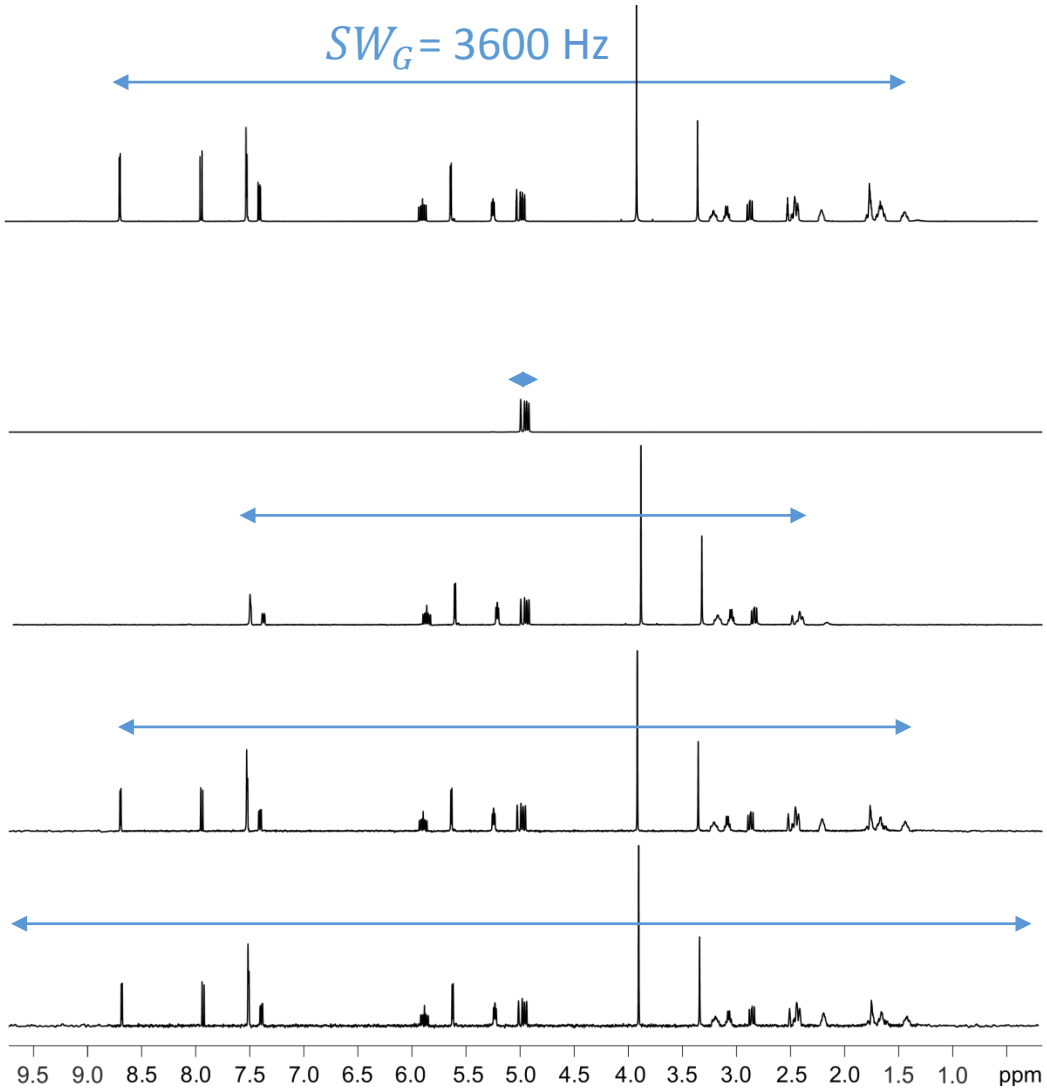
$$G = \frac{2\pi}{\gamma}\frac{SW_G}{L}$$



^{1}H NMR

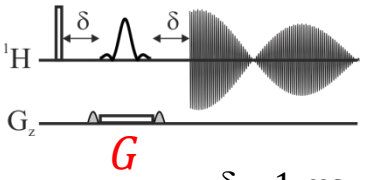
Setting up encoding gradients

$$G = \frac{2\pi}{\gamma}\frac{SW_G}{L}$$



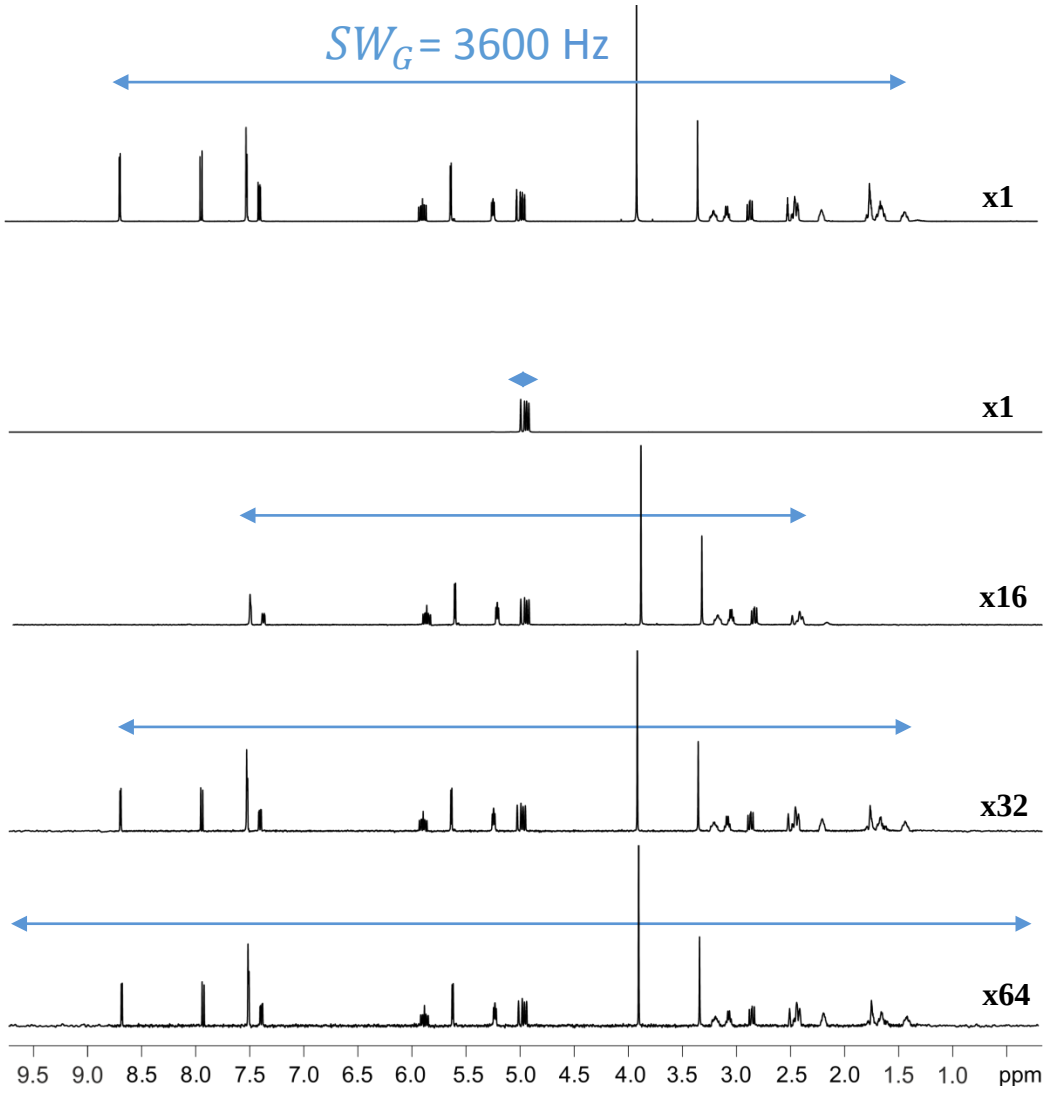
^{1}H NMR

Slice selection selective spin echo



δ = 1 ms

$G = \frac{2\pi}{\gamma}\frac{SW_G}{L}$



^{1}H NMR

Slice selection selective spin echo

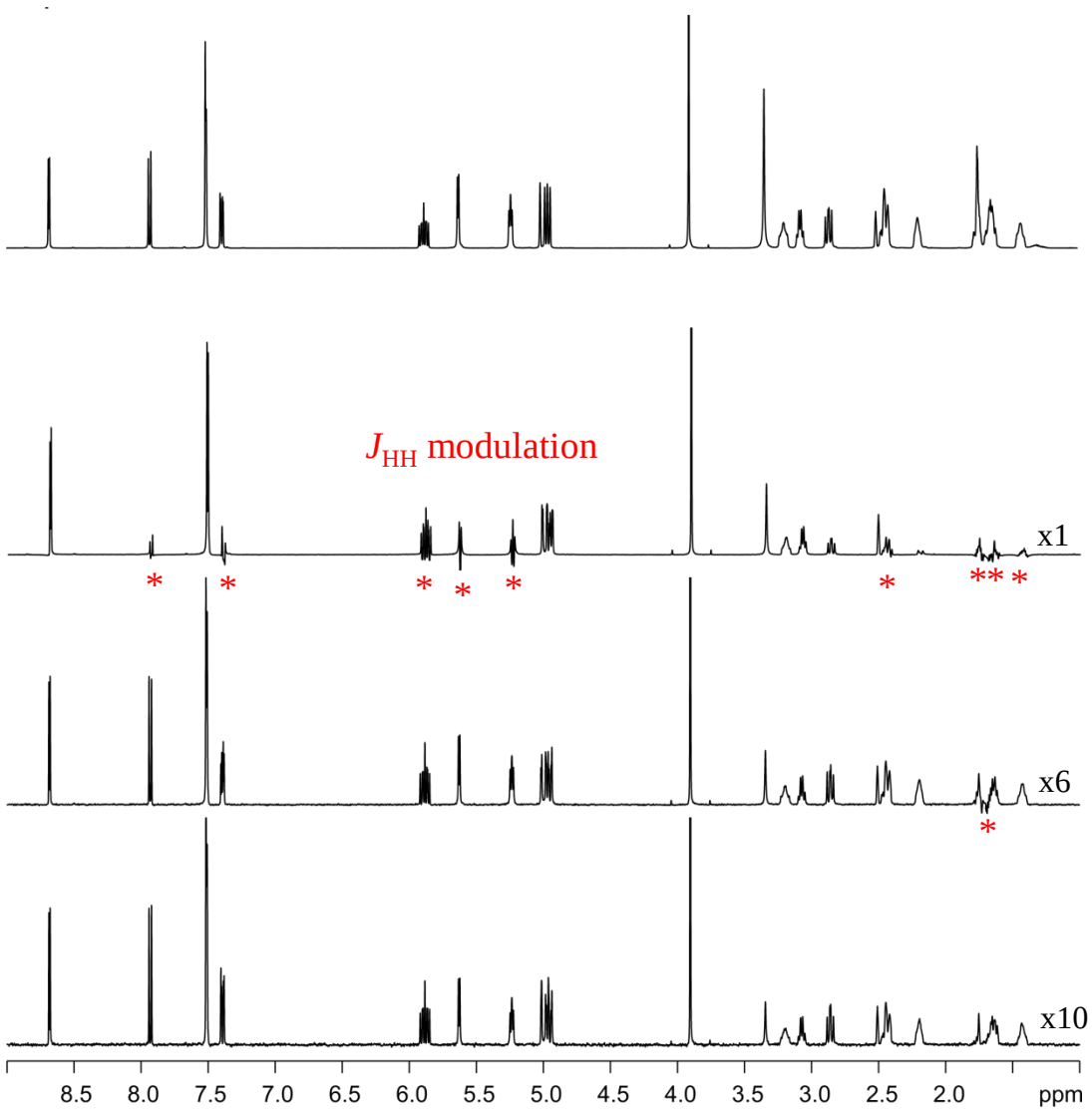
Sensitivity

Slice thickness:

$\Delta z = \Delta\nu / \frac{\gamma}{2\pi} G$

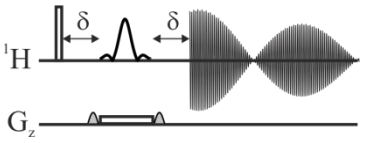
$\downarrow G \rightarrow \uparrow \Delta z \rightarrow \uparrow$SNR

Setting up selective pulses



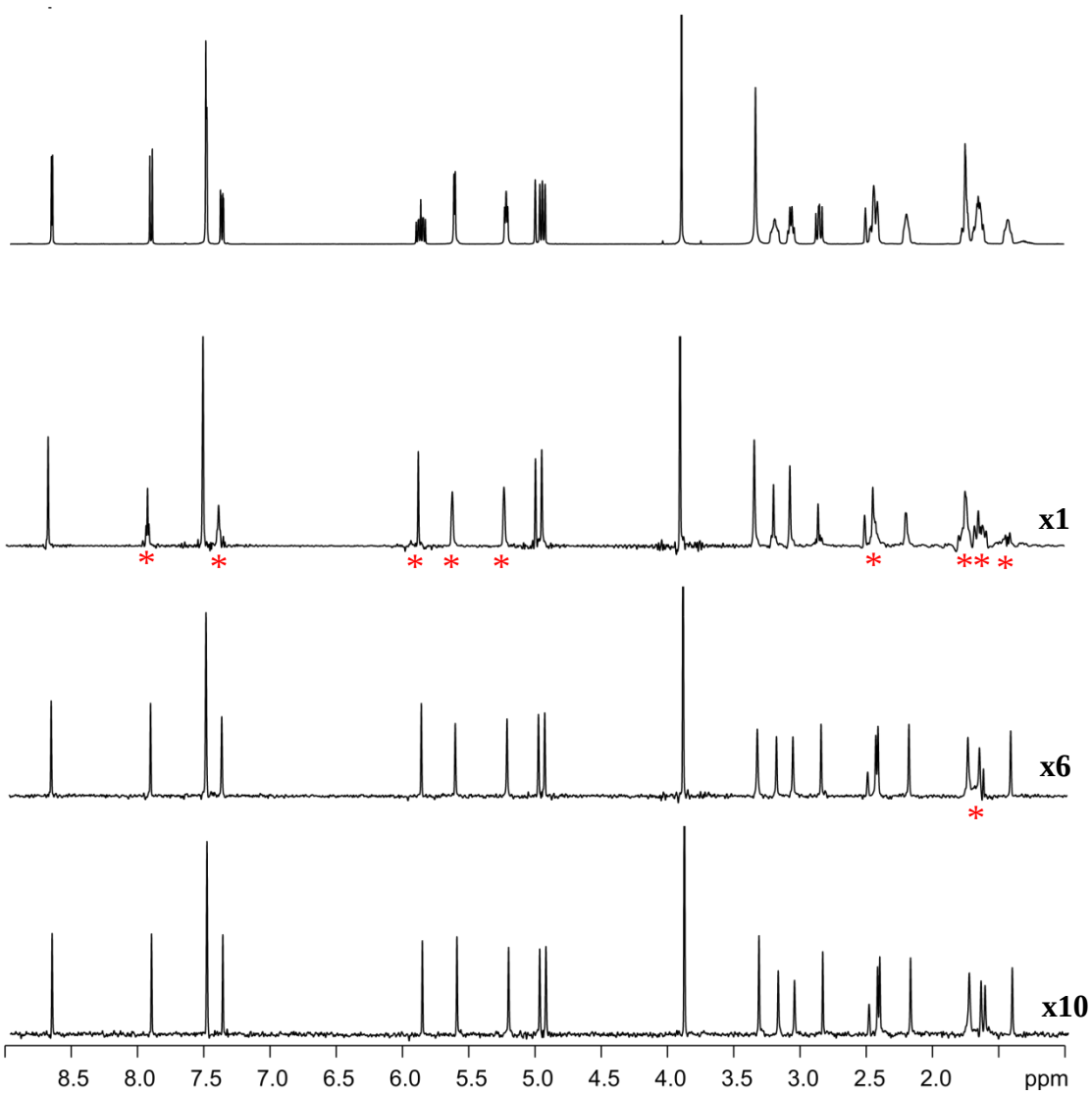
^{1}H NMR

Slice selection selective spin echo



δ = 50 ms
G = 0.52 G/cm

Setting up selective pulses



^{1}H NMR

ZS interferogram

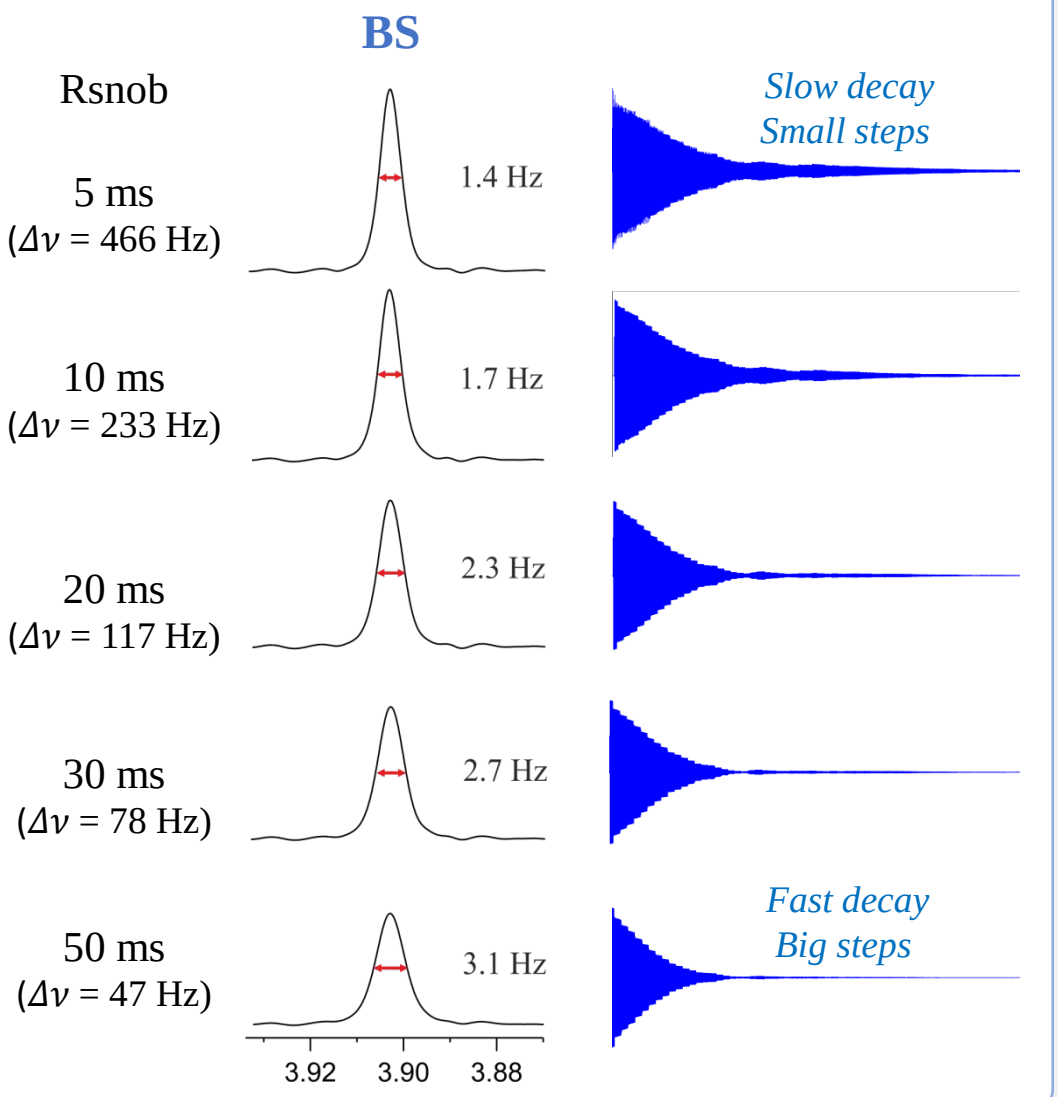
Sensitivity

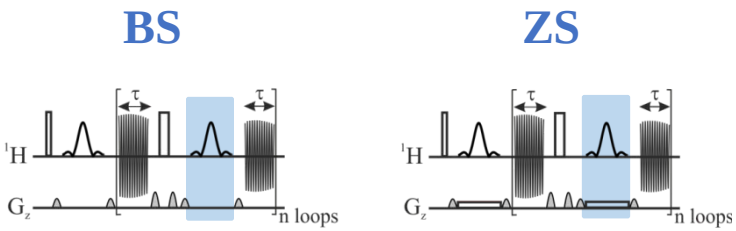
Slice thickness:

$$\Delta z = \Delta\nu / \frac{\gamma}{2\pi} G$$

↑$\Delta\nu$ ➡ ↑Δz ➡ ↑SNR

Real-time pure shift: resolution limited by selective pulse duration





Increase the selectivity

⬇

Increase the duration

⬇

Longer gap between chunks

⬇

Bigger step in the FID

Faster FID decay ⬇ Greater linewidth

Bigger chunking artefacts

Outline

Introduction:

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Pure shift methods:

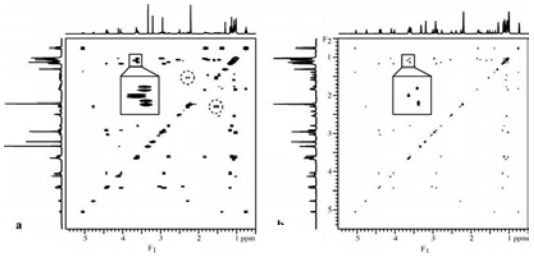
- Zangger-Sterk (ZS)
- Band-selective (BS)

Practical implementation:

- Band-selective: selective pulses
- Zangger-Sterk: spatial encoding gradient and selective pulses

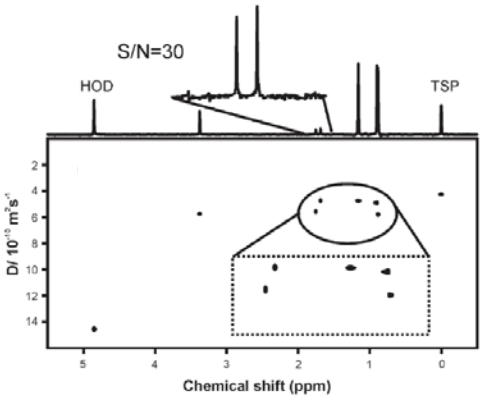
Applications

Structure analysis of small and medium size molecules



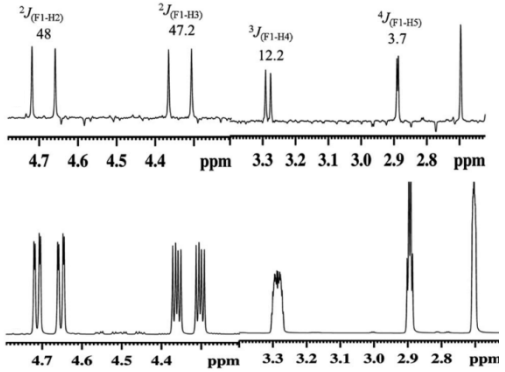
J. Am. Chem. Soc. **132**, 12771 (2010)

Diffusion studies



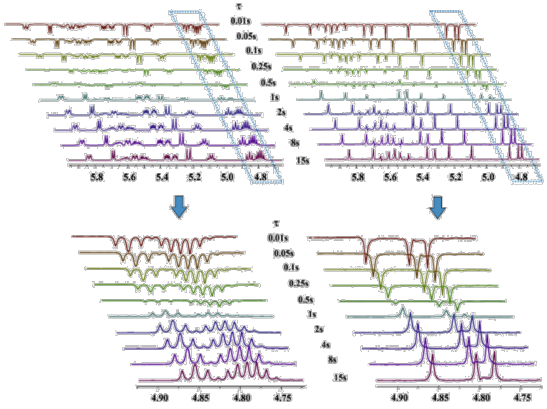
Chem. Commun. 933 (2007)

Measurement of scalar and residual dipolar coupling



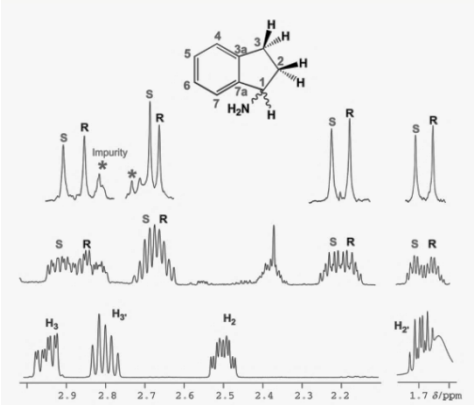
RSC Adv. **4**, 15018 (2014)

Dynamic processes



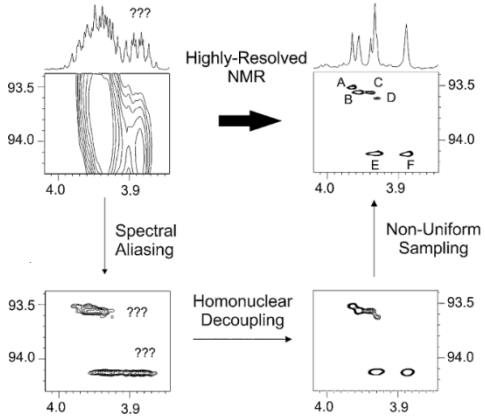
J. Magn. Reson. **244**, 30 (2014)

Enantiomeric and diasteromeric studies



ChemPhysChem. **15**, 854 (2014)

Study of complex mixtures



Chem. Eur. J. **21**, 7682 (2015)

Review: *Magn. Reson. Chem.* **53**, 399 (2015)

Outline

Introduction:

- Set the scene
- Shift selection
- Slice and shift selection

Pure shift methods:

- Zangger-Sterk (ZS)
- Band-selective (BS)

Practical implementation:

- Band-selective: selective pulses
- Zangger-Sterk: spatial encoding gradient and selective pulses

Applications

Summary

Summary

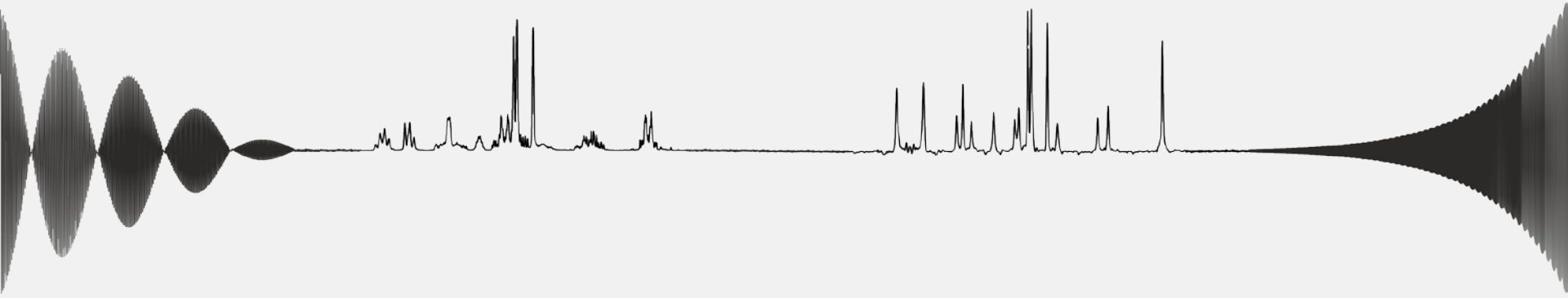
Zangger- Sterk:

- **Broadband homodecoupled spectrum**
- **Low sensitivity**. It depends on the requirements of the sample:
  - Selectivity needed (selective pulse)
  - Range of frequencies sampled (encoding gradient)
- SNR can be improved using multiple-frequency modulated pulses or polarization sharing methods
- Compatible with both real-time and interferogram based acquisition

Band-selective:

- **Selective homodecoupled spectrum** containing:
  - A single signal (frequency selection)
  - Several signals (multiple-frequency selection; only works if the signals excited are not coupled)
- **Excellent sensitivity**
- Compatible with both real-time and interferogram based acquisition
- Very useful for the analysis of:
  - NH and H_α protons in peptides and proteins
  - Enantiomers and diastereoisomers

Thank you very much for your attention



Questions?

A Pure Shift NMR Workshop

11.00	Gareth Morris	**Welcome, introduction and history**
11.30	Peter Kiraly	**Interferogram and real-time acquisition methods**
12.00	Laura Castañar	**Zangger-Sterk and band-selective methods**
12.30	**Mohammadali Foroozandeh**	**PSYCHE**
13.00		*Lunch and poster session*
14.00	Ralph Adams	**Other pure shift and related methods**
14.30	Mathias Nilsson	**Practical implementations**
15.00	Adolfo Botana	**JEOL pure shift implementation**
15.10	Vadim Zorin	**MestreNova pure shift implementation**
15.20	Ēriks Kupče	**Bruker shaped pulse implementation**
15.30		*Question and answer session*

University of Manchester, 12th September 2017