Introduction to pure shift NMR

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Menu

- The definition and the reason
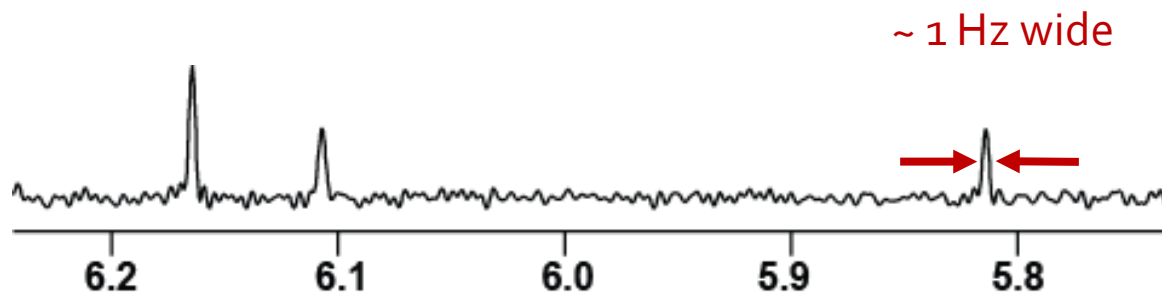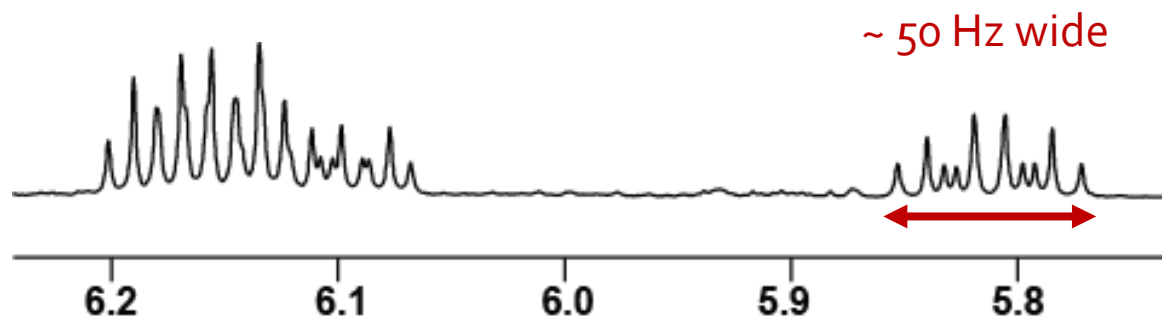
- One-dimensional experiments

      The Zangger-Sterk pulse sequence
      The ZS-BIRD-Hybrid
      How to use them

- Multi-dimensional experiments

      3D Variants
      2D variants based on real-time compression

      Constant-time versions
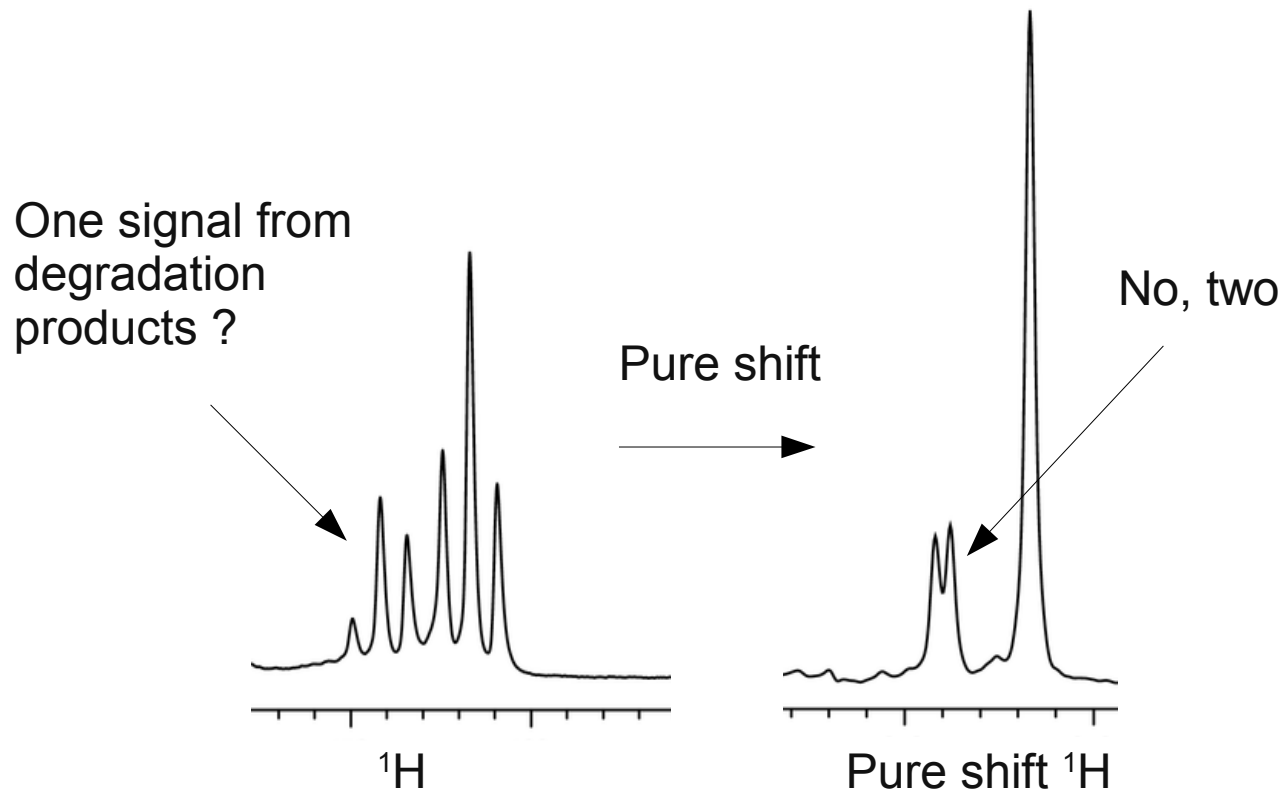
- Questions
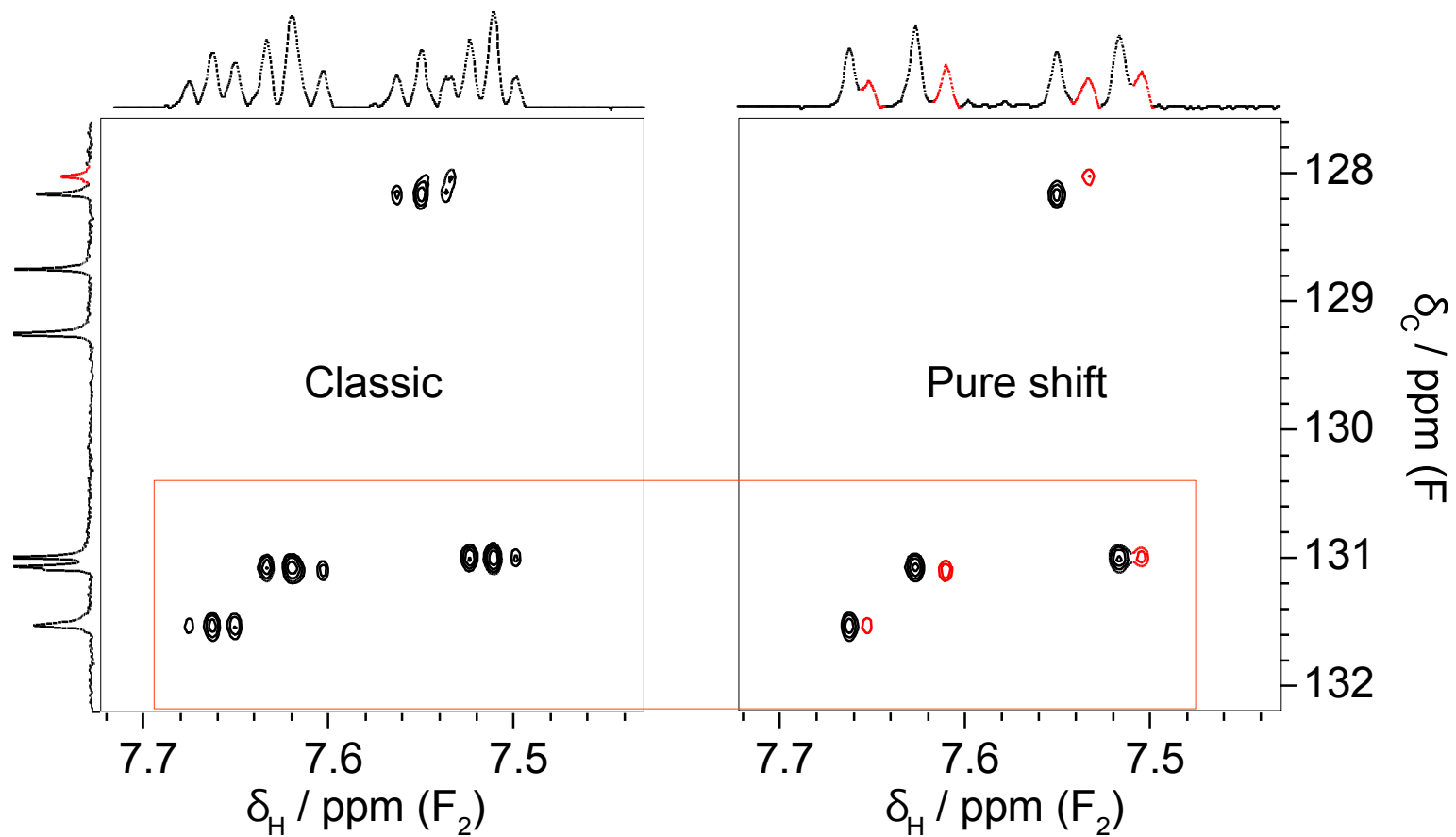
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What is it?

~ 50 Hz wide

~ 1 Hz wide

Single signal for each chemical site

Why do you want to use these methods?

One signal from degradation products ?

Pure shift

No, two

^1H

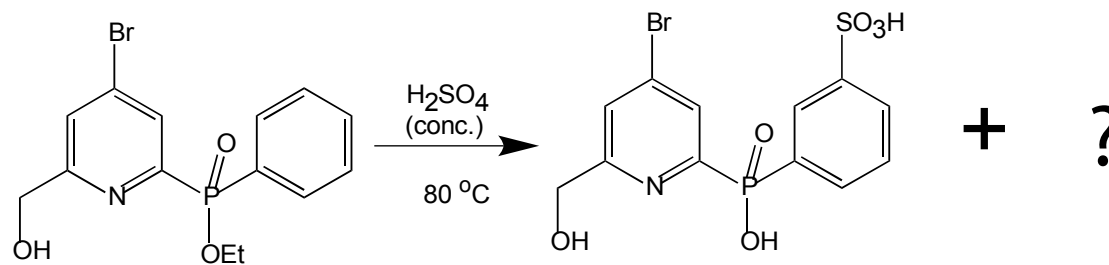Pure shift ^1H

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Surely 2D-NMR makes it unnecessary:
HSQC

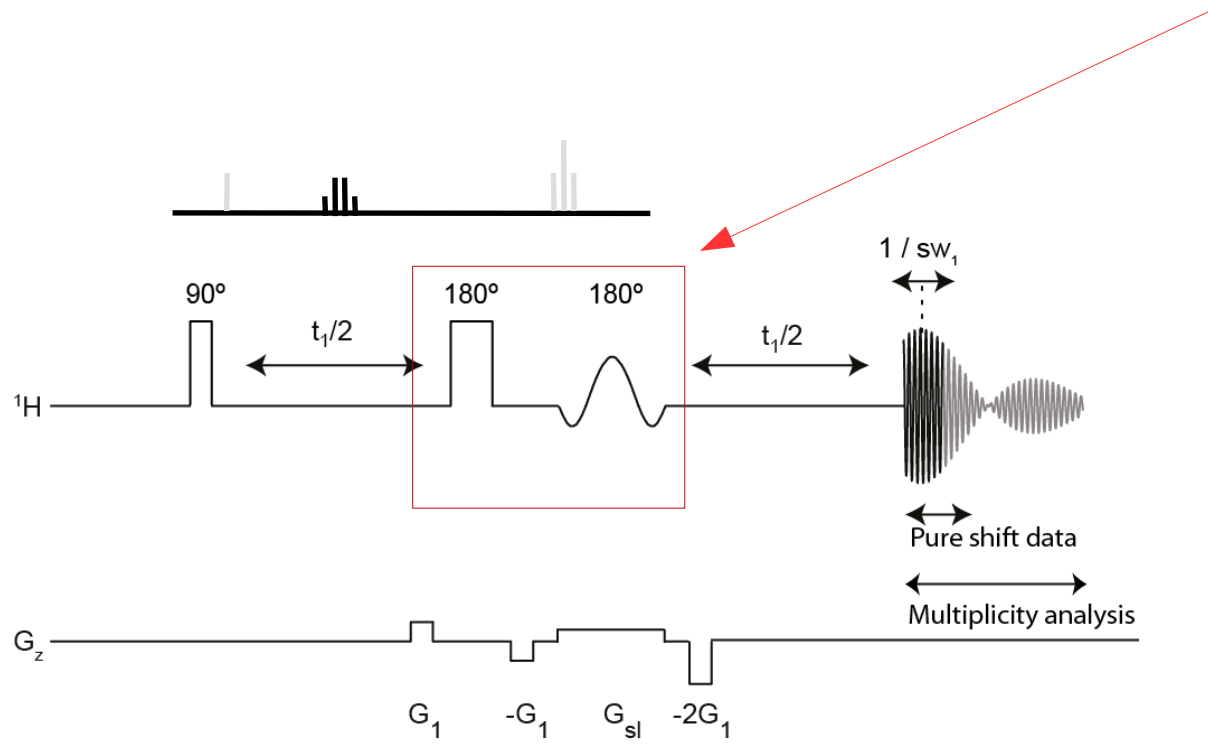# Surely 2D-NMR makes it unnecessary:
COSY

Classic

True pure shift

In order to produce unambiguous data true pure shift was necessary, i.e. both H-H and H-P splittings had to be suppressed

Pure shift NMR is a broader concept than that of homo-decoupling

A

^{19}F

-110.1   -110.2   -110.3 ppm

B

6.7 Hz   4.6 Hz | 10.3 Hz

Pure shift ^{1}H

Notice this is not a true pure shift spectrum because H-F couplings are present. This, however, is useful.

H-F couplings were hard to measure from either ^{1}H or ^{19}F spectra but easier from the pure shift experiment.

*n | *n

*n || *n

C

^{1}H

8.4   8.0   7.6   7.2   6.8   ppm
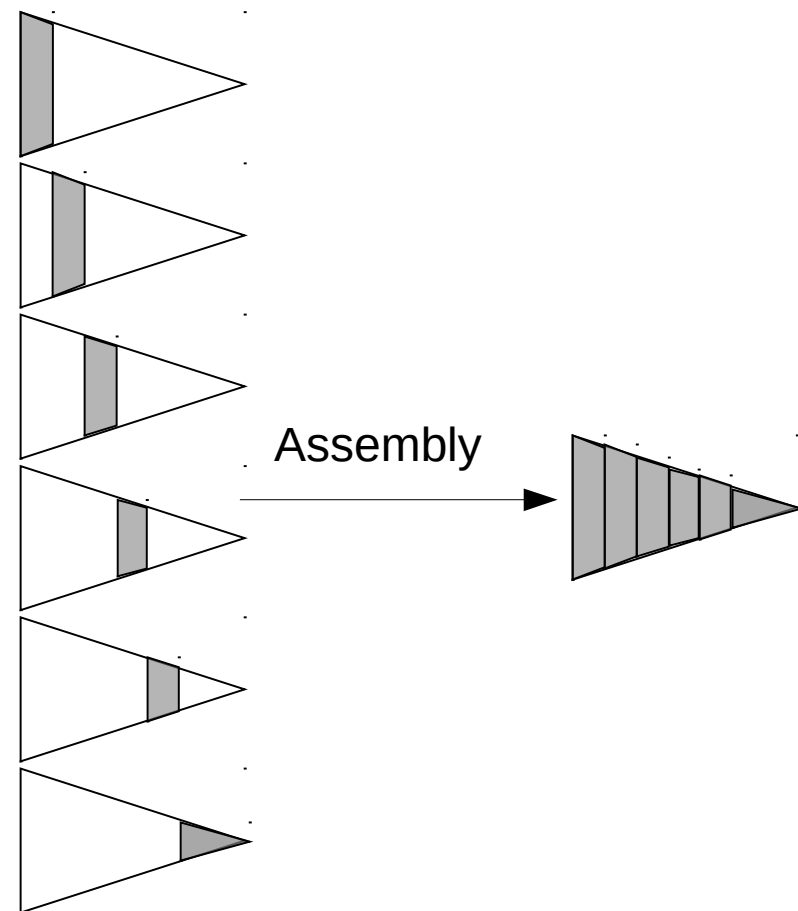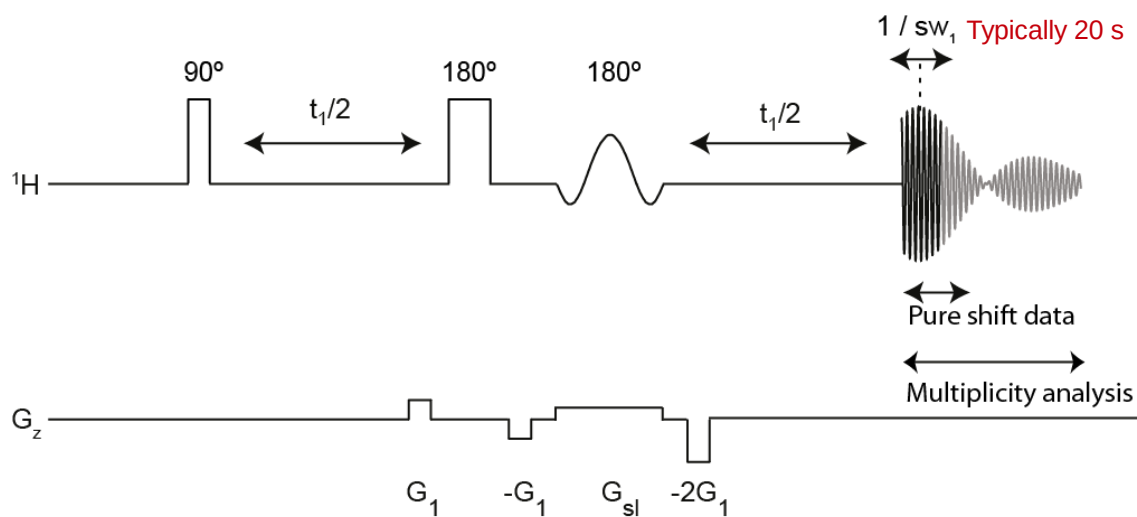
Zangger and Sterk: J-refocusing

The combination of selective and non-selective 180 rotations:

- refocuses the evolution under the coupling
- but allows that of the chemical shift to evolve

Zangger and Sterk: (2D) Chemical shift sampling

Increment t_1 stepwise,
Typically 32-64 blocks of 20 ms [*]

1 / sw$_1$ Typically 20 s

90°   180°   180°

$t_1/2$ $t_1/2$

¹H

Pure shift data

Multiplicity analysis

G$_z$

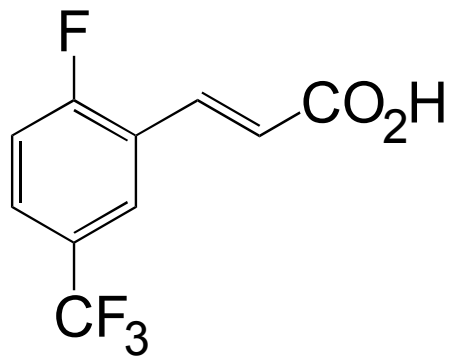G$_1$ -G$_1$ G$_{sl}$ -2G$_1$

Assembly

Typical experimental time: 5-10 minutes using a 5-10 mM sample

[*] J modulation is slow, so a block of data points lasting $1/sw_1 \ll 1/J$ can be measured for each value of t_1
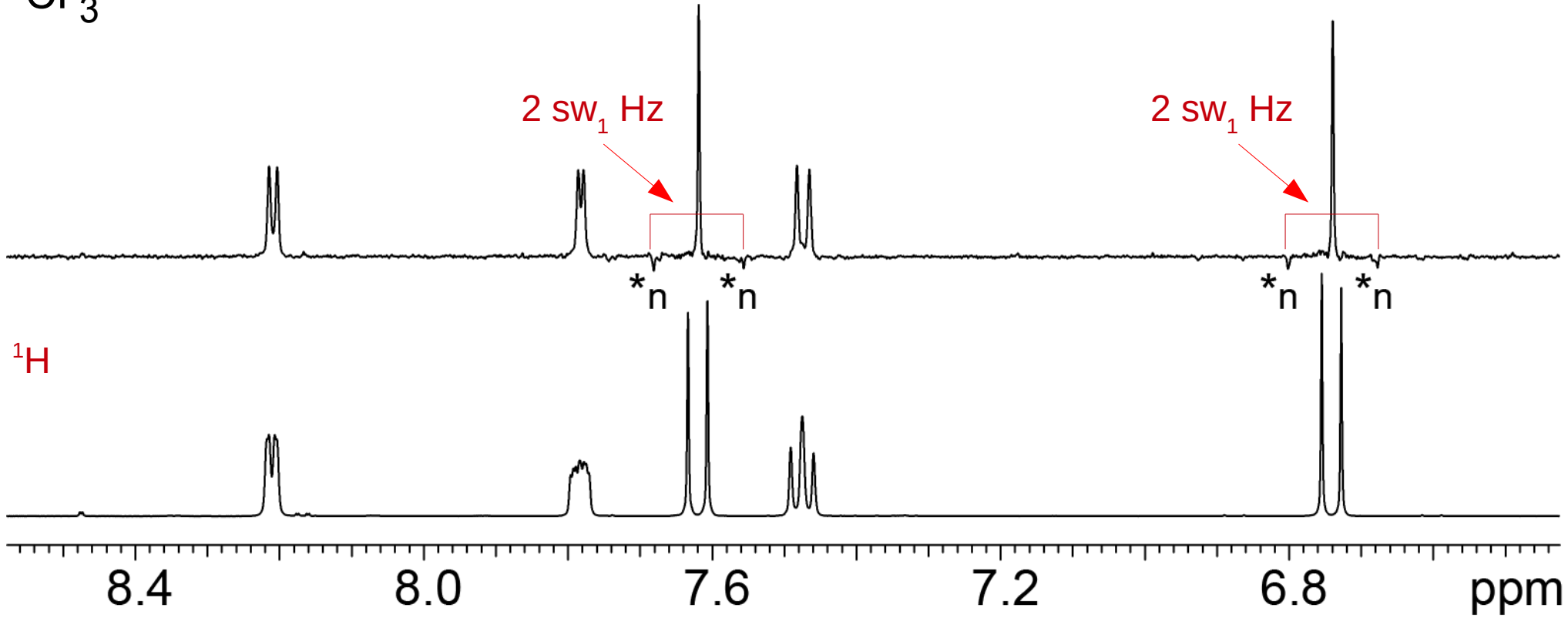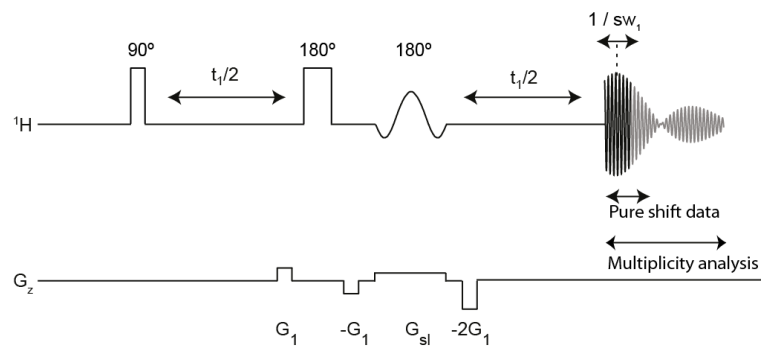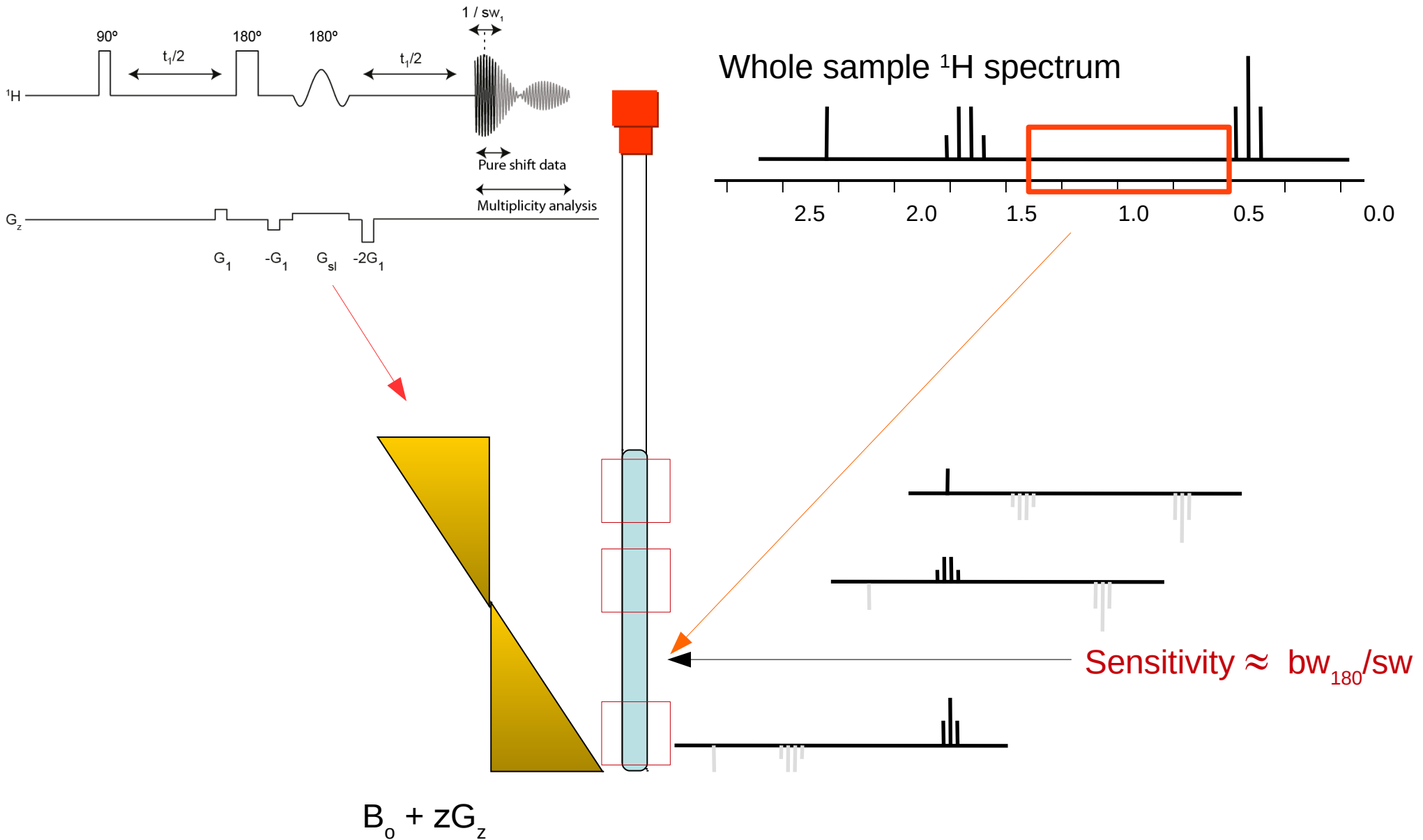
The consequences of chunking

Chunking artefacts are usually not seen.

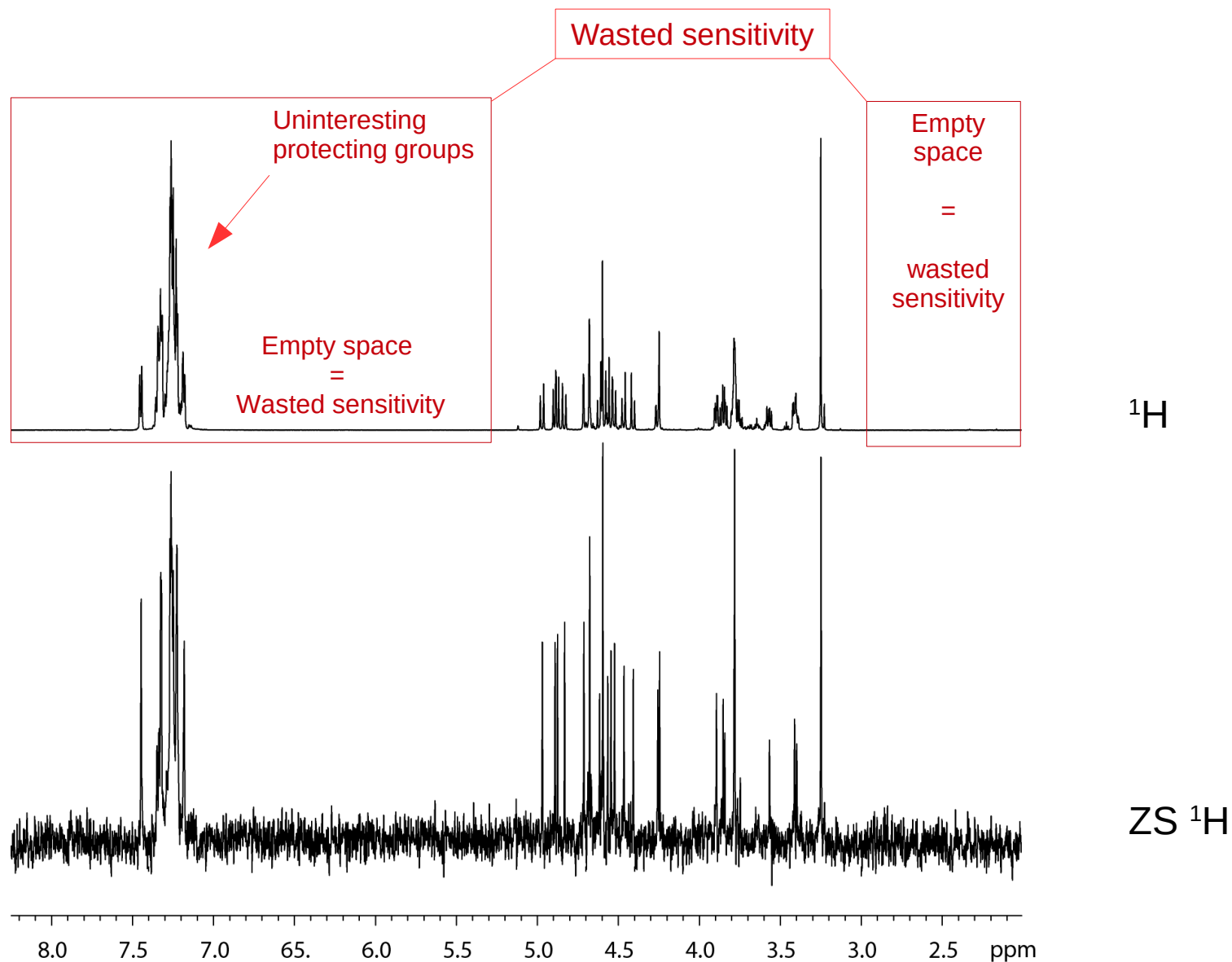They can be seen in this sample because the concentration is high and because some couplings are high.

Cleaner results can be produced reducing the chunking time.

$2\ sw_1$ Hz

$2\ sw_1$ Hz

^{1}H

Zangger and Sterk: multiplexing

Whole sample ¹H spectrum

Pure shift data

Multiplicity analysis

$B_o + zG_z$
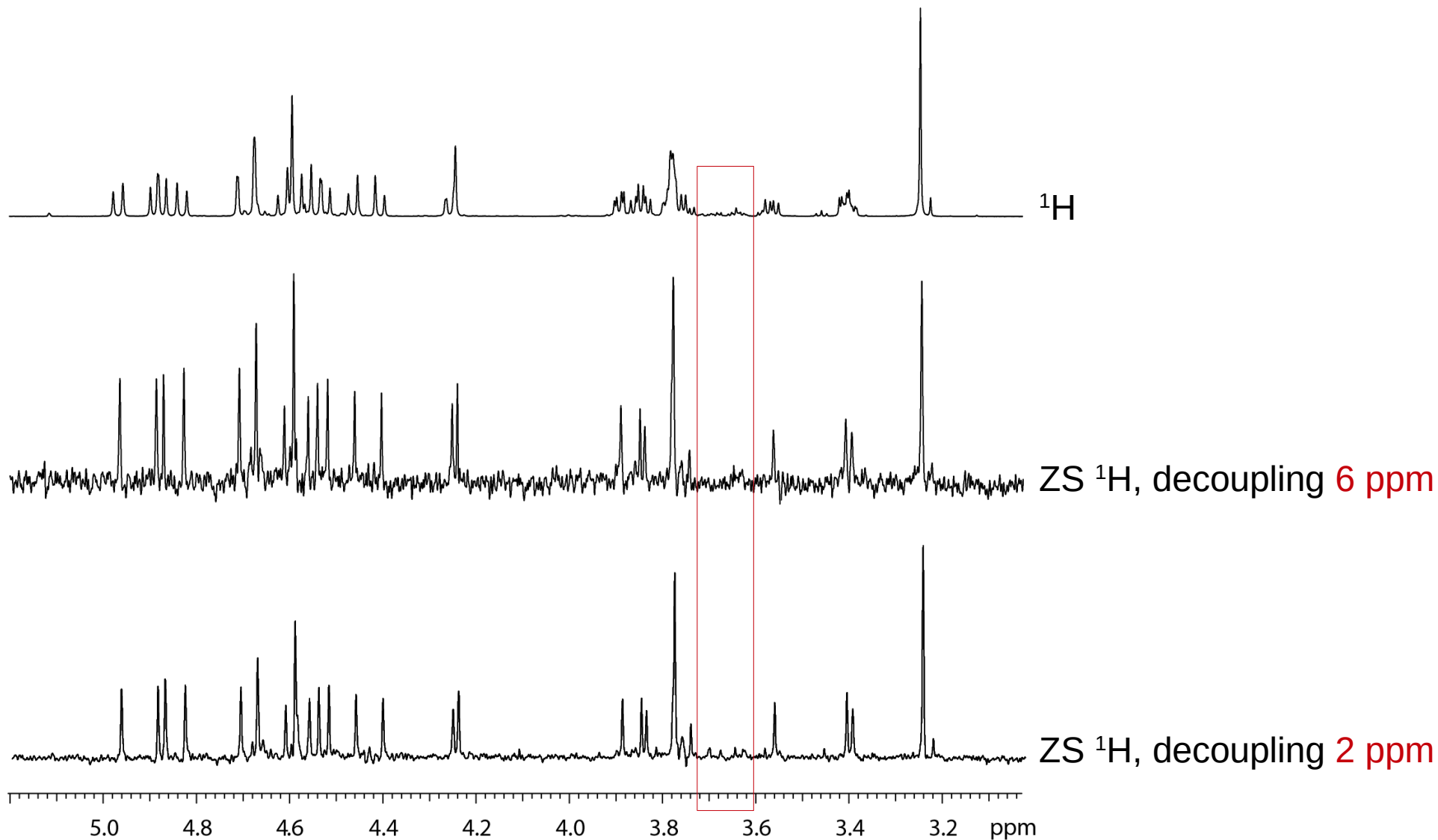
Sensitivity $\approx$ bw_{180}/sw

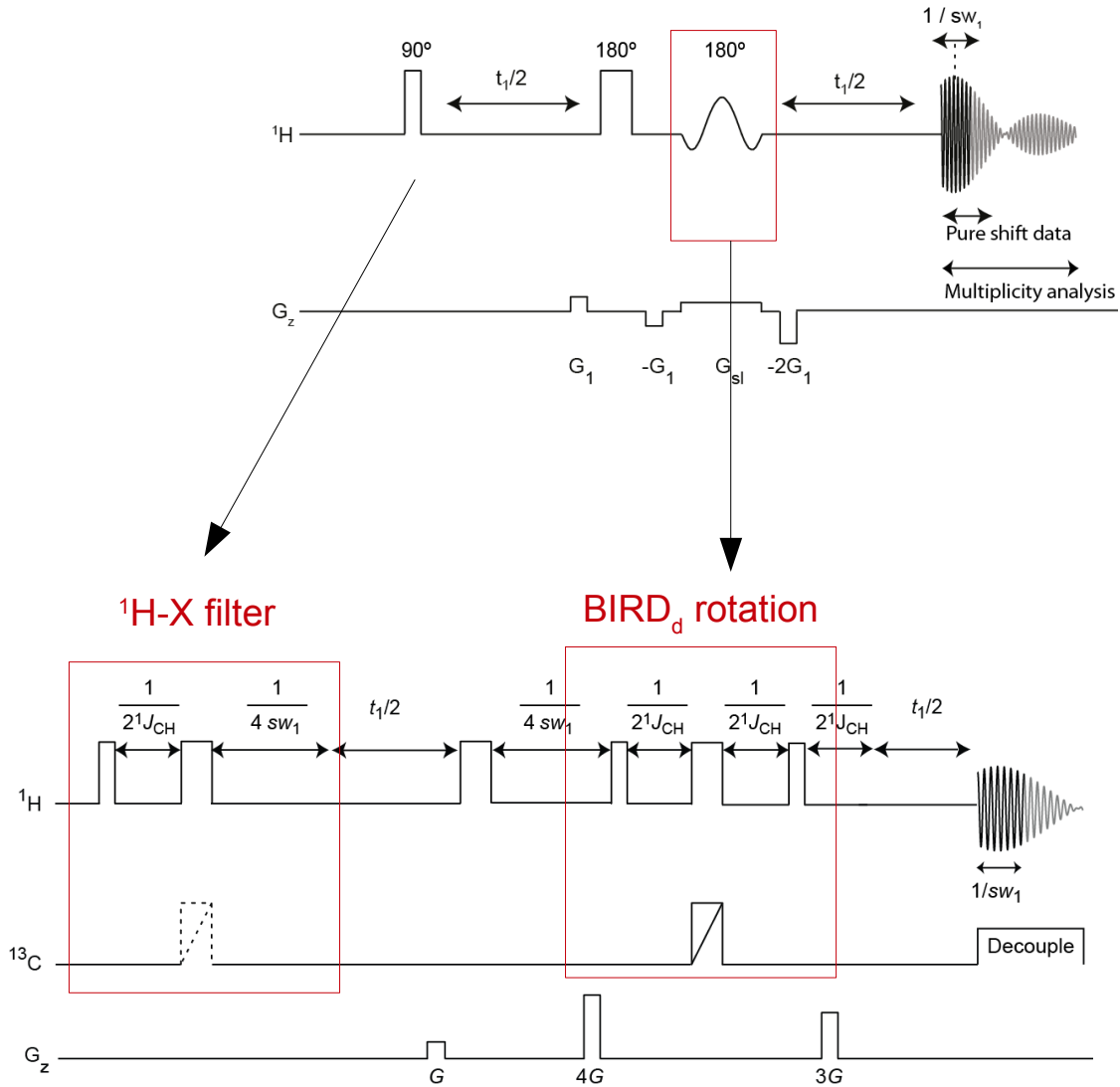# Focus on the area that that contains the problem

Focus on the area that that contains the problem

- Less hardware demanding
- Fewer distortions
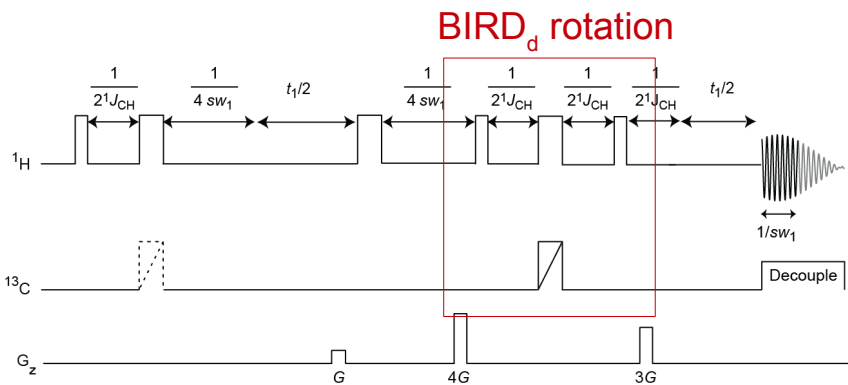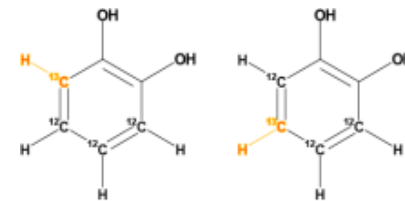- Better sensitivity

The BIRD - Zangger-Sterk hybrid

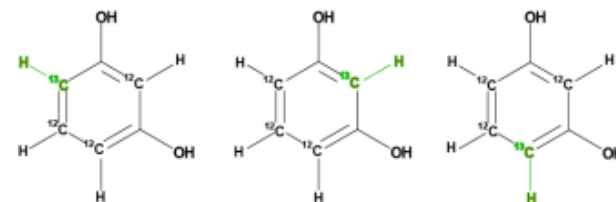The BIRD_d rotation inverts only protons directly coupled to ^{13}C

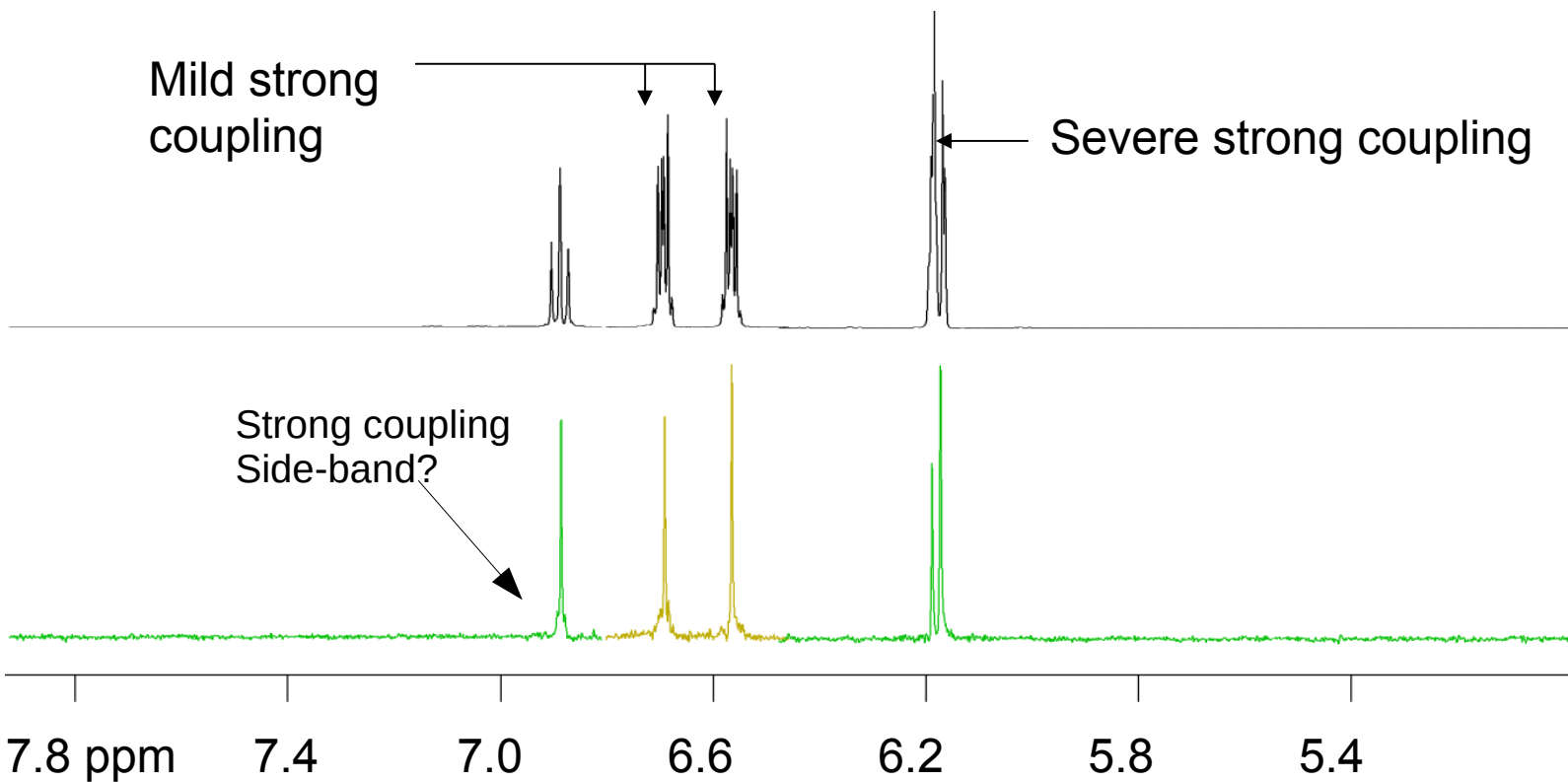Isotopic dilution ensures that their coupled partners are not inverted

BIRD$_d$ rotation

$\frac{1}{2^1J_{CH}}$ $\frac{1}{4\,sw_1}$ $t_1/2$ $\frac{1}{4\,sw_1}$ $\frac{1}{2^1J_{CH}}$ $\frac{1}{2^1J_{CH}}$ $\frac{1}{2^1J_{CH}}$ $t_1/2$

^{1}H

$1/sw_1$

^{13}C   Decouple
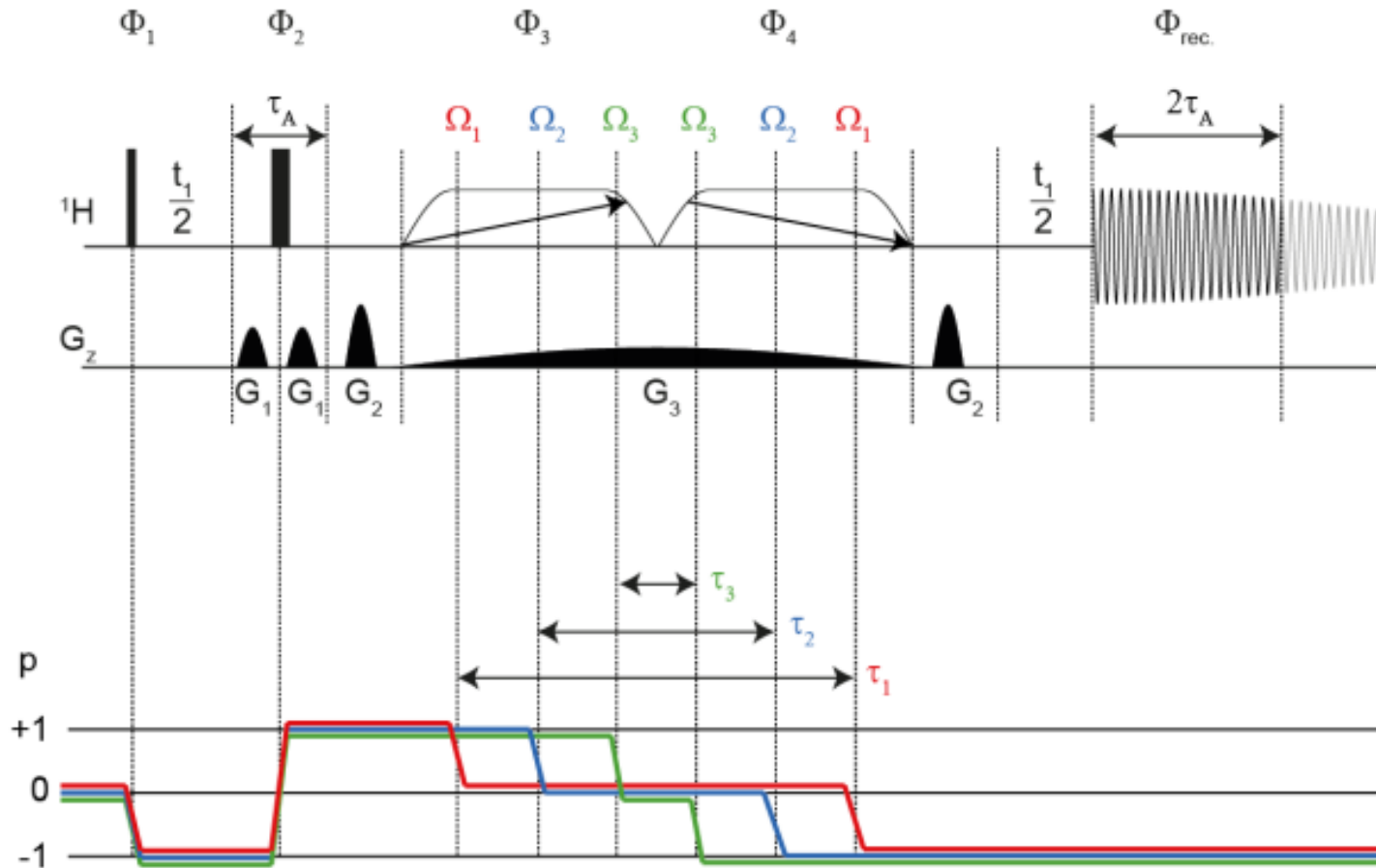
G$_z$ G   4G   3G

Catechol isotopomers

Resorcinol isotopomers

The BIRD$_d$ rotation inverts only protons directly coupled to ^{13}C
Isotopic dilution ensures that their coupled partners are not inverted

Mild strong coupling

Severe strong coupling

Strong coupling Side-band?

7.8 ppm   7.4   7.0   6.6   6.2   5.8   5.4

The PSYCHE- Zangger-Sterk hybrid

Improved sensitivity (it avoids sample slicing, pulse field gradients are only used for signal selection)
Improved performance regarding strong coupling

Zangger-Sterk

Zangger-Sterk - BIRD

+ Sensitive when the bandwidth (sw) is narrow

$\approx$ bw_{180}/sw

- More sensitive to strong coupling

+ Fully decouples geminals (usually)
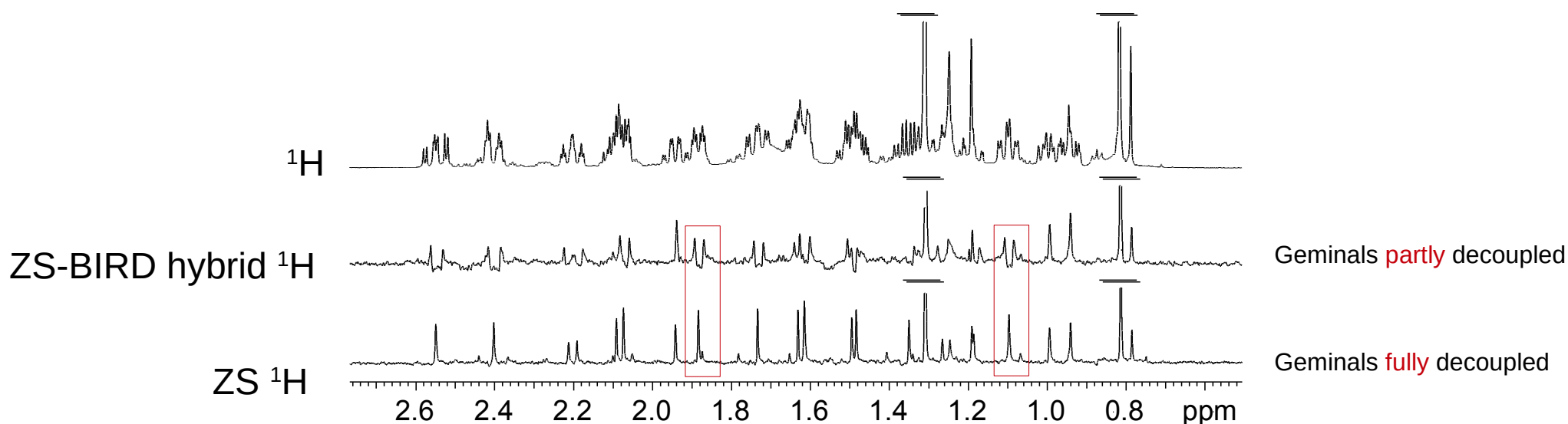
Bottom line:
Ideal to decouple aliphatic regions

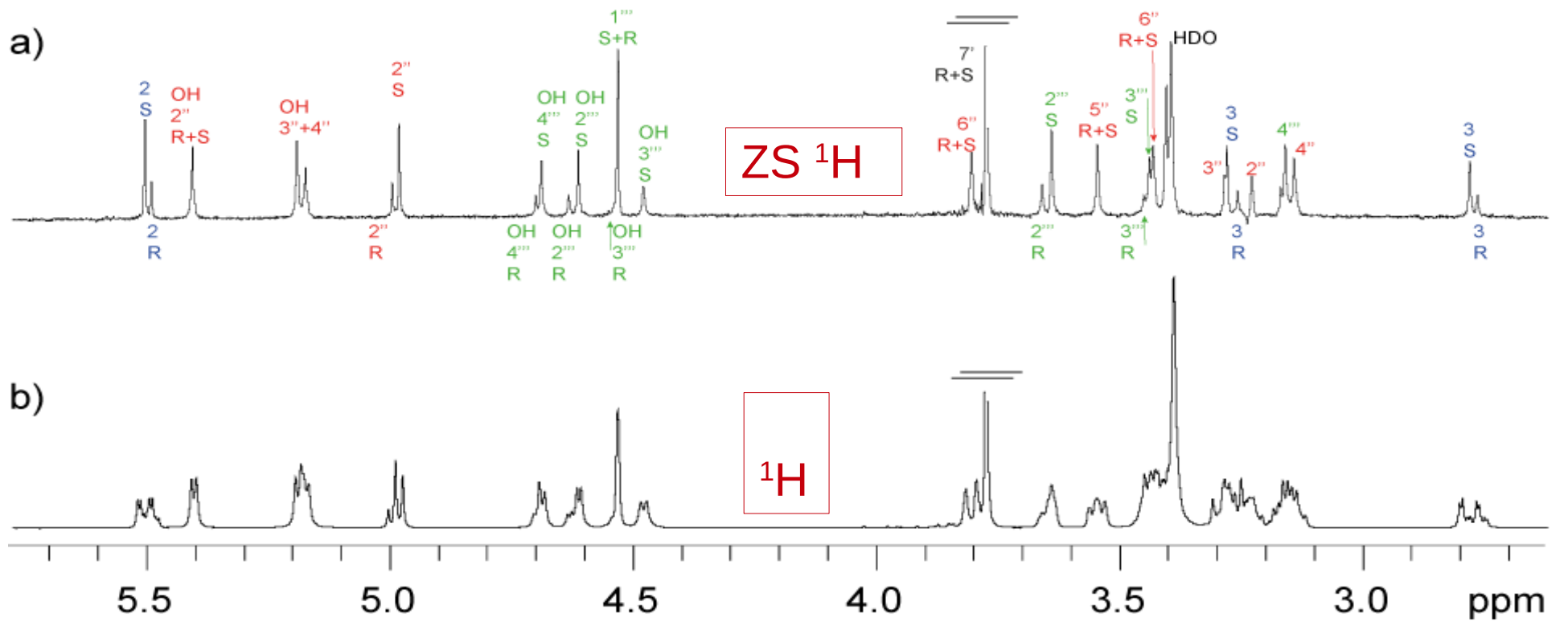- Typically less sensitive but its sensitivity, is <u>almost</u> independent of the bandwidth, < 1 %
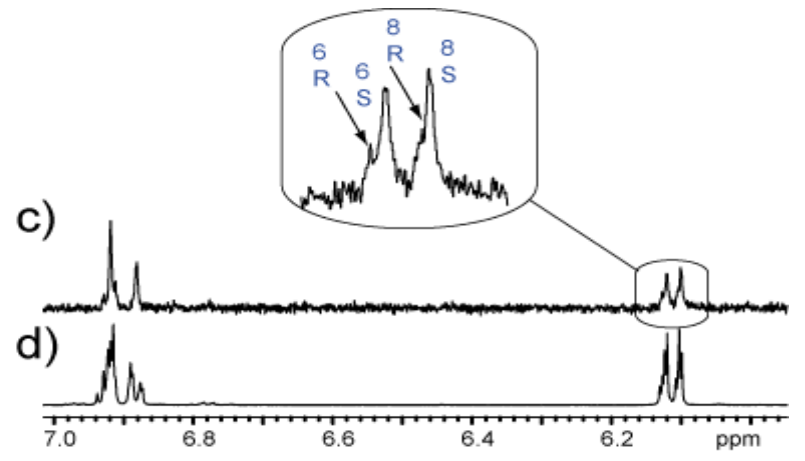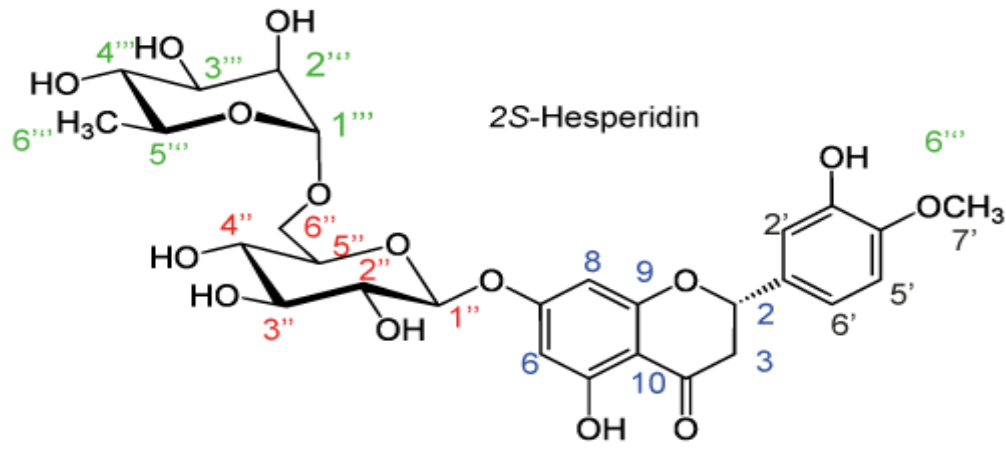
+ Less sensitive to strong coupling
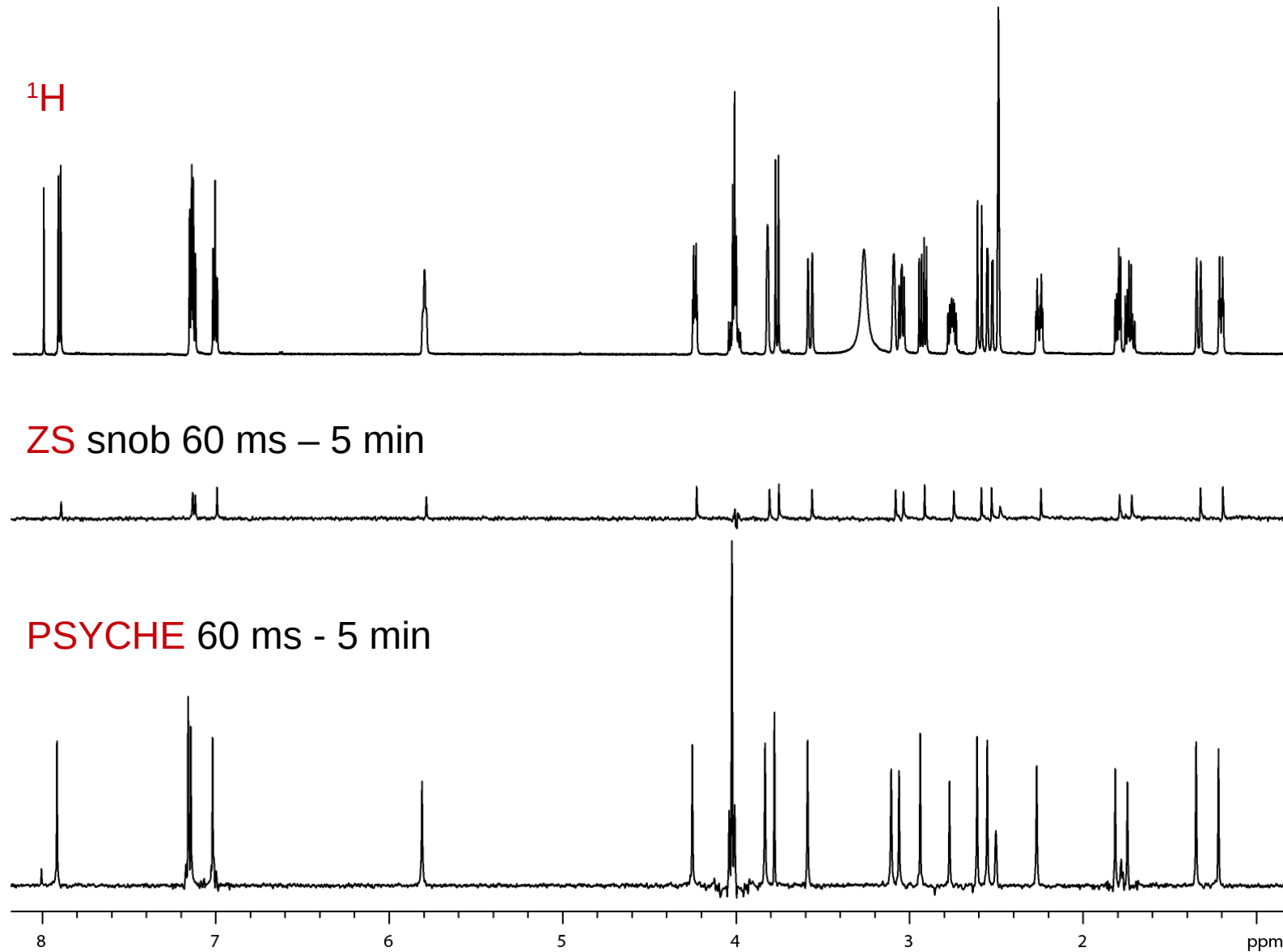
- Partially decouples geminals
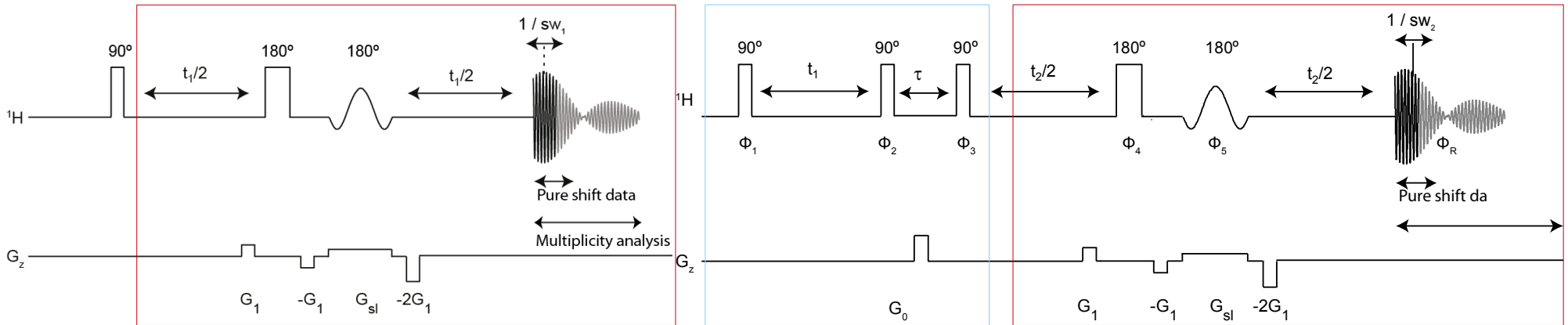
Bottom line:
Ideal to decouple aromatic regions

^{1}H

ZS-BIRD hybrid ^{1}H

Geminals partly decoupled

ZS ^{1}H

Geminals fully decoupled

2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 ppm

ZS-BIRD hybrid ¹H

2S-Hesperidin

c)

d)

a)

ZS ¹H

b)

¹H

The PSYCHE hybrid

^{1}H

ZS snob 60 ms – 5 min

PSYCHE 60 ms - 5 min

Multi-dimensional pure shift experiments
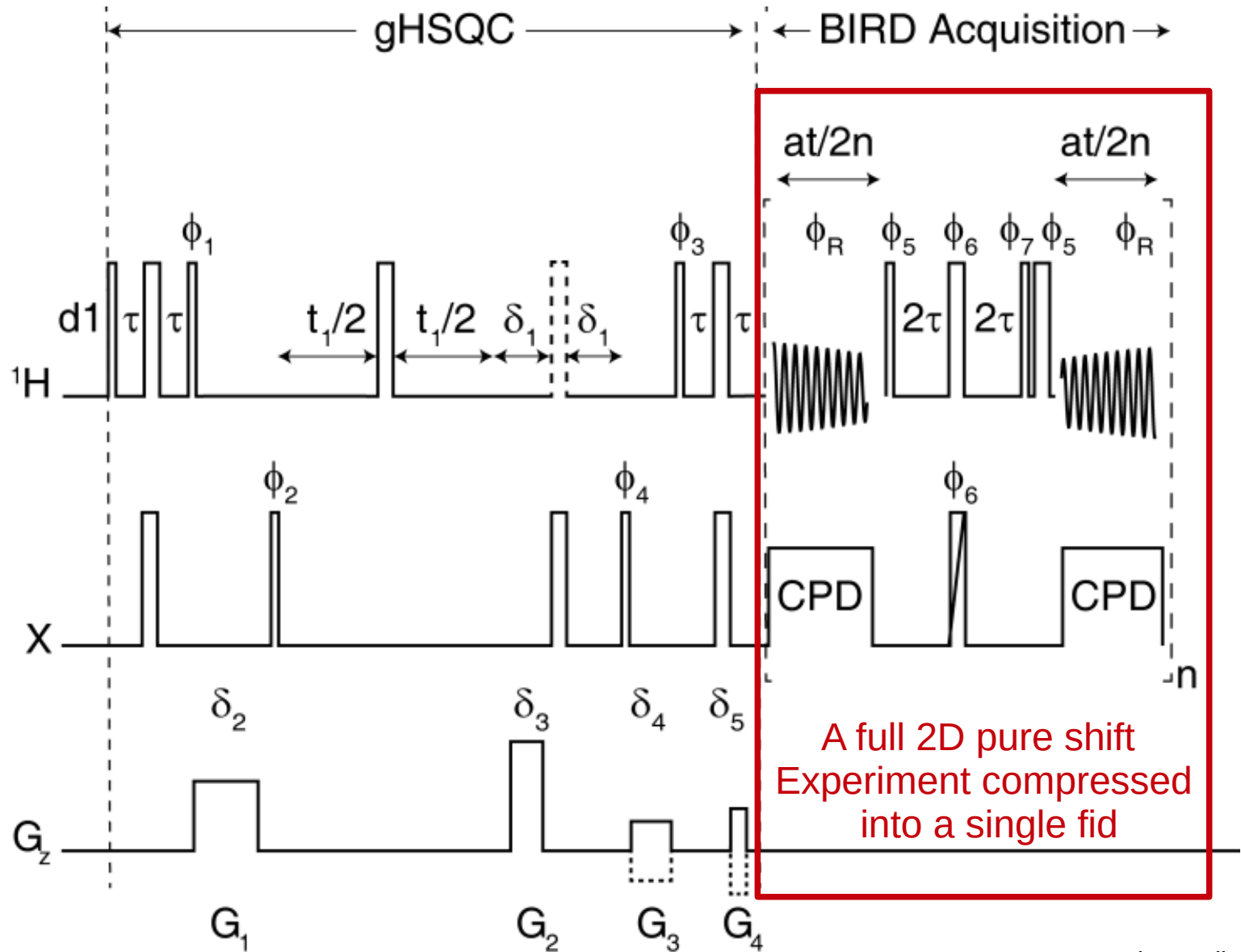

Pure shift ^1H
with classic 2D
chemical shift sampling

NOESY (2D)
+
Pure shift with classic 2D
chemical shift sampling
= 3D experiment (long)

How-to: Merge the pure shift sequence with your experiment (except for COSY)

The problem: The experiment will now be 32-64 times longer
The solution: Compress the whole 2D chemical shift sampling scheme into a single acquisition
using real-time compression.

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Multi-dimensional pure shift experiments with real-time compression

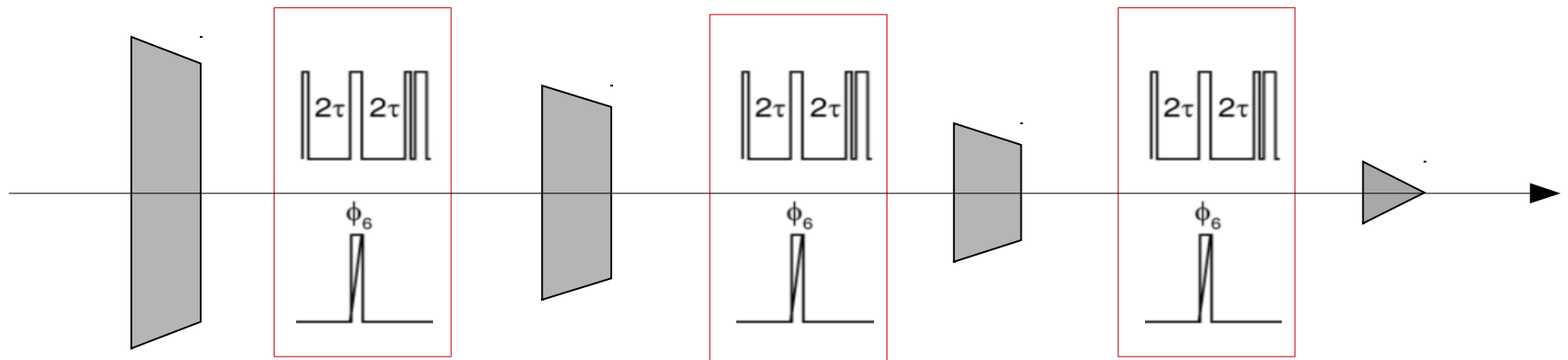A full 2D pure shift Experiment compressed into a single fid
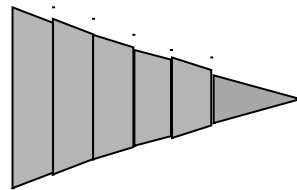
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Real-time compression

How-to

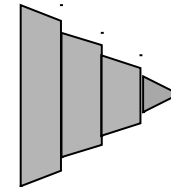Compress a full 2D sampling scheme into a single acquisition

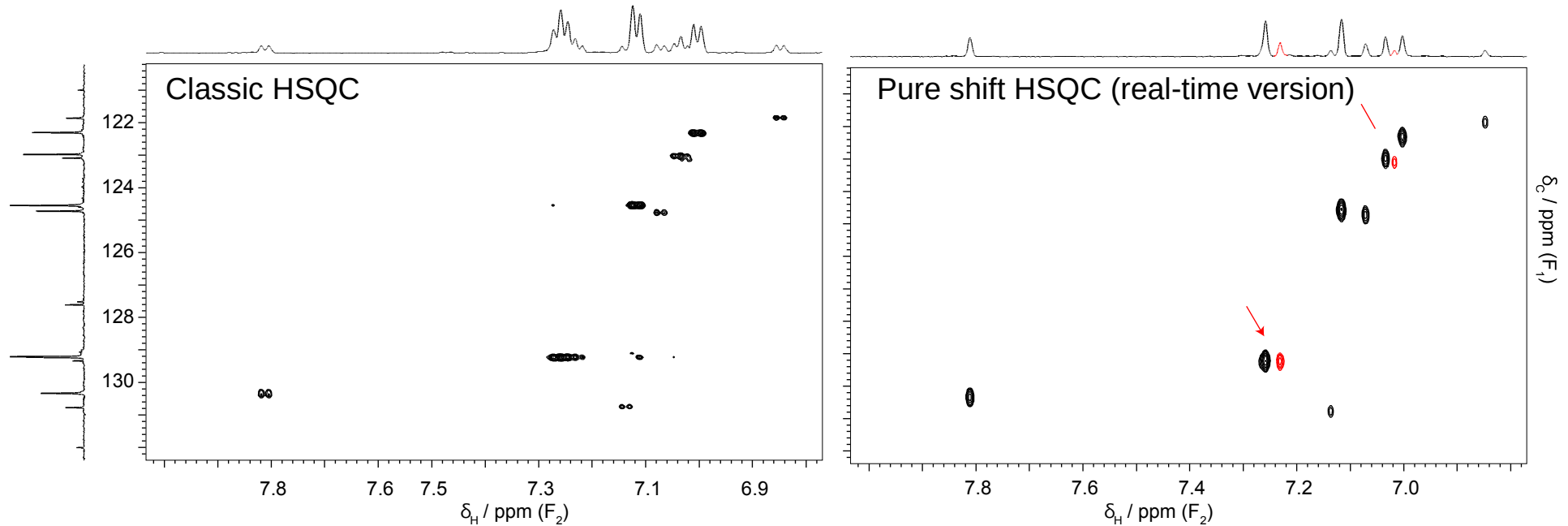Acquire – J-refocus - acquire – J-refocus - acquire - J-refocus – acquire

Original fid
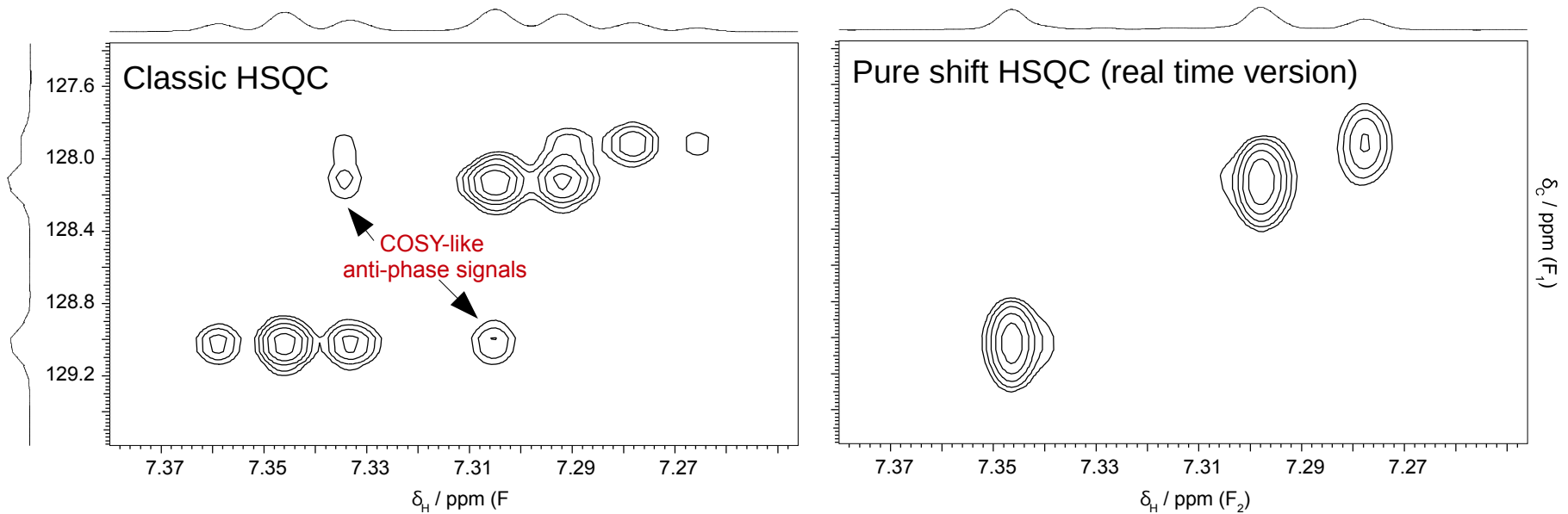
Shortened fid = broadening

Broadening in context
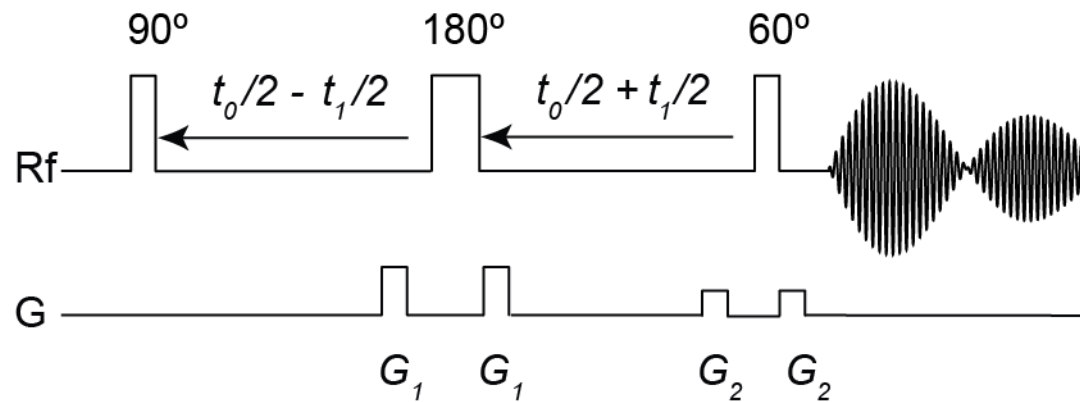
Undesirable but better off with than without

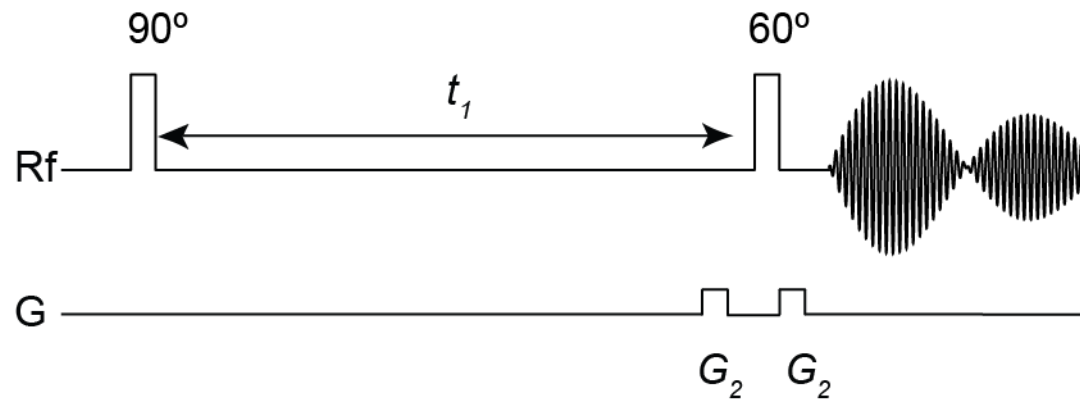## Important but obvious

- Make sure that the fid is long enough to be able to tell the difference between a singlet and a multiplet
  Typical HSQC acquisition times are inappropriate to produce pure shift data.

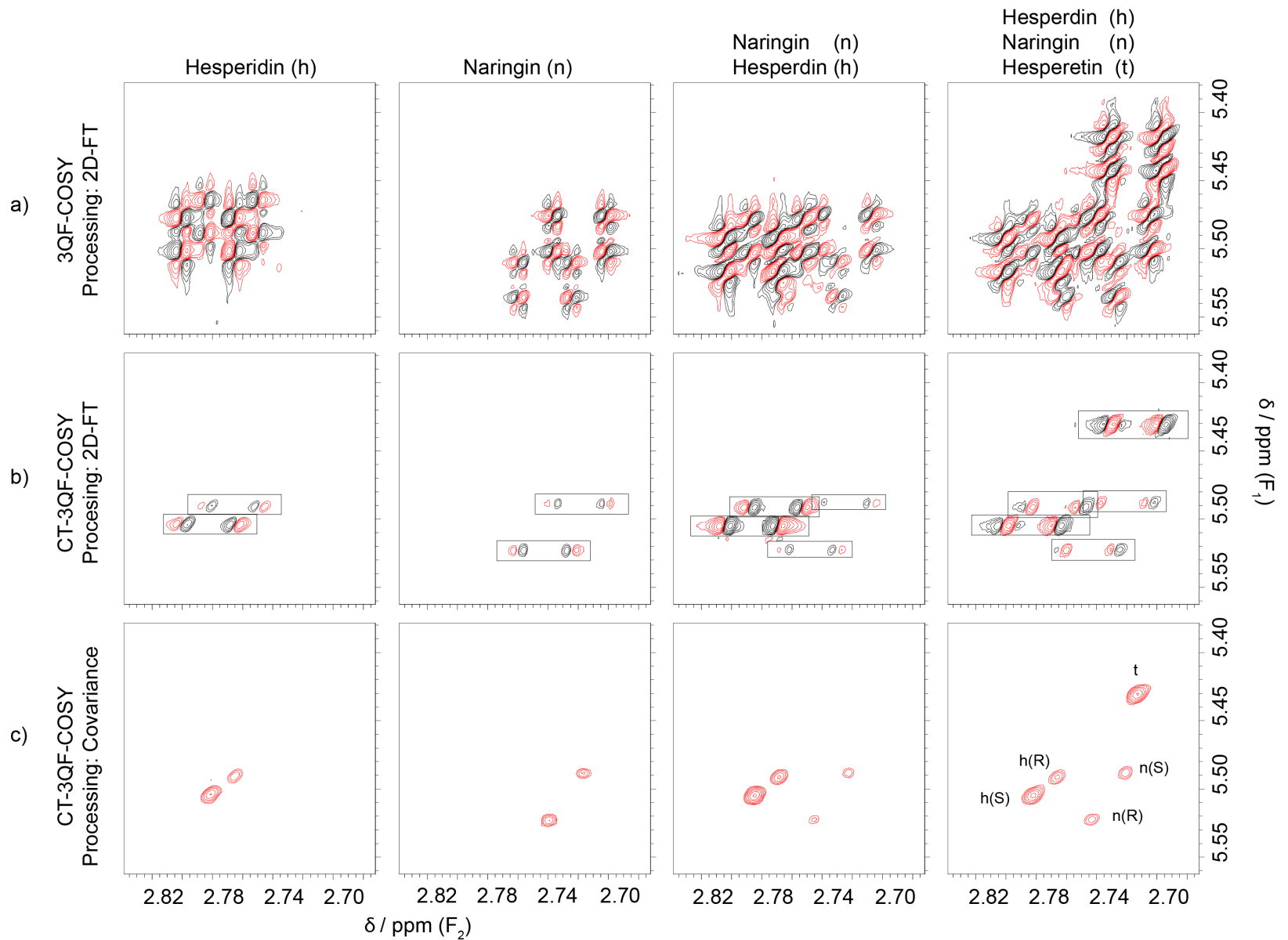- Make sure your pulses are decently calibrated, you are going to produce multiple rotations

Unexpected benefits: attenuation of anti-phase peaks

Constant-time techniques

Constant-time techniques

Thanks to:

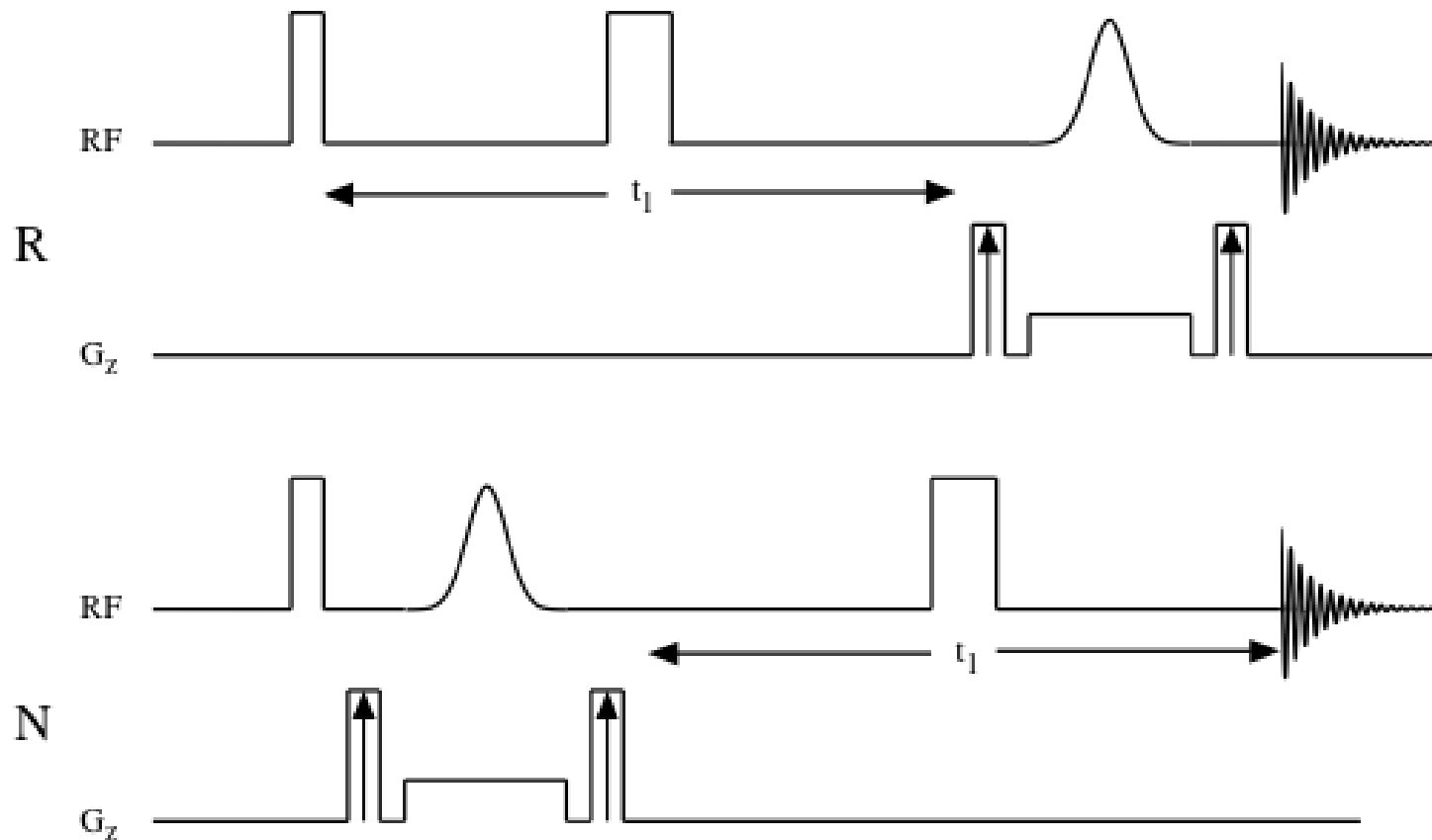# Multiplicity determination using ZS-type sequences

- Always acquire full fids,
  not only 20 ms ones (except for the
  ZS-BIRD hybrid).

- Do not use the reconstruction macro,
  use a double FT instead.

For these matters is preferable a phase sensitive J-resolved Pell-Keeler-ZS variant.
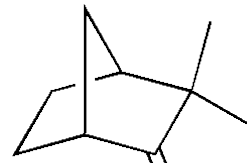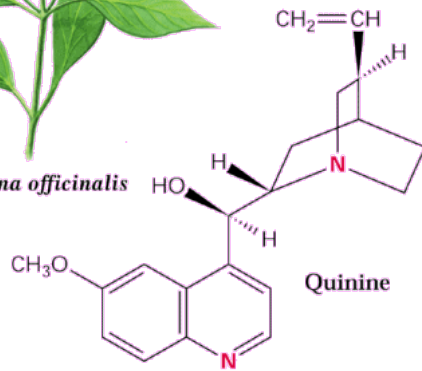
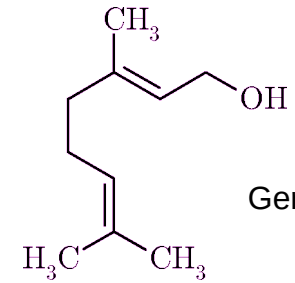# Phase sensitive J-resolved
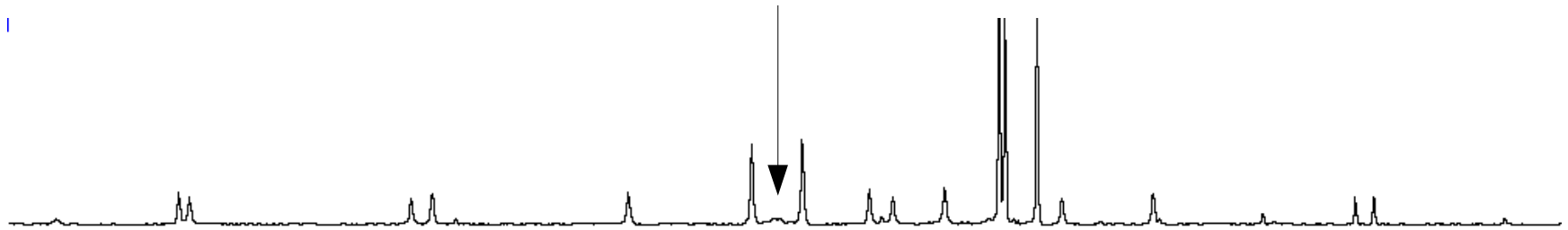## Pell-Keeler-ZS

Strong coupling artefacts (*)
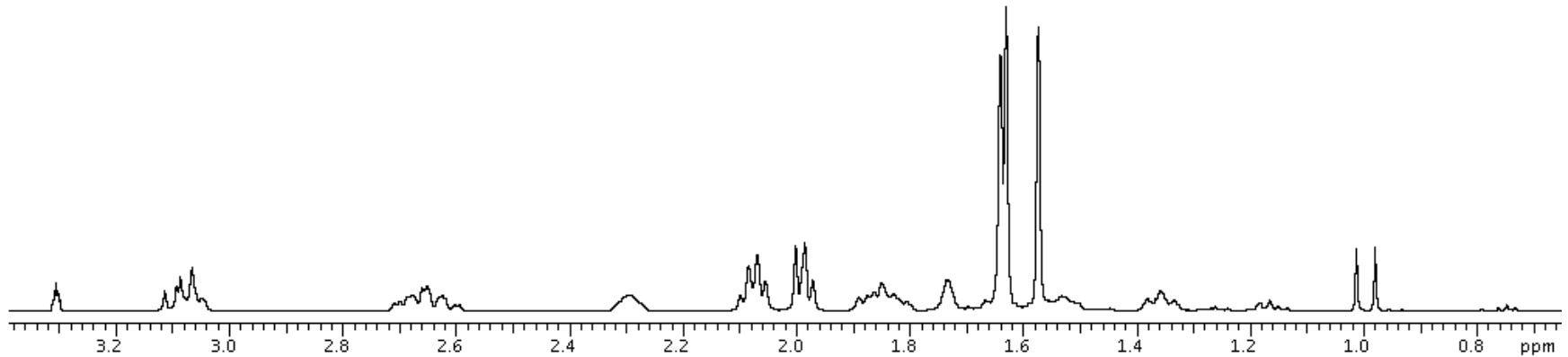

Cinchona officinalis
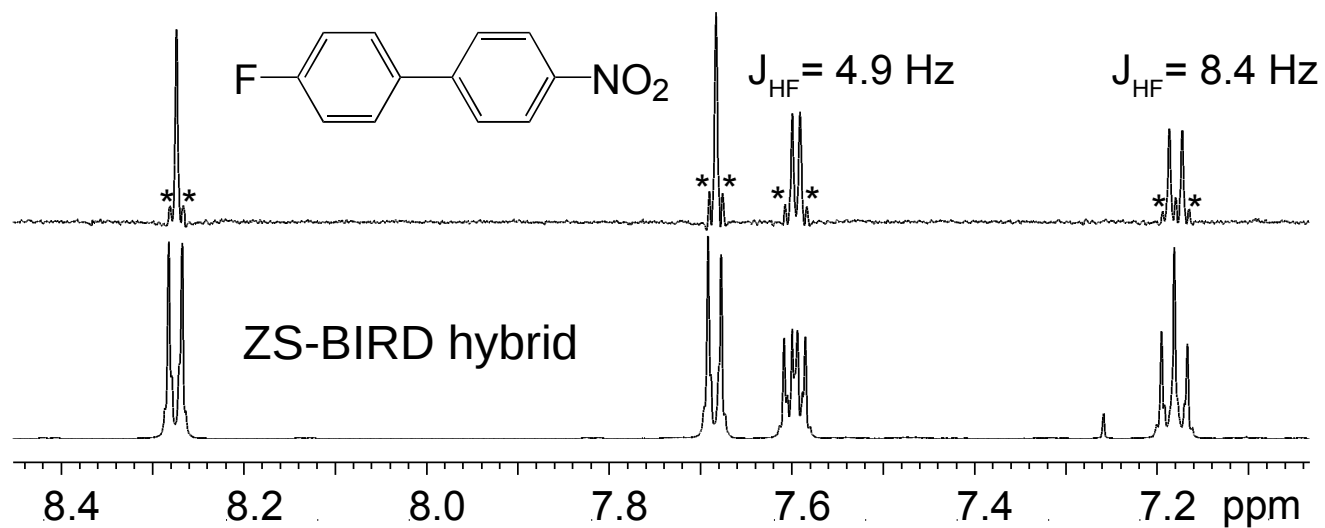
Quinine

Camphene

Geraniol

Strong coupling (*)

ZS ¹H

¹H

Strong coupling artefacts (*)

$J_{HF} = 4.9$ Hz $J_{HF} = 8.4$ Hz

F—⬡—⬡—NO$_2$

ZS-BIRD hybrid

8.4   8.2   8.0   7.8   7.6   7.4   7.2 ppm

PSYCHE

12°   ×36
21°   ×12.4
38°   ×5.6
67°   ×4.6
Normal   ×1

7.8   7.6   7.4   7.2   [ppm]

Chunking artefacts

Chunk size= 40 ms

Chunk size= 20 ms

Chunk size= 10 ms

Chunk size= 5 ms

^1H

500 MHz spectra of EtOH in Methanol-d_4