PSYCHE

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The University of Manchester

Pure Shift Workshop
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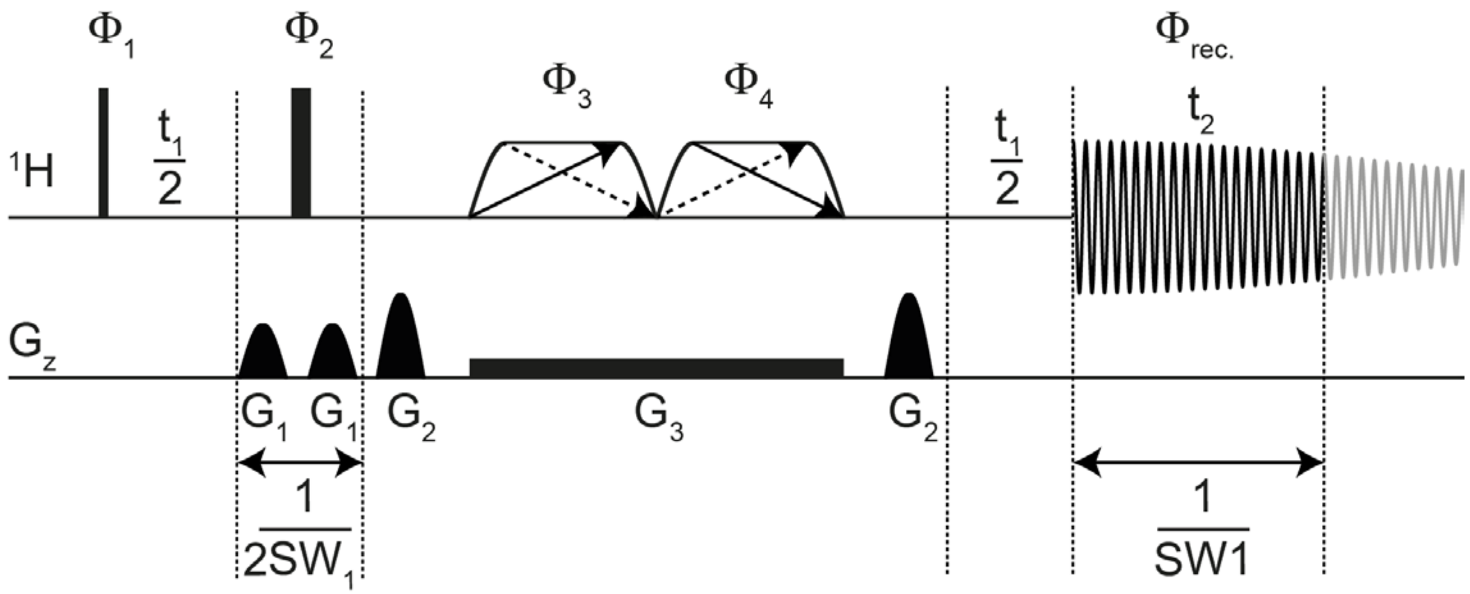
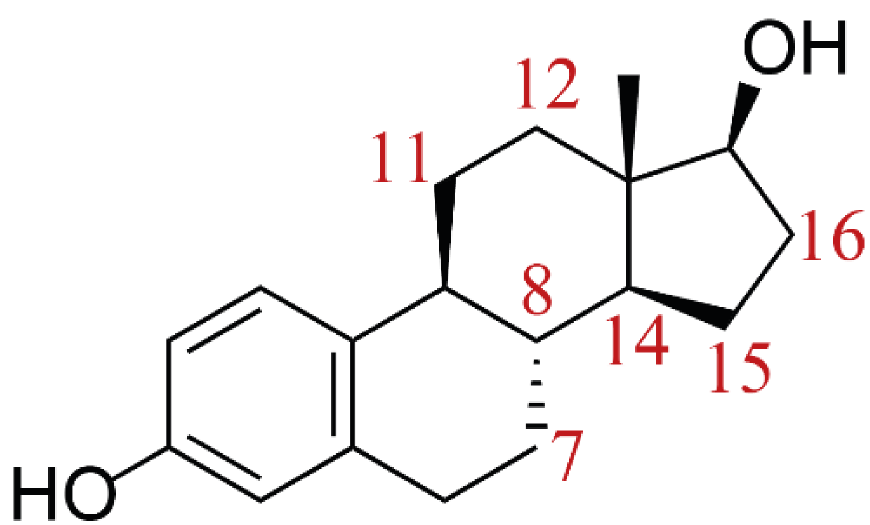
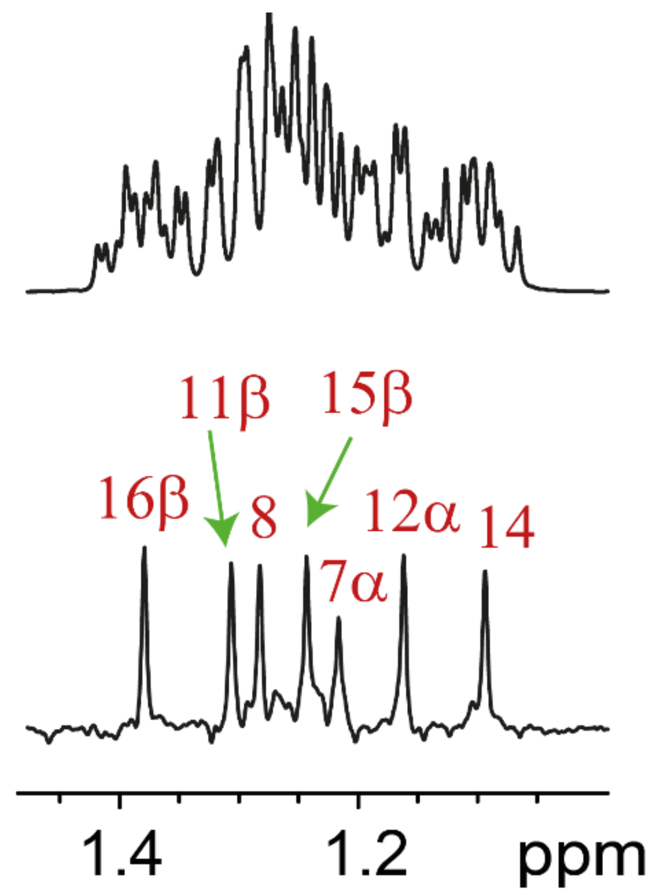
Manchester

PSYCHE NMR







Angew. Chem. Int. Ed., **2014**, *53*, 6990.

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- Triple Spin Echo PSYCHE
- PSYCHE-2D *J*
- F_1-PSYCHE-TOCSY
- PSYCHE-*i*DOSY

General mechanisms for J-refocusing

In general refocusing of J-couplings can be achieved by three approaches:

- Separation of chemical shift and J-coupling evolutions (2D J)
- Inversion of coupling partners (BS, ZS, and BIRD)
- Simplification of coupling patterns using low-flip angle pulses (anti *z*-COSY and PSYCHE)

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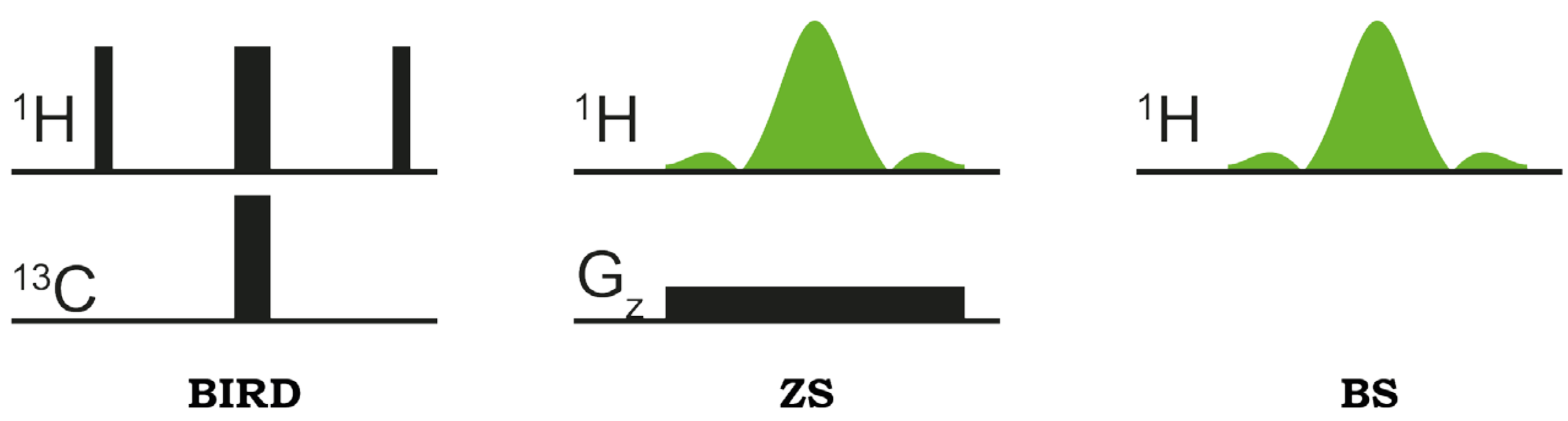

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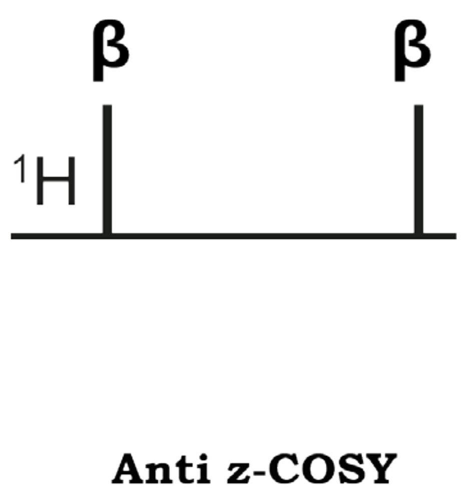
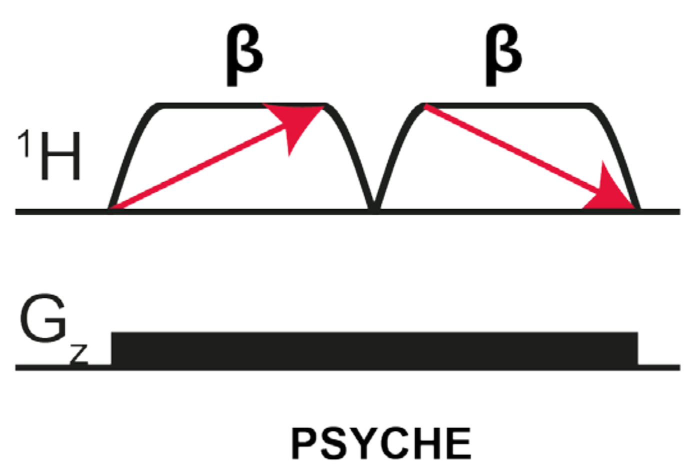
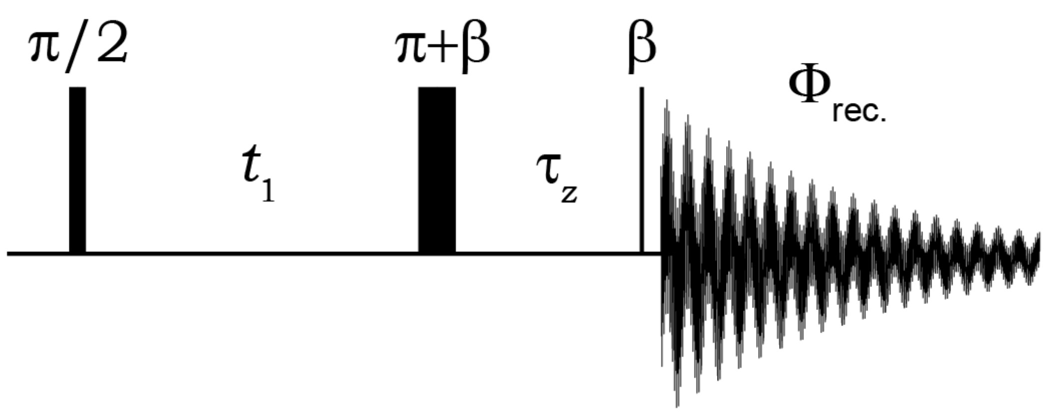
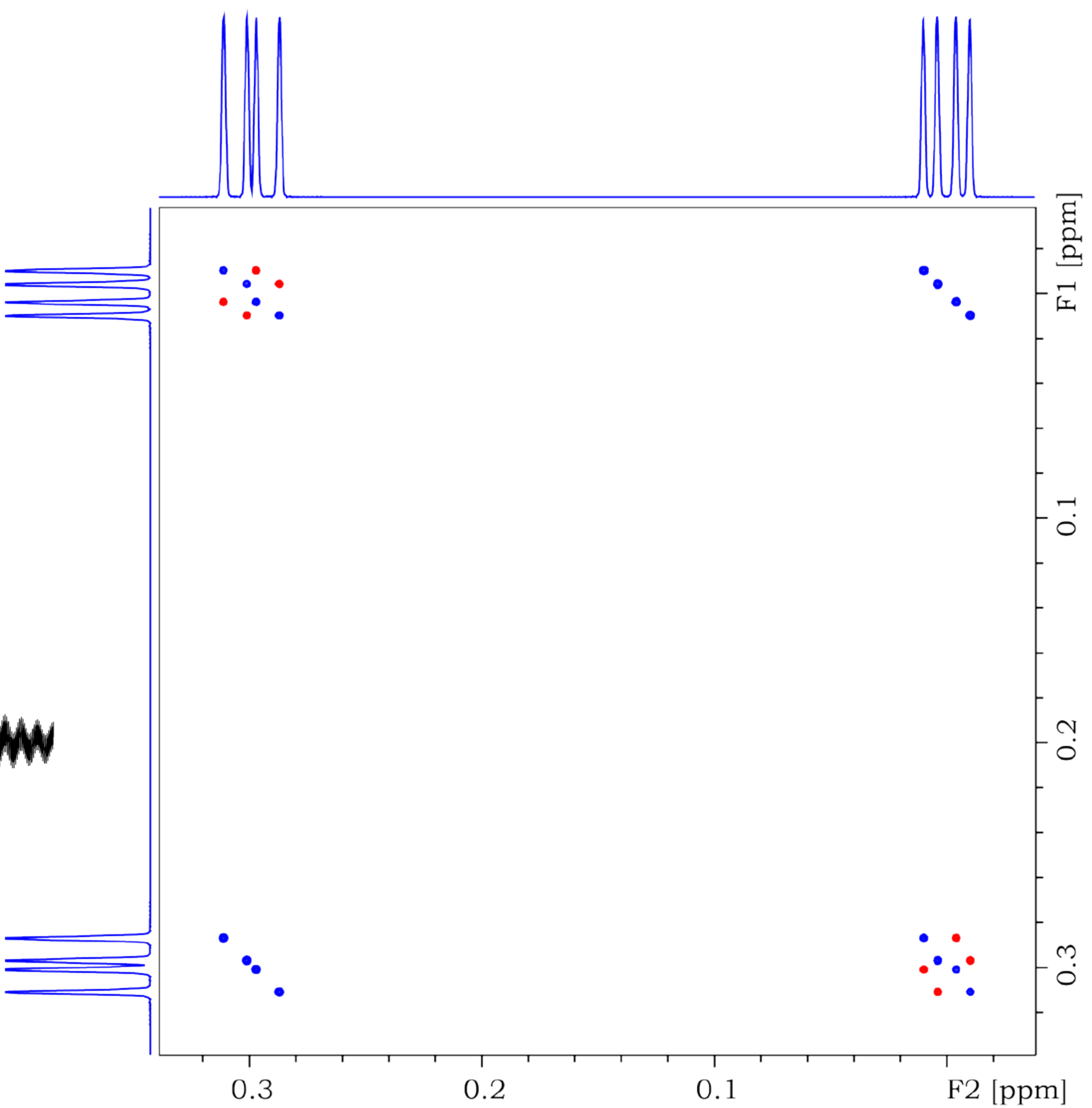




Anti z-COSY

Anti z-COSY experiment uses low-flip angle pulses in order to simplify the multiplet patterns of cross-peaks.

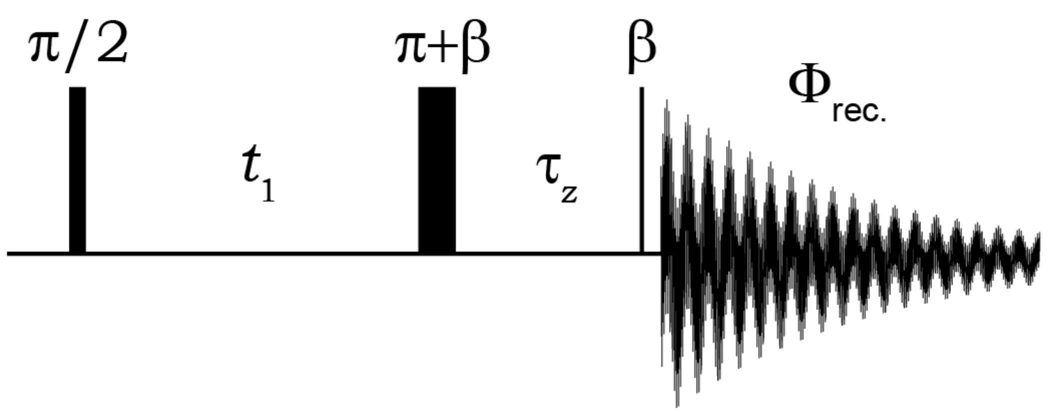


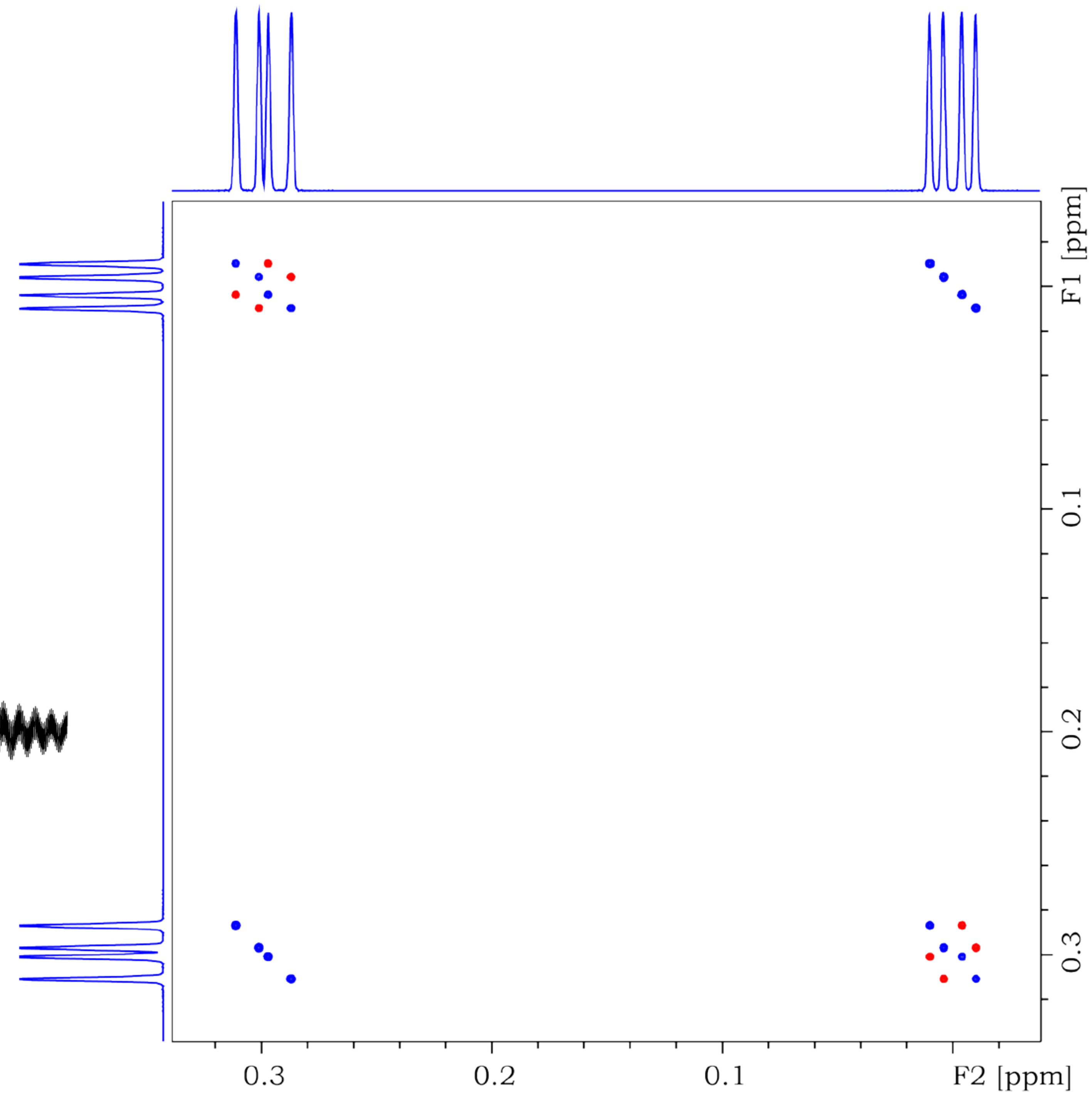


- *J. Magn. Reson.*, **1986**, *69*, 559.

Anti *z*-COSY

The effect of low-flip angle pulses on the diagonal signals can be harnessed to achieve pure shift spectra.





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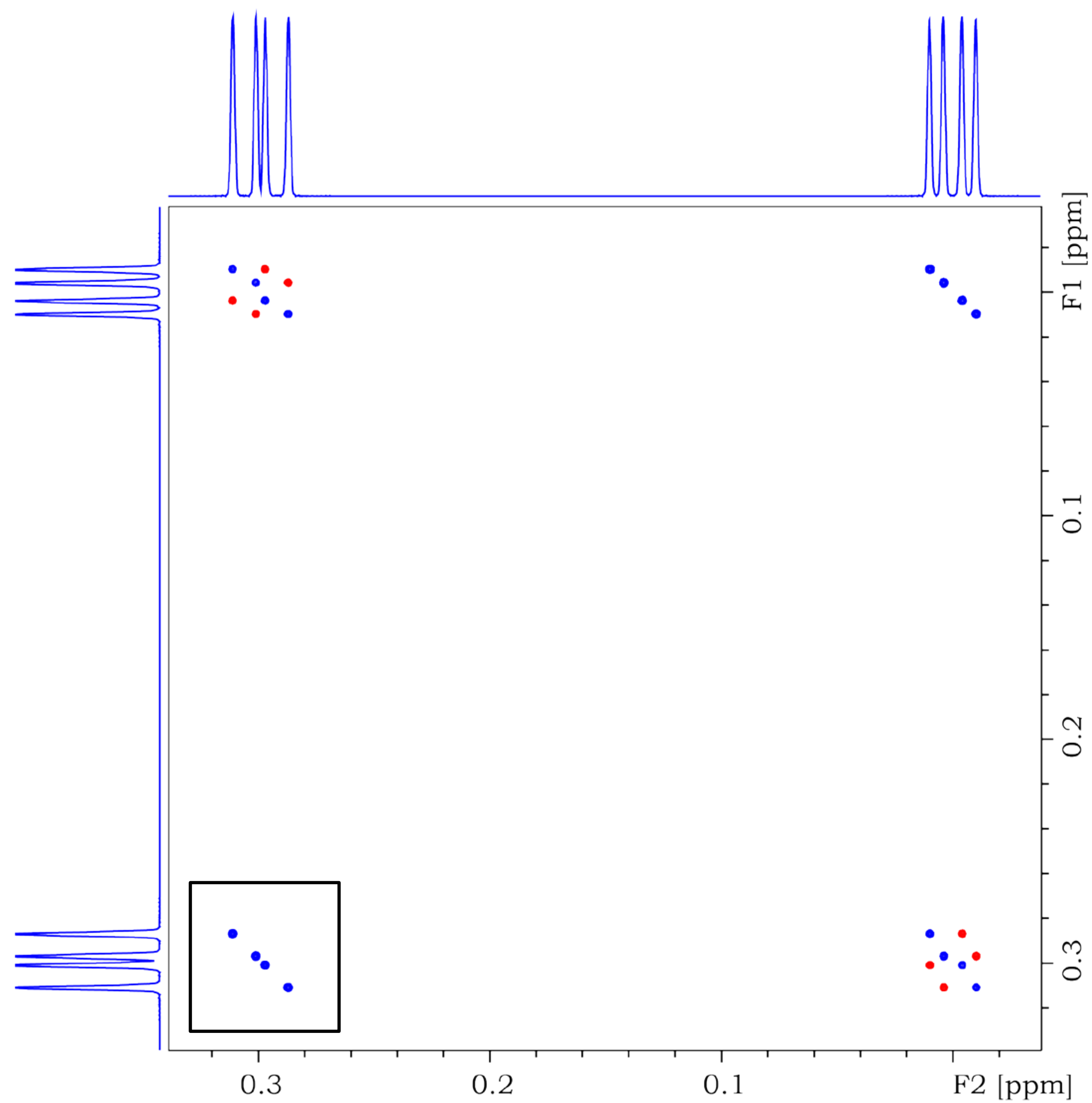

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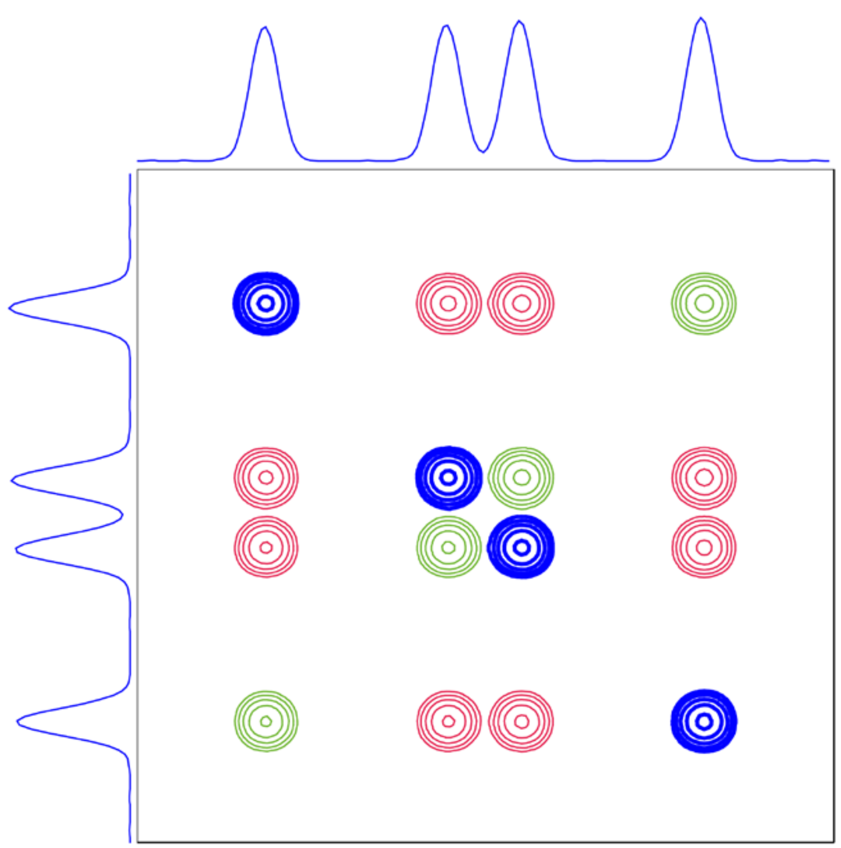

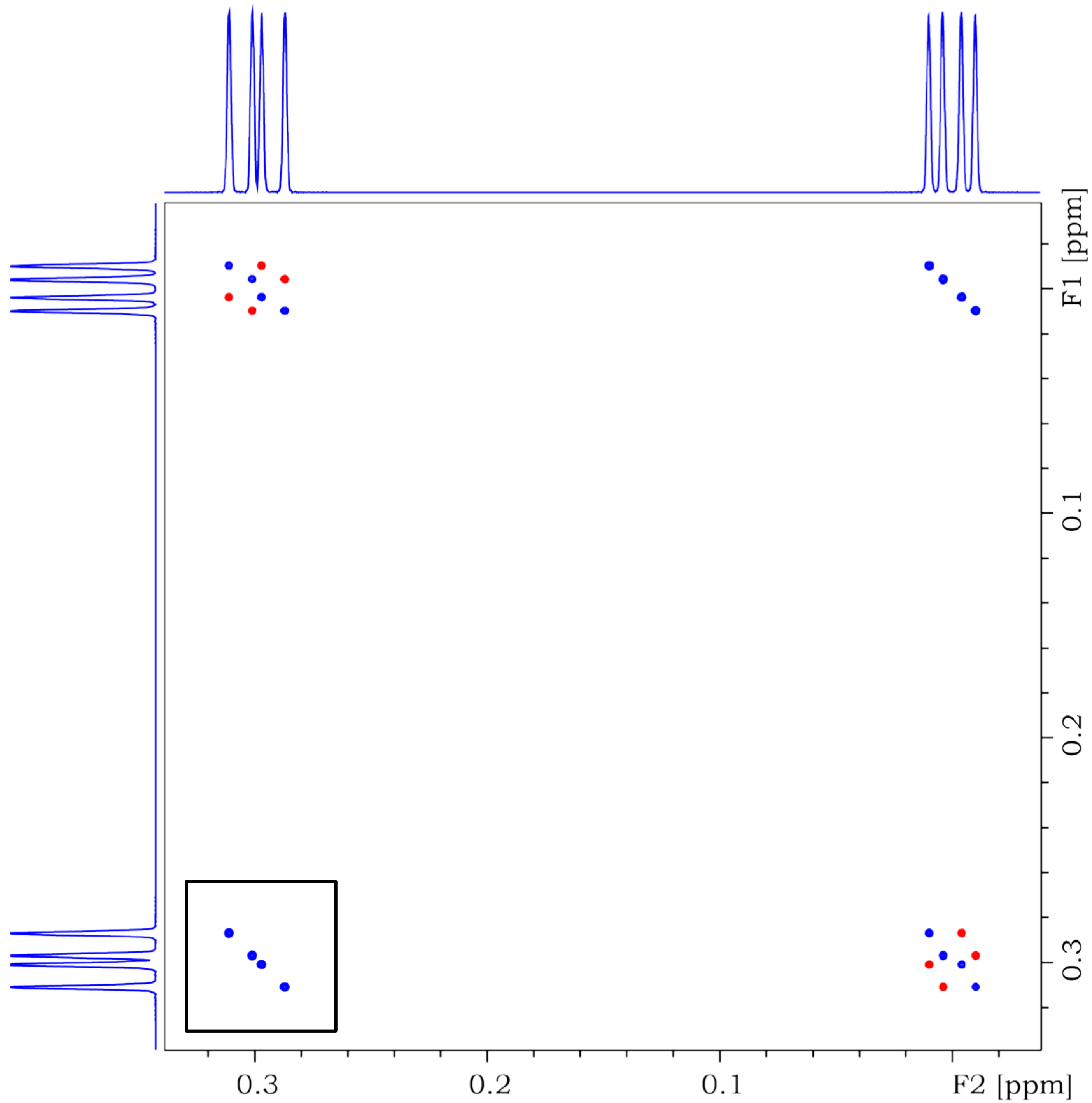

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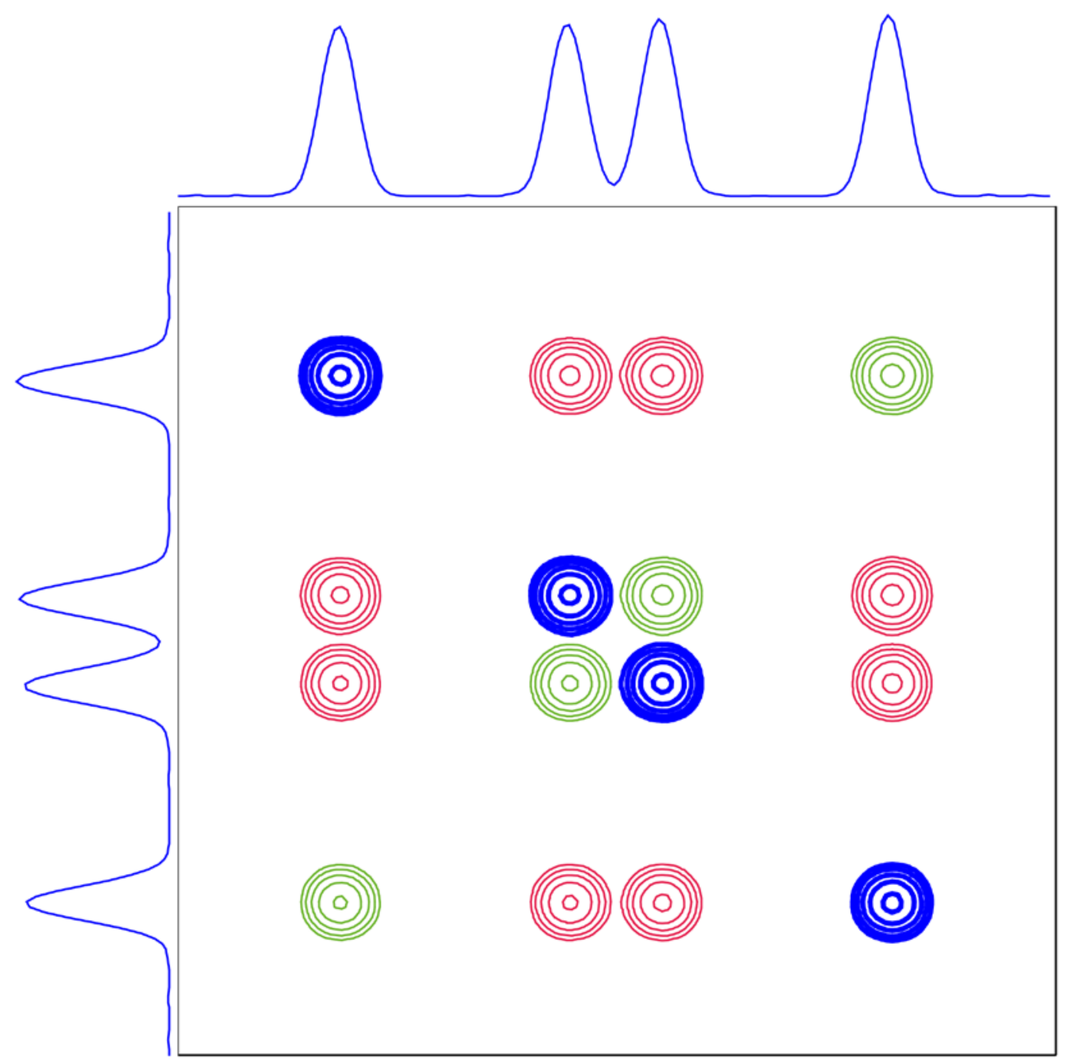
The effect of flip angle

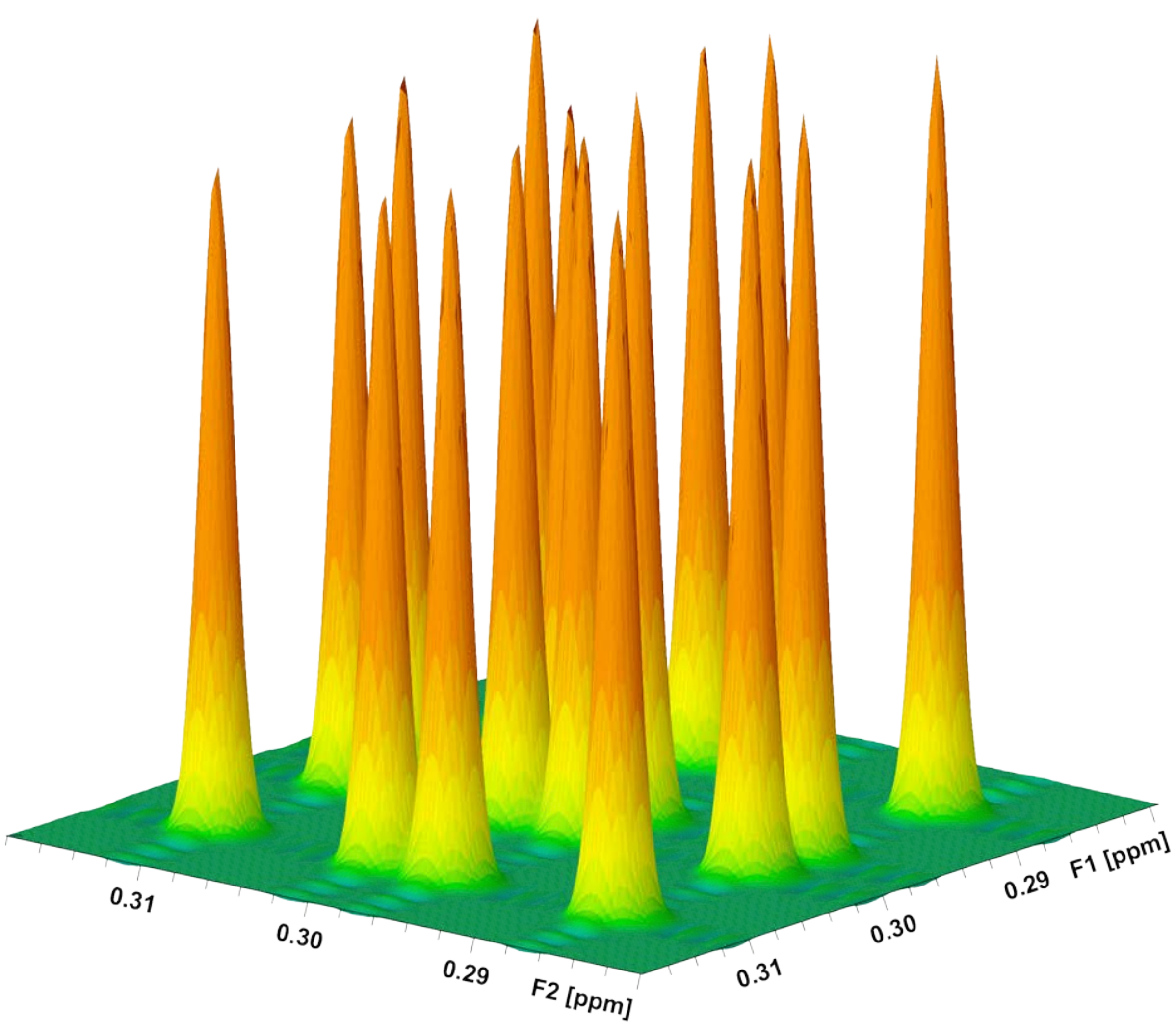
Signals within one of the diagonal multiplets can be considered in three sub-categories: i) **diagonal** (green), ii) **anti-diagonal** (blue), and iii) **off-diagonal** (red). Intensities of these signal as a function of flip angle can be written as:



The effect of flip angle

$\beta = 90^{\circ}$

$\times 1$



Off-diagonal : 100 %

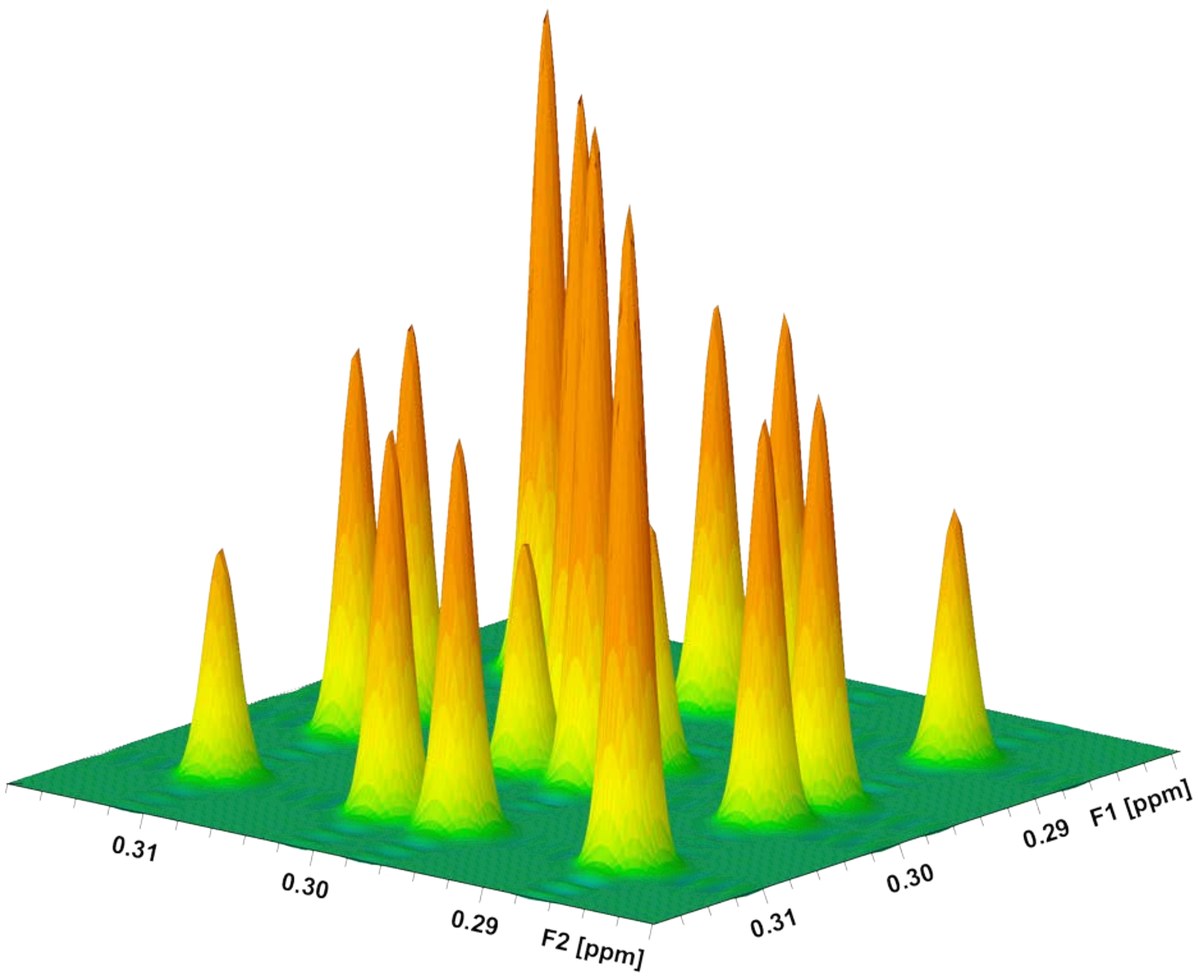
Diagonal : 100 %

Decoupling factor = 1

The effect of flip angle

$\beta = 60^\circ$

$\times 1.3$



Off-diagonal : 60 %

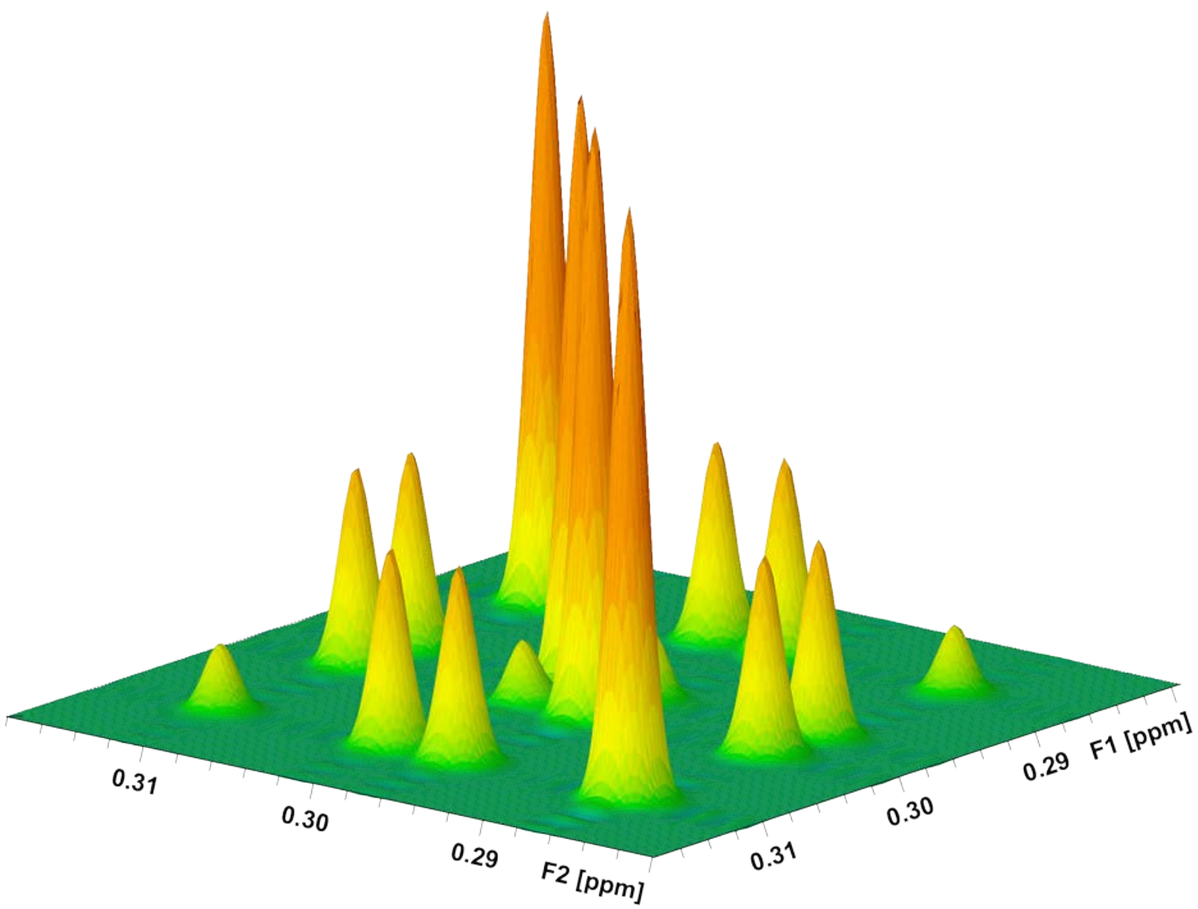
Diagonal : 36 %

Decoupling factor = 1.7

The effect of flip angle

$\beta = 45^\circ$

$\times 2$



Off-diagonal : 33.3 %

Diagonal : 11.1 %

Decoupling factor = 3

The effect of flip angle

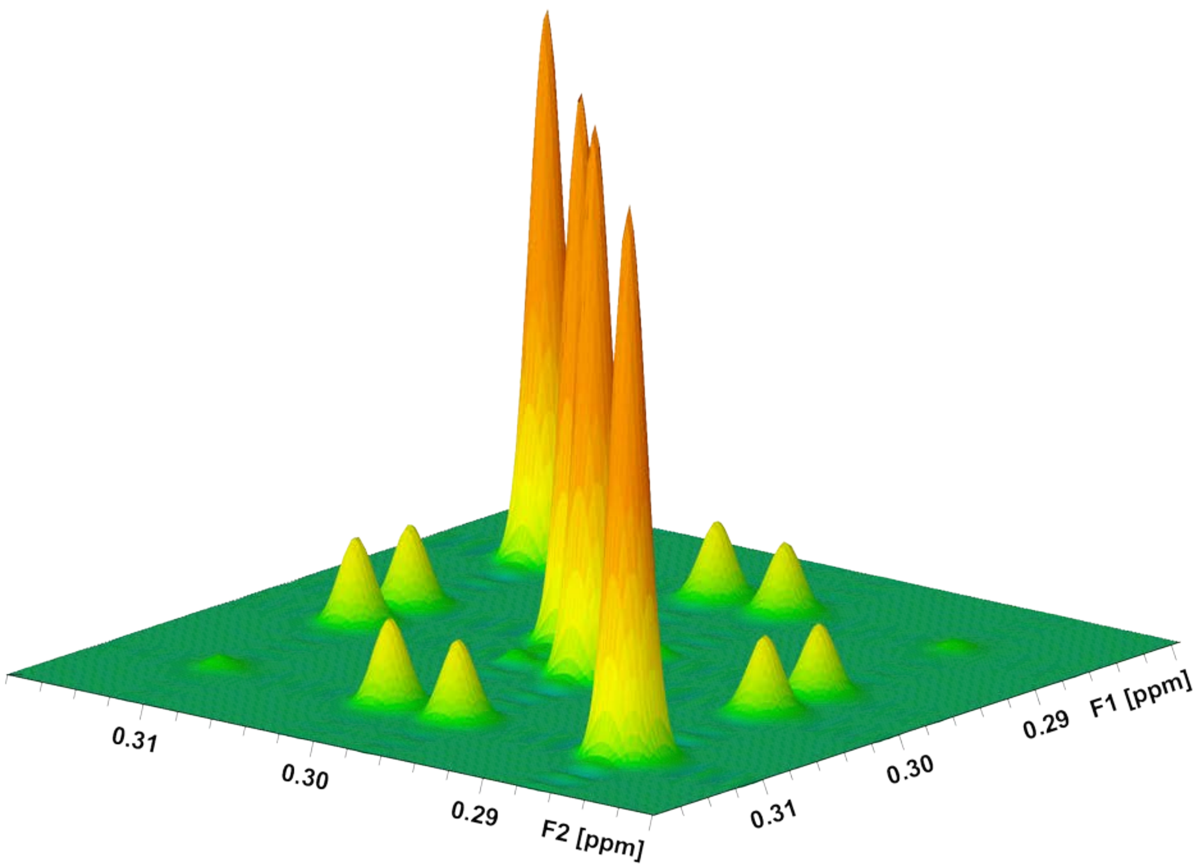
$\beta = 30^\circ$

$\times 4$

Off-diagonal : 14.3 %

Diagonal : 2 %

$\boxed{\text{Decoupling factor} = 7}$



The effect of flip angle

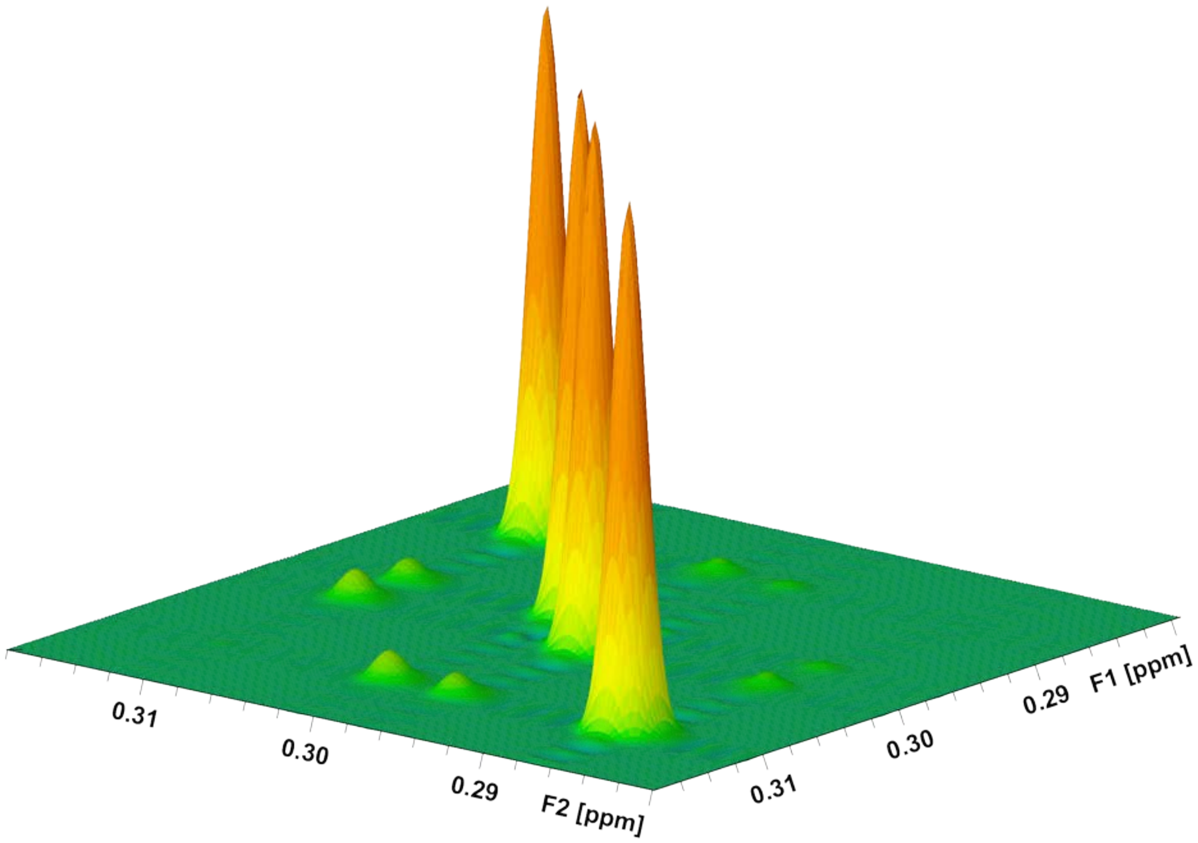
$\beta = 15^{\circ}$

$\times 15$

Off-diagonal : 3.5 %

Diagonal : 0.12 %

$\boxed{\text{Decoupling factor = 28.6}}$



The effect of flip angle

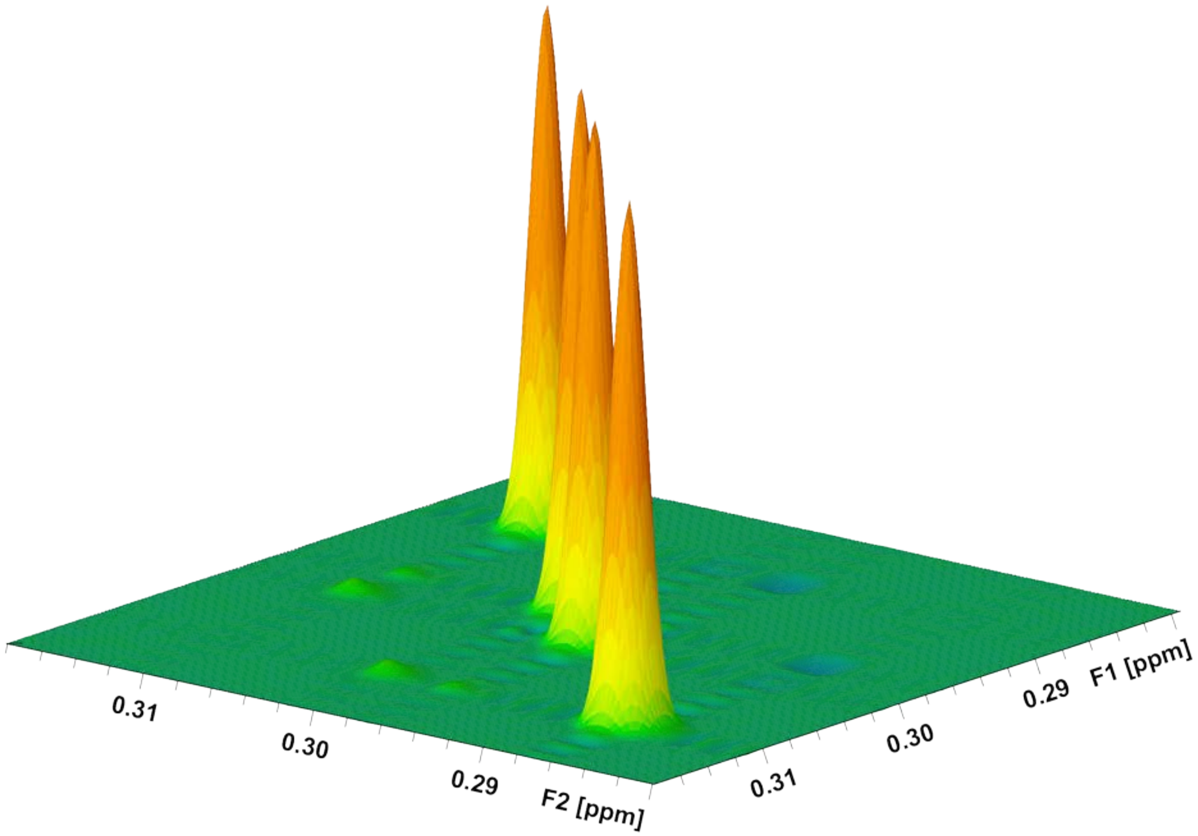
$\beta = 5°$

$\times 132$

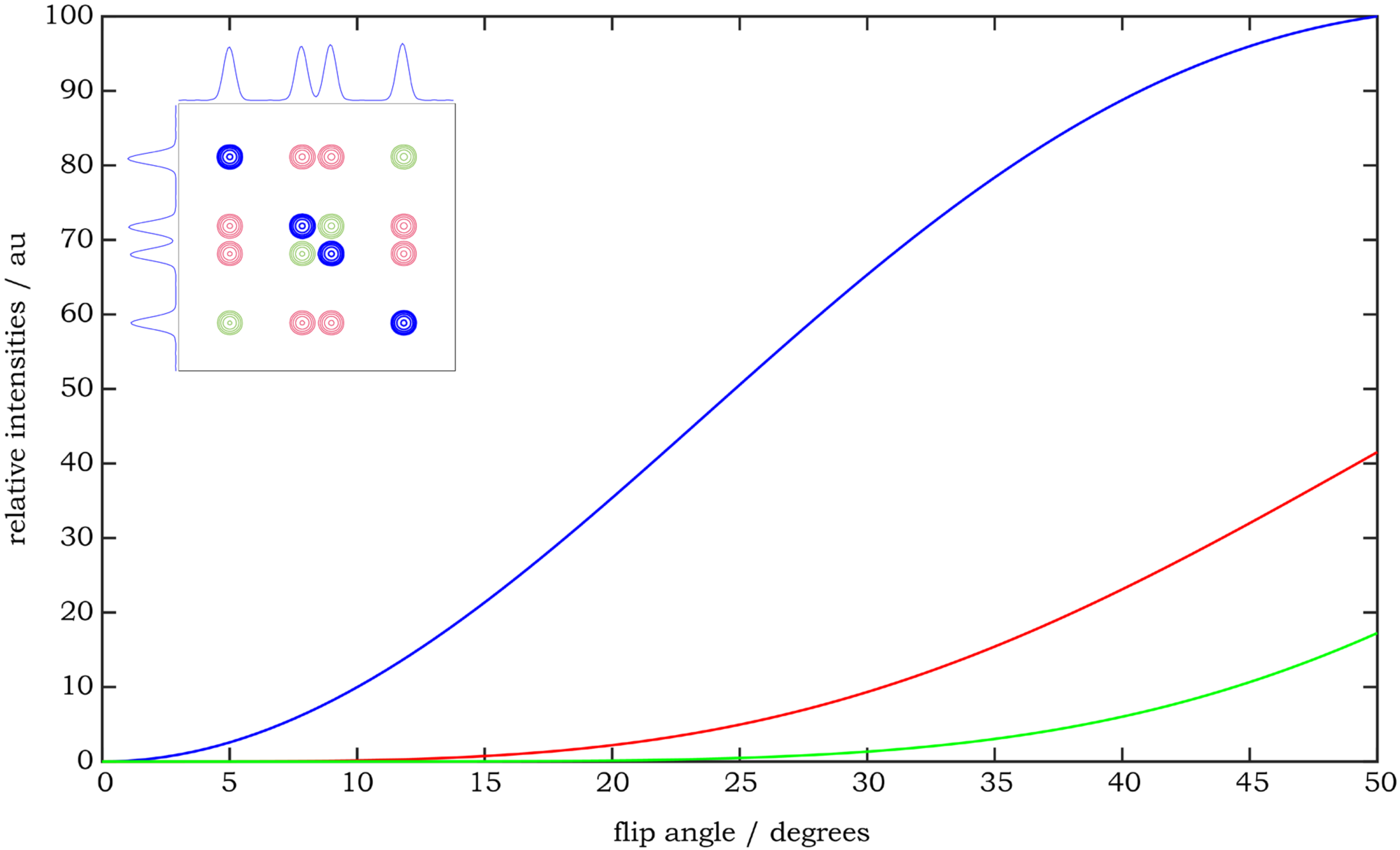
Off-diagonal : 0.4 %

Diagonal : 0.001 %

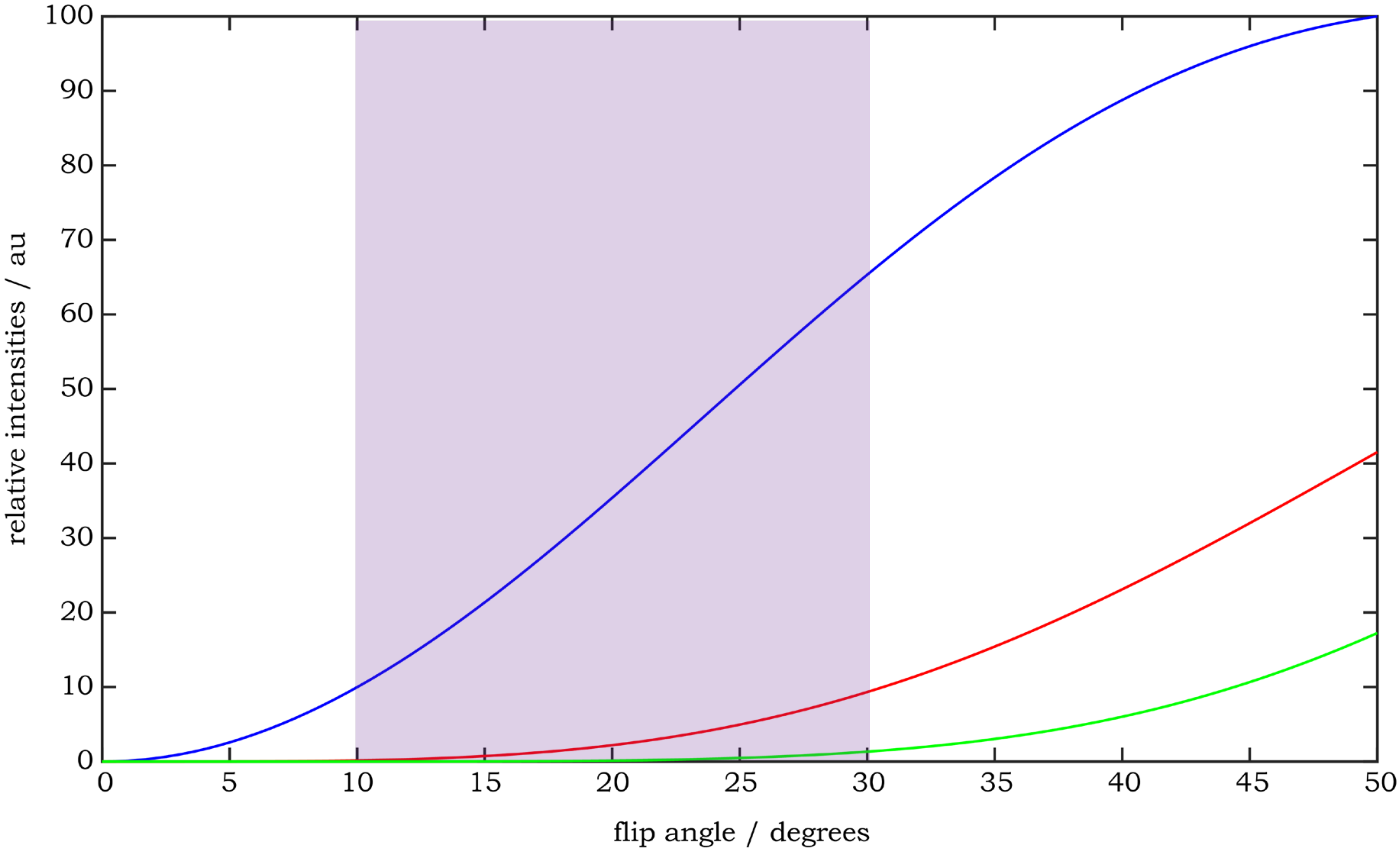
$\boxed{\text{Decoupling factor = 250}}$



The effect of flip angle



The effect of flip angle



Types of responses in spectra

Wanted signals

- Signals of interest i.e. decoupled signals in pure shift spectra

Unwanted signals

- Recoupling signals
- Zero Quantum signals
- COSY type responses
- Strong coupling signals

Artefacts

- Chunking artefacts
- Fast pulsing artefacts
- Digital filter artefacts

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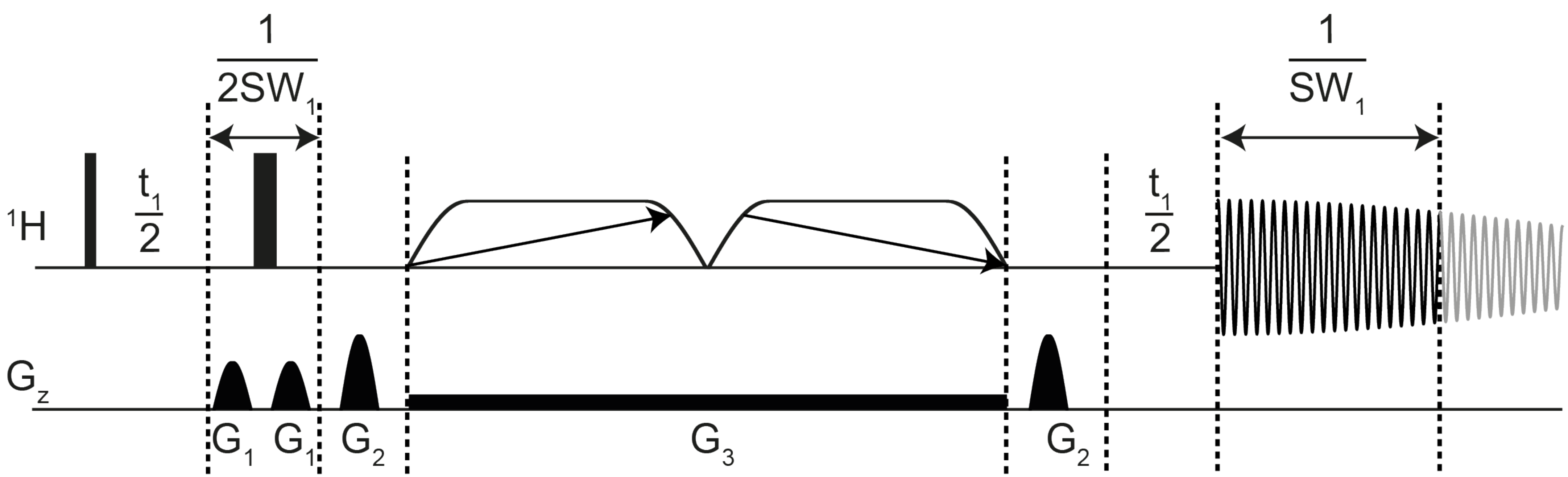
Suppression of unwanted signals

Unwanted responses in PSYCHE experiment include zero-quantum signals, COSY type responses, and strong coupling signals. All of these have time-dependent phases, so by averaging a series of experiments and varying the times during which these coherences evolve we can suppress them.

Spatio-temporal averaging

PSYCHE uses **spatio-temporal** averaging in order to attenuate unwanted responses.

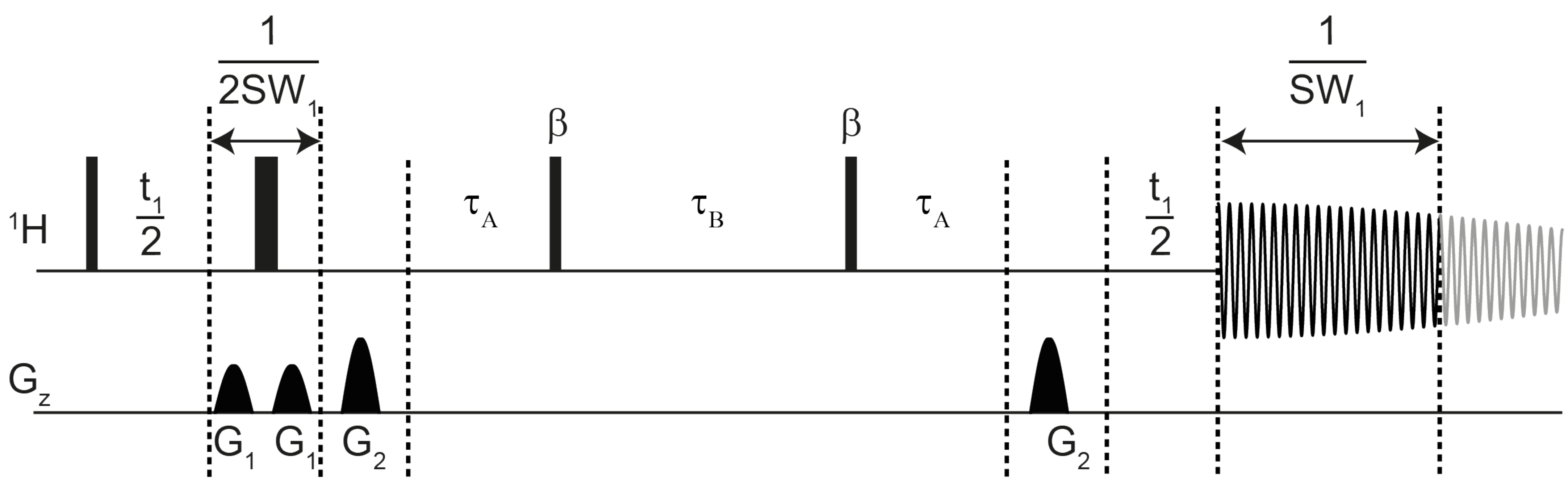


Spatio-temporal averaging

PSYCHE uses **spatio-temporal** averaging in order to attenuate unwanted responses.

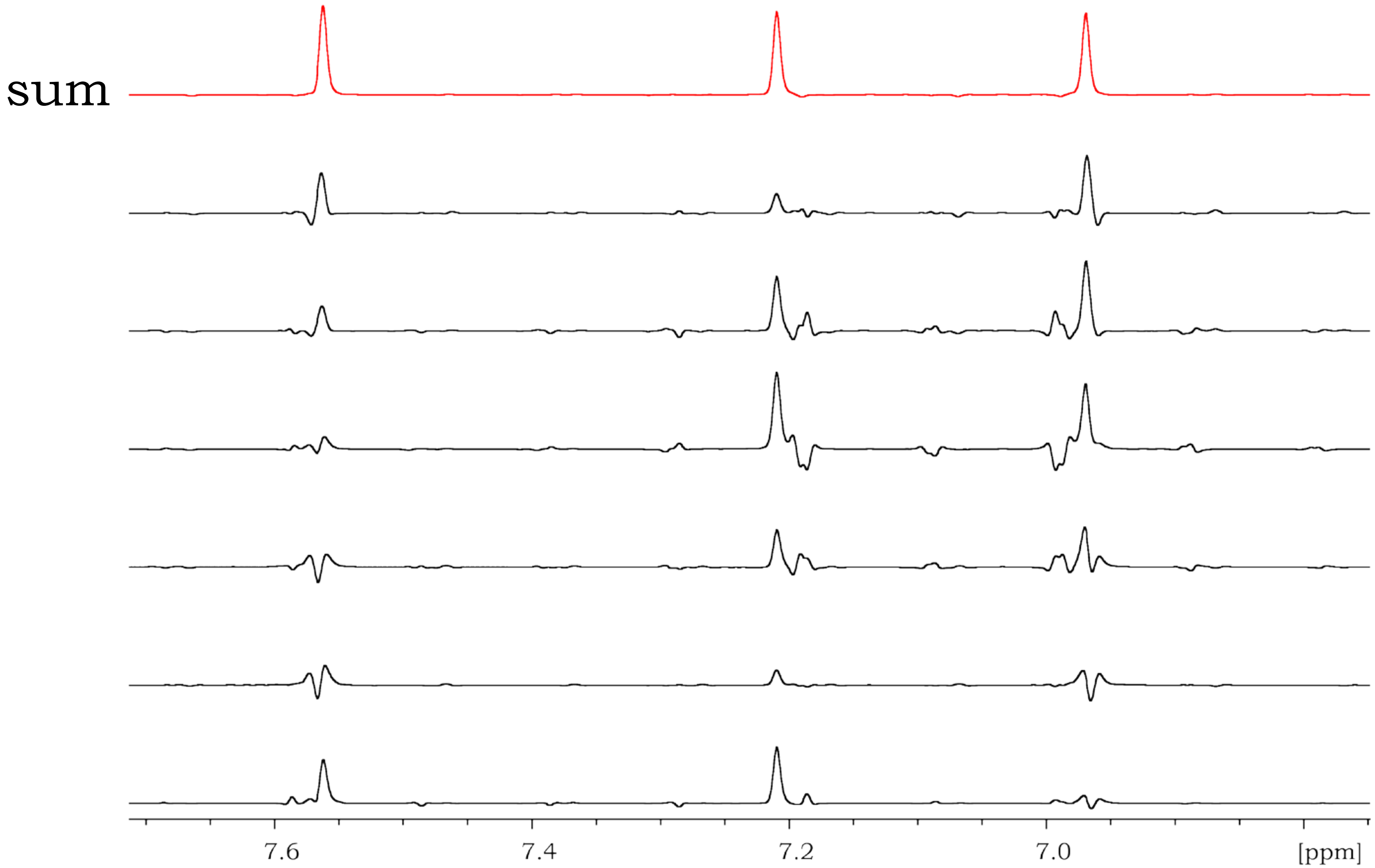
A simplified model of PSYCHE experiment will be helpful to see spatial and temporal effects separately. This model is close to anti *z*-COSY experiment.

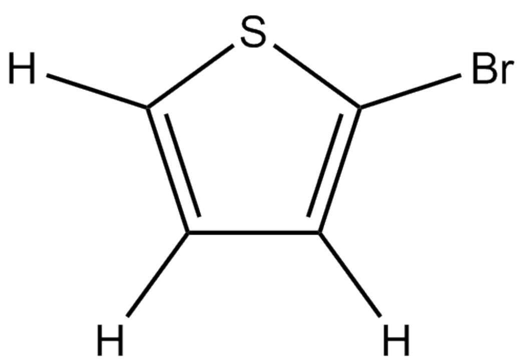
This pure shift experiment is run multiple times while incrementing τ_A and decrementing τ_B.



Temporal averaging

Since the wanted signals (pure shift singlets) have time-invariant phase, summing over variable delays suppress the unwanted signals, while retaining the wanted singlets.

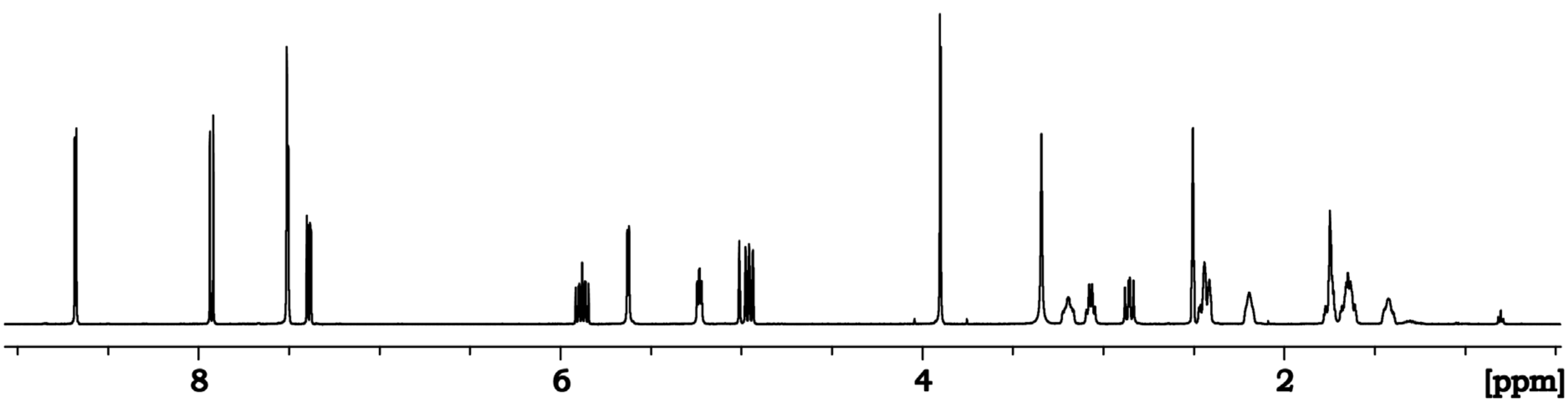




An AMX spin system

Swept-frequency (chirp) pulses

- These pulses are applied in many magnetic resonance experiments for broadband inversion and refocusing.
- Generally they sweep the frequency across the spectral window in a linear fashion.
- Here we use them as swept-frequency low-flip angle pulses over the chemical shift range of ^{1}H spectrum, c.a. 10 ppm.



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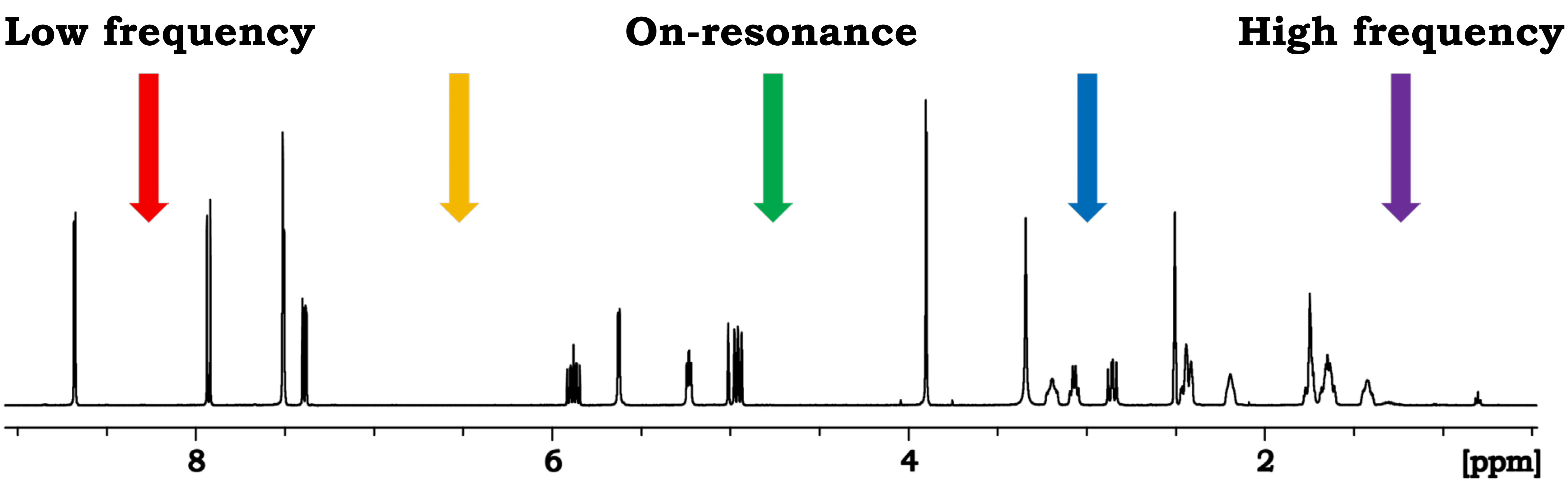
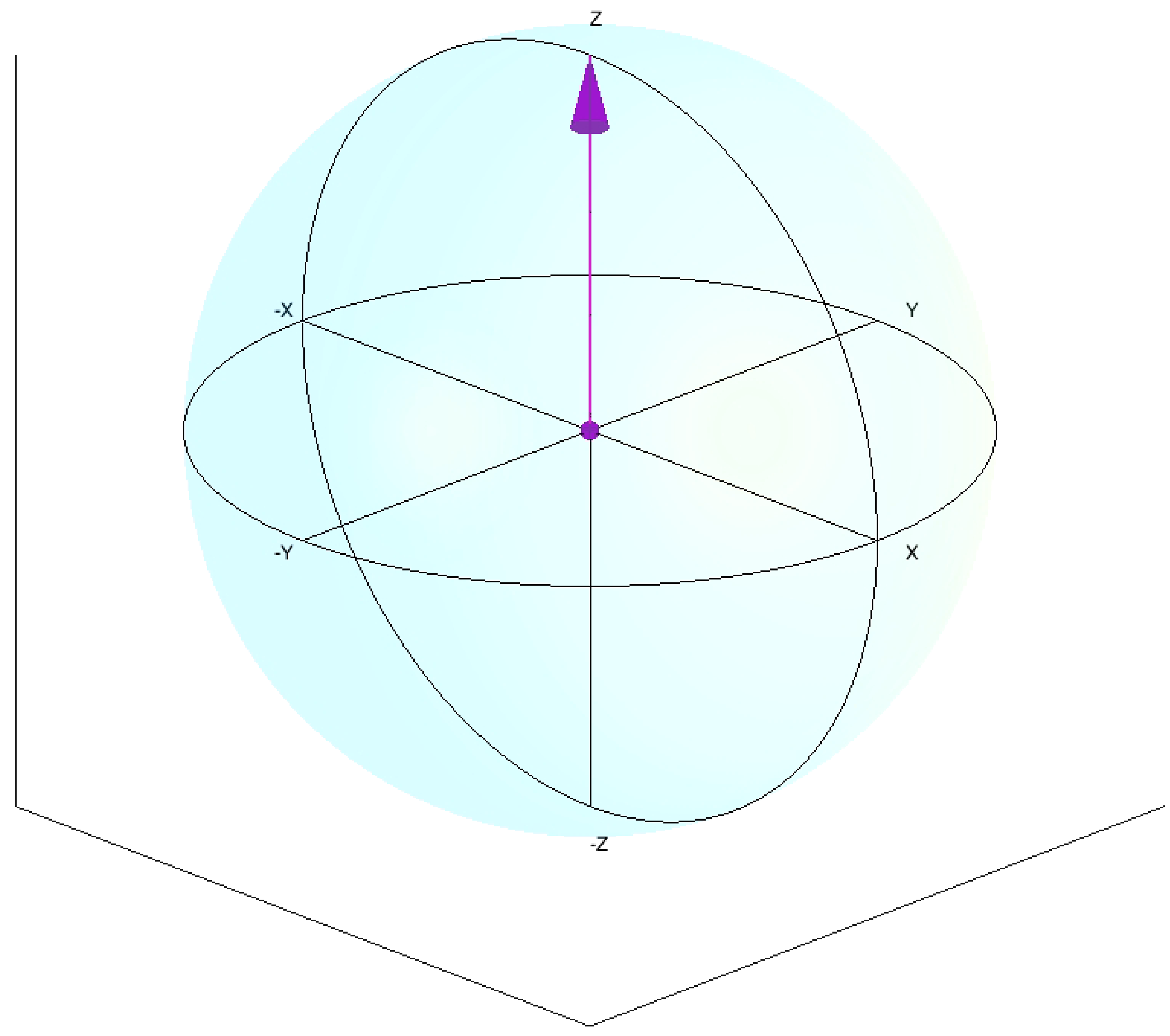
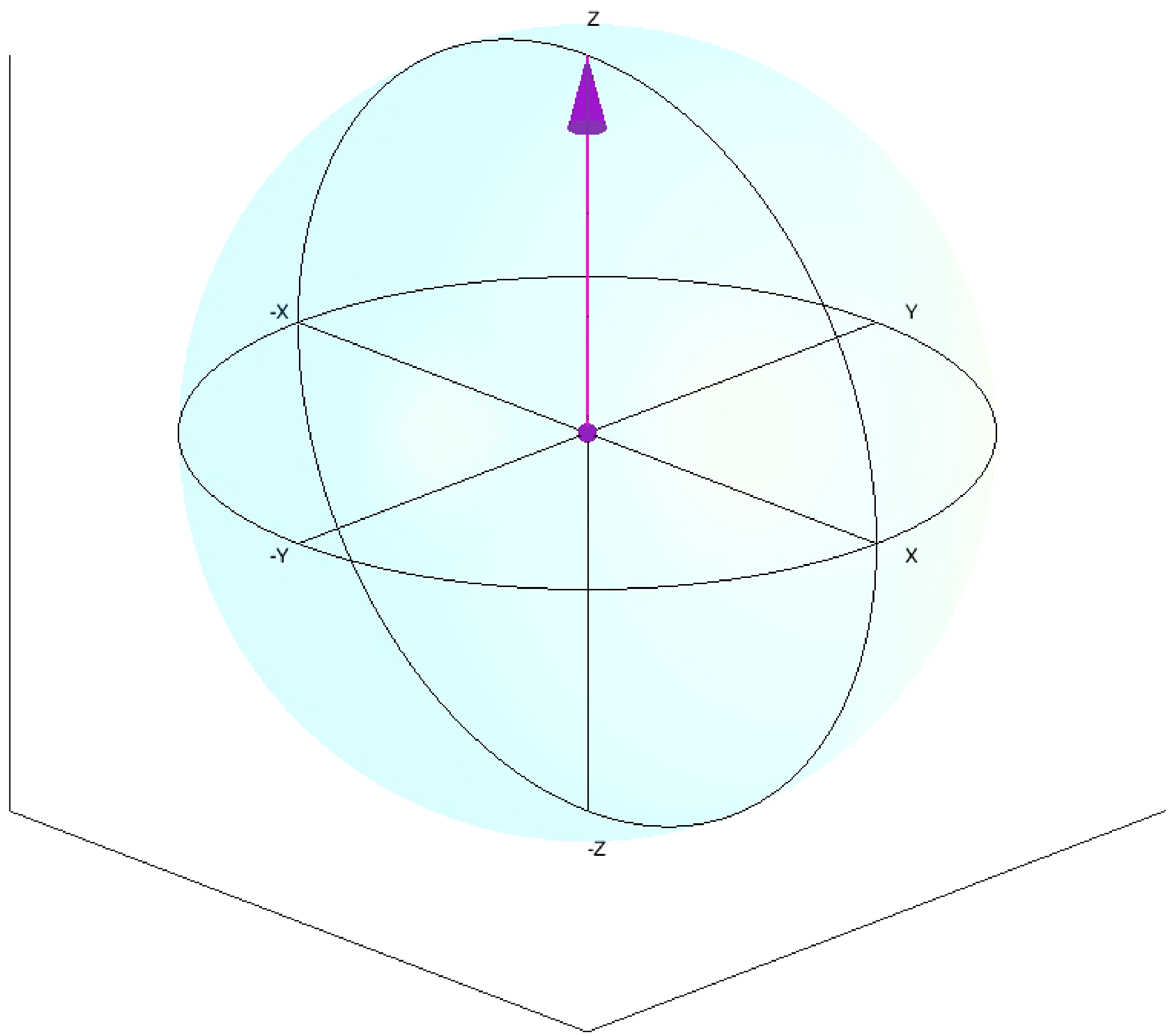


180-degree chirp



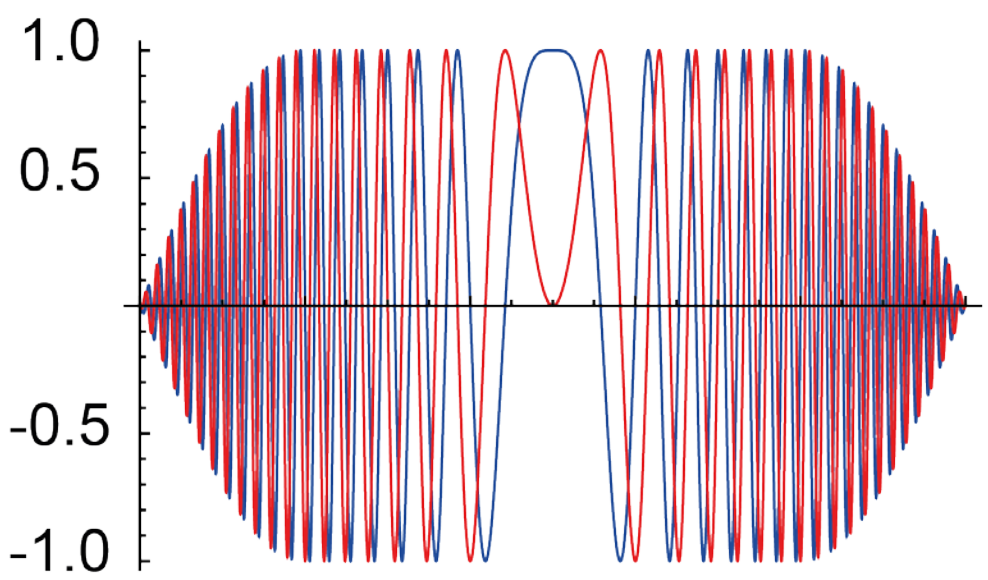
Low-flip angle chirp

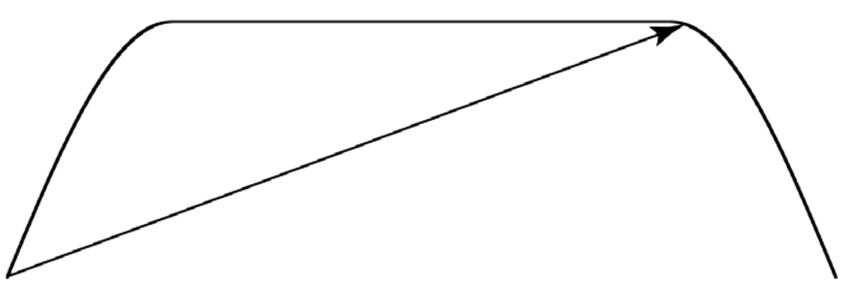


Chirp pulses

A normal (unidirectional) chirp pulse, with **Low-to-High** frequency sweep, sweeps a frequency range of ΔF (Hz) from $-\Delta F/2$ to $+\Delta F/2$, during a time τ_p (sec), and with r.f. amplitude of A (Hz):

$$Chirp(t) = A\left\{\cos\left(\pi\left(\Delta F/\tau_p\right)t^2\right) + i\sin\left(\pi\left(\Delta F/\tau_p\right)t^2\right)\right\}$$

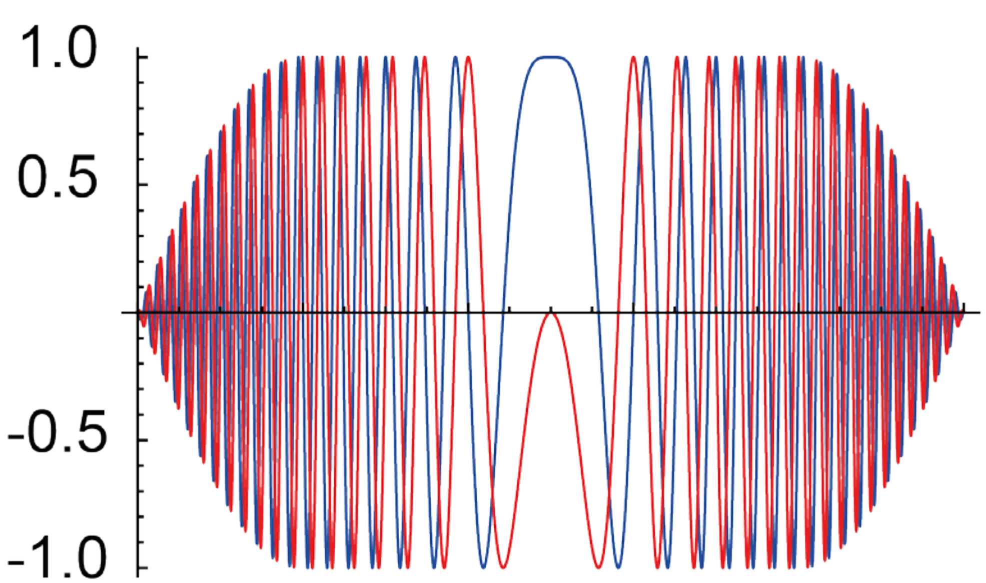


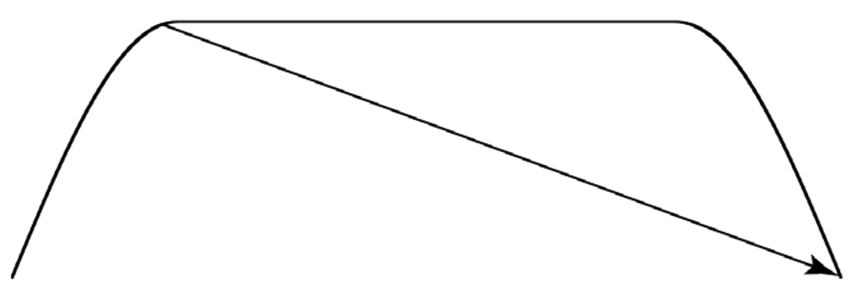


Chirp pulses

A normal (unidirectional) chirp pulse, with **High-to-Low** frequency sweep, sweeps a frequency range of ΔF (Hz) from $+\Delta F/2$ to $-\Delta F/2$, during a time τ_p (sec), and with r.f. amplitude of A (Hz):

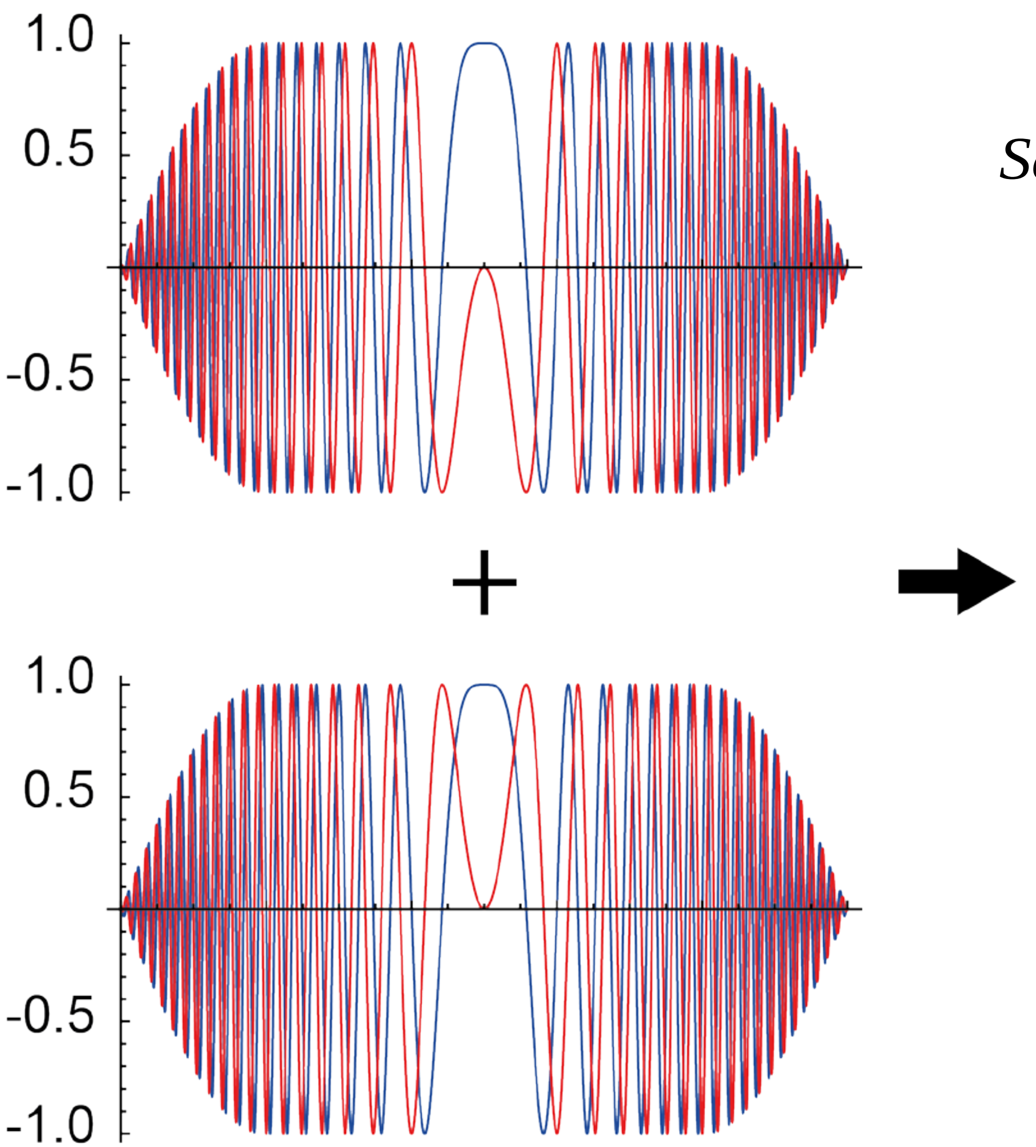
$$Chirp(t) = A\left\{\cos\left(\pi\left(\frac{\Delta F}{\tau_p}\right)t^2\right) - i\sin\left(\pi\left(\frac{\Delta F}{\tau_p}\right)t^2\right)\right\}$$



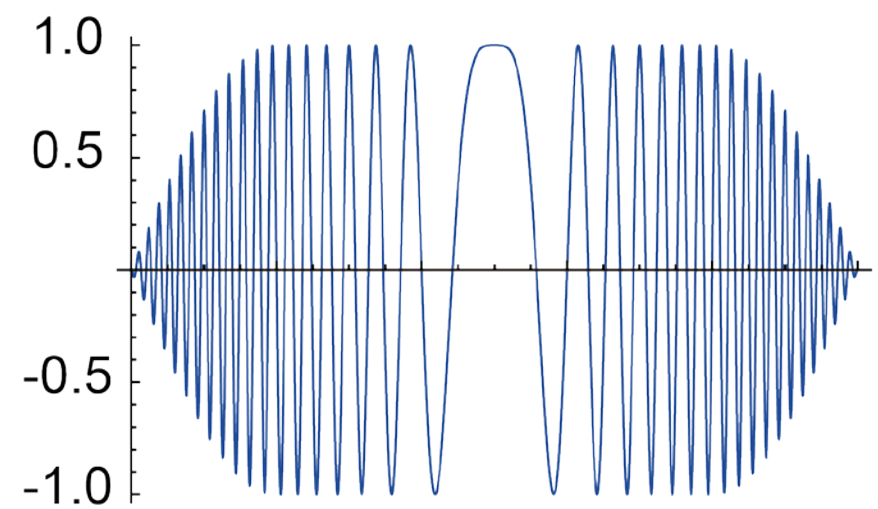


Saltire chirp pulses

A **saltire chirp** is the average of chirps with low-to-high and high-to-low frequency sweep, resulting in a pure real waveform.

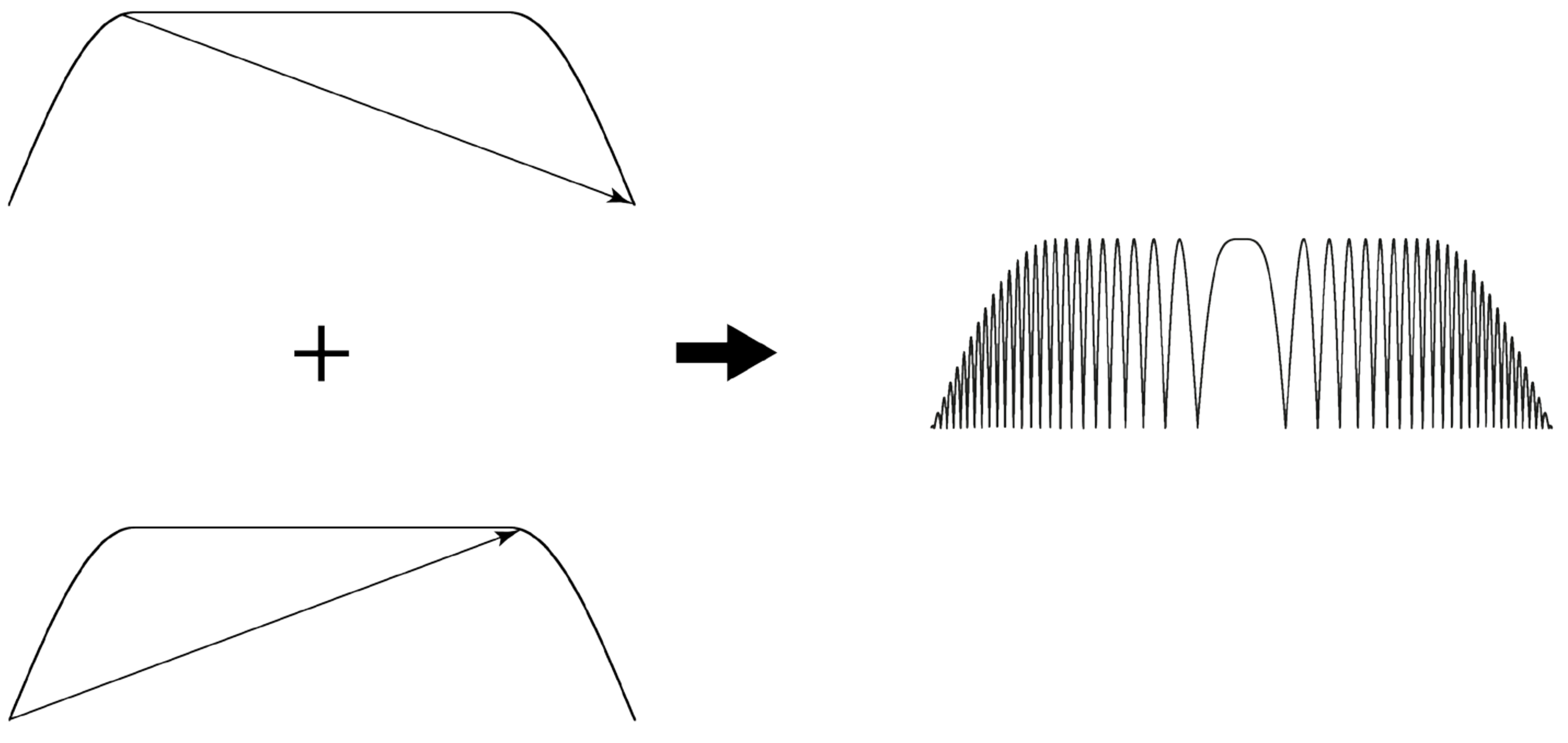


$$Saltire\_Chirp(t) = A\cos\left(\pi\left(\Delta F / \tau_p\right)t^2\right)$$



Saltire chirp pulses

The absence of imaginary part of the waveform makes the saltire chirp pulse an amplitude modulated pulse with constant phase.



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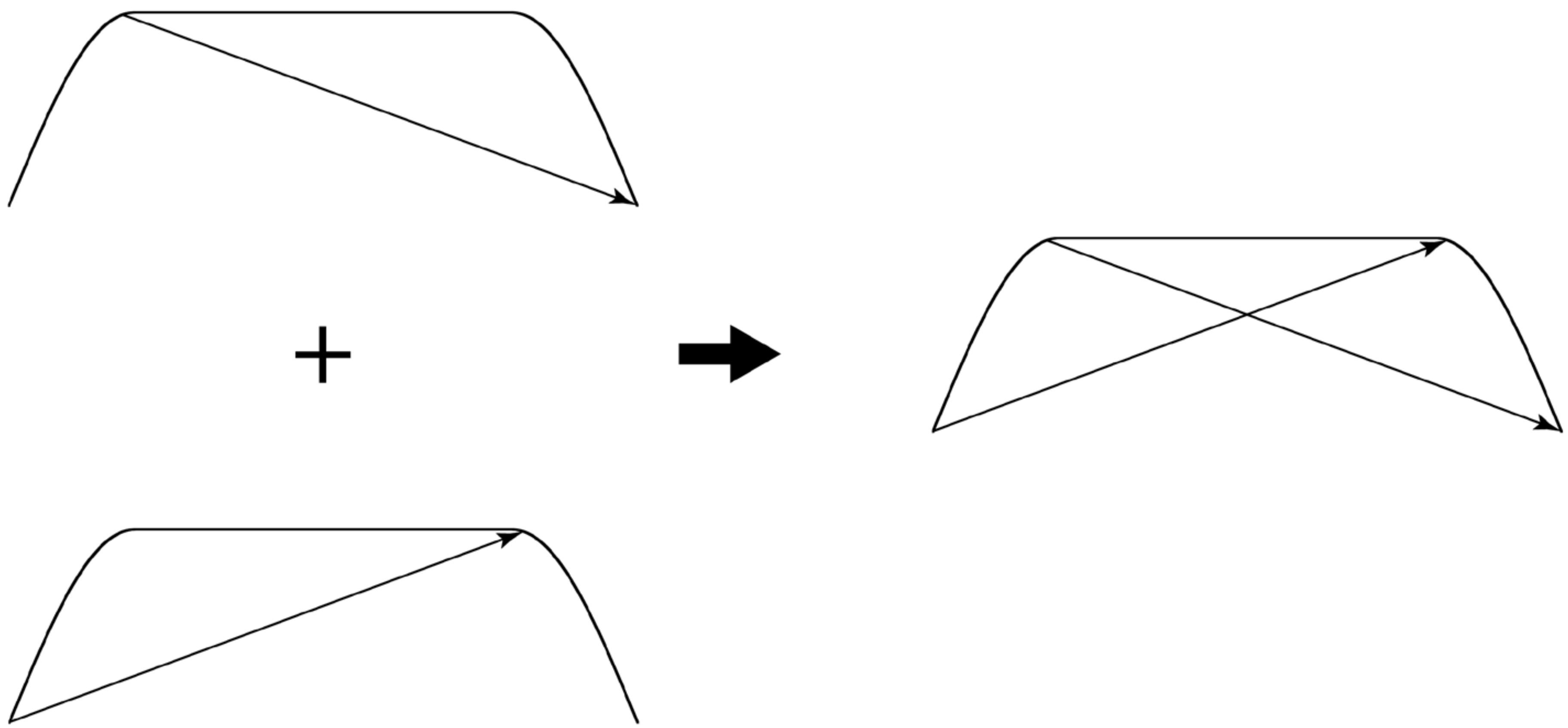
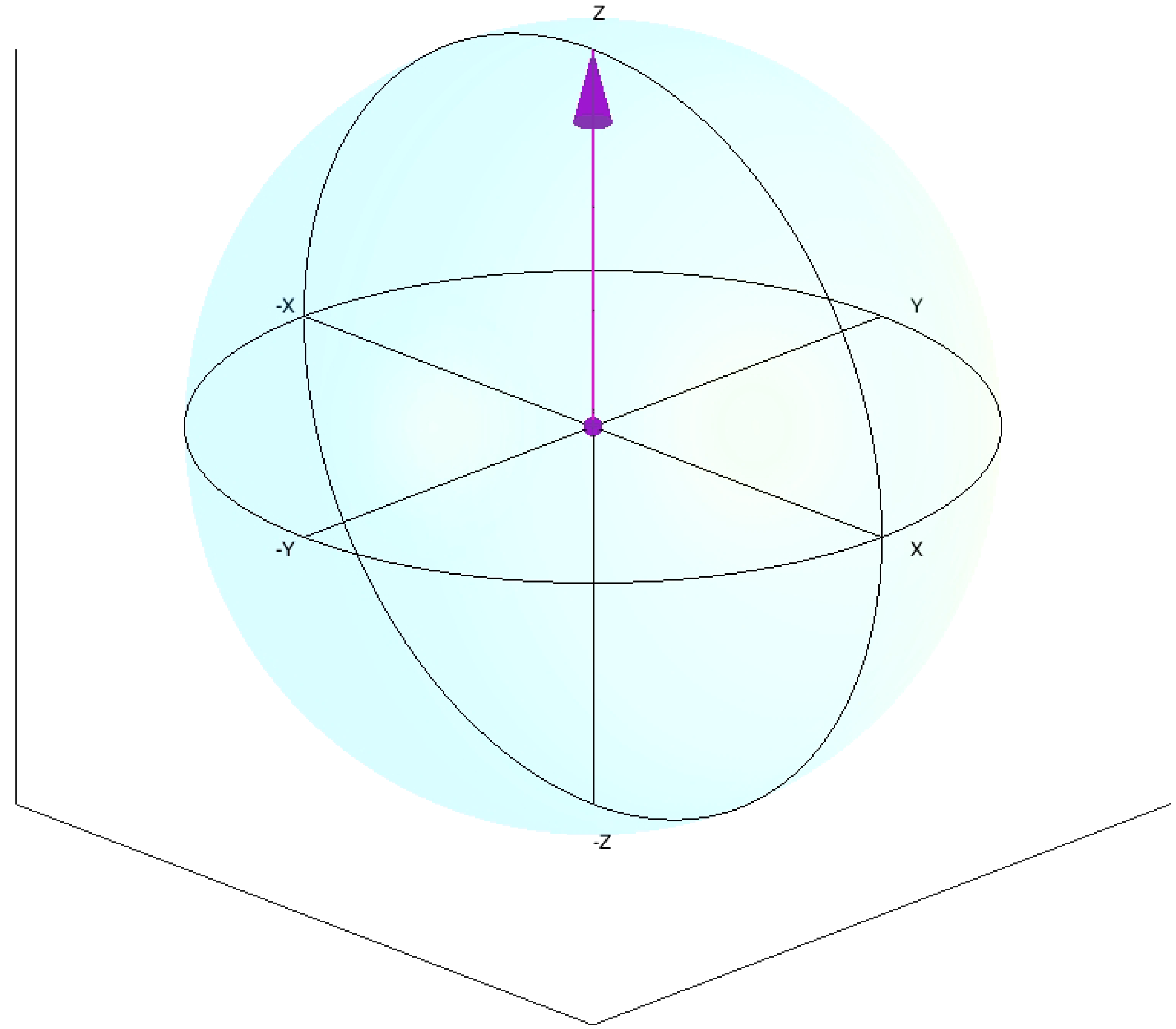


Low-flip angle saltire chirp



r.f. amplitude of a saltire chirp

Since this is an amplitude modulated pulse, its flip angle (in degrees) is the integral of the amplitude envelope with respect to time.

$$\beta = 360 \times A \int_{-\infty}^{+\infty} \cos\left(\pi \left(\Delta F / \tau_p \right) (t - t_0)^2 \right) dt$$

$$= 360 \times A \sqrt{\frac{\tau_p}{2\Delta F}}$$

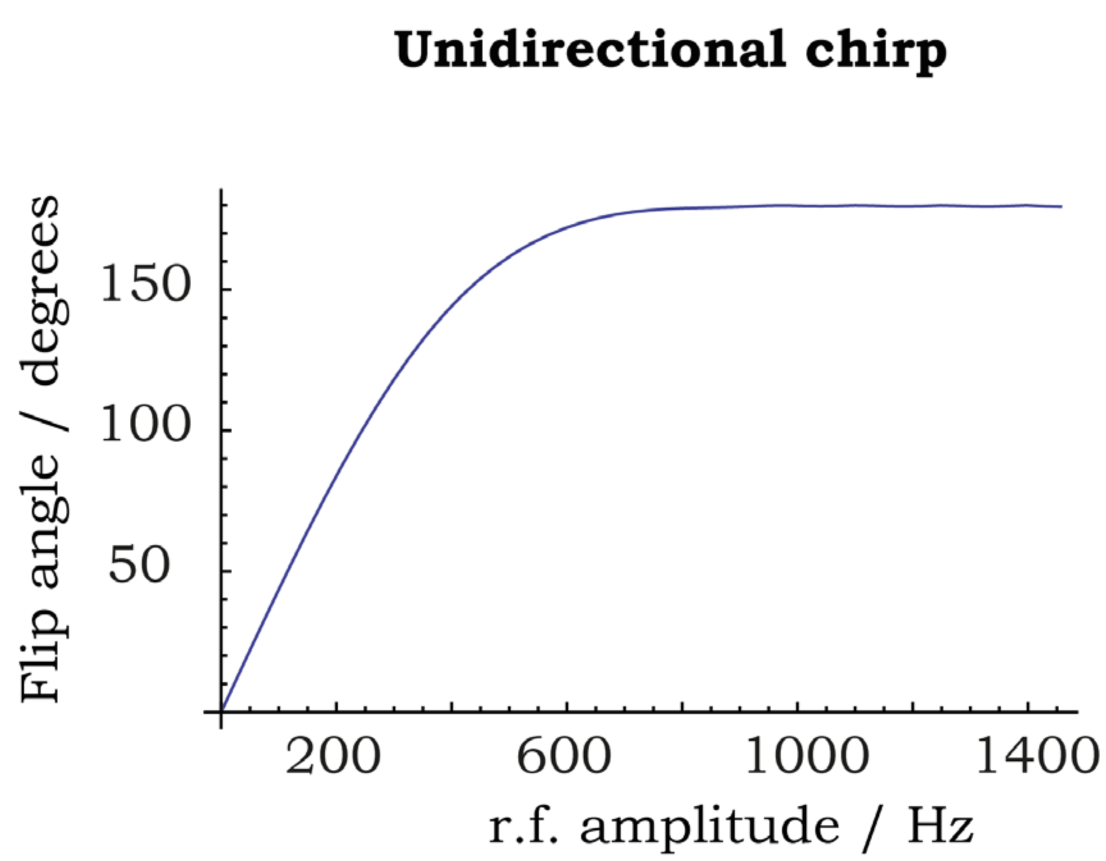
The r.f. amplitude of a saltire chirp pulse with a sweep-width of ΔF Hz, duration of τ_p sec, and flip angle of $\beta°$ is:

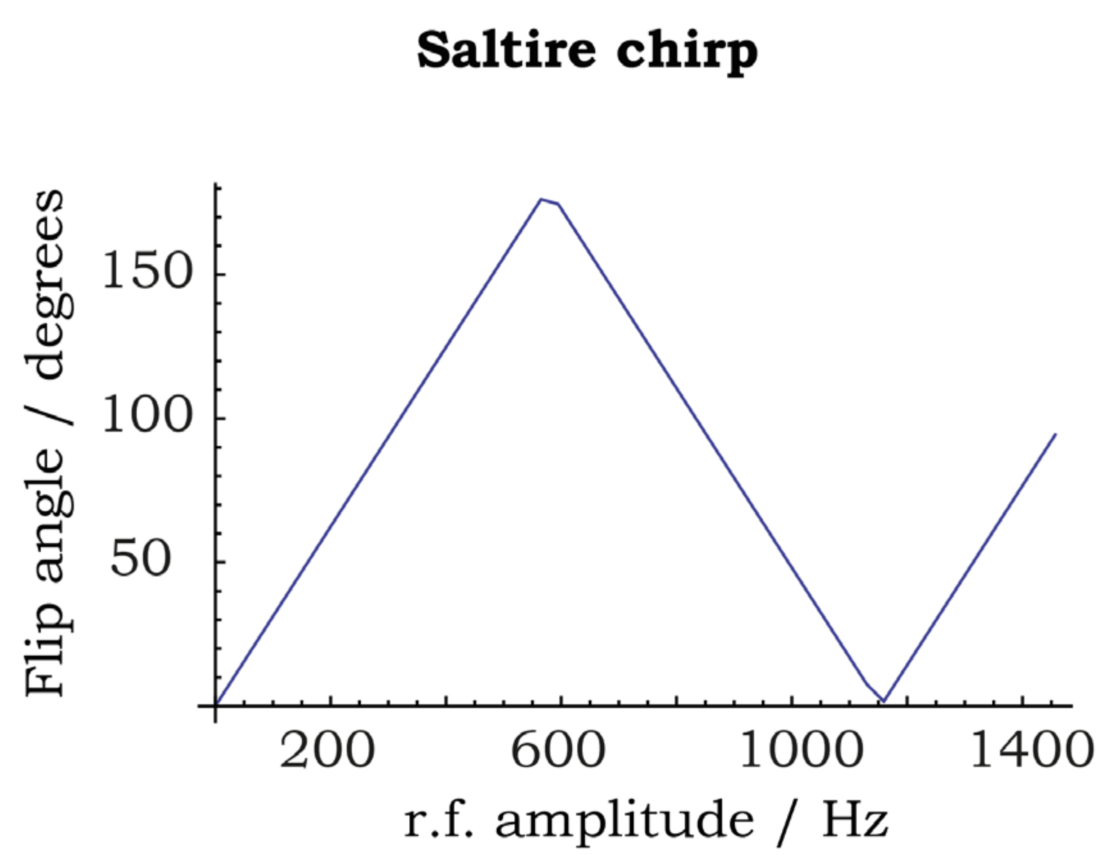
$$\boxed{A = \left(\frac{\beta}{360} \right) \times \sqrt{\frac{2\Delta F}{\tau_p}}}$$

r.f. amplitude of a saltire chirp

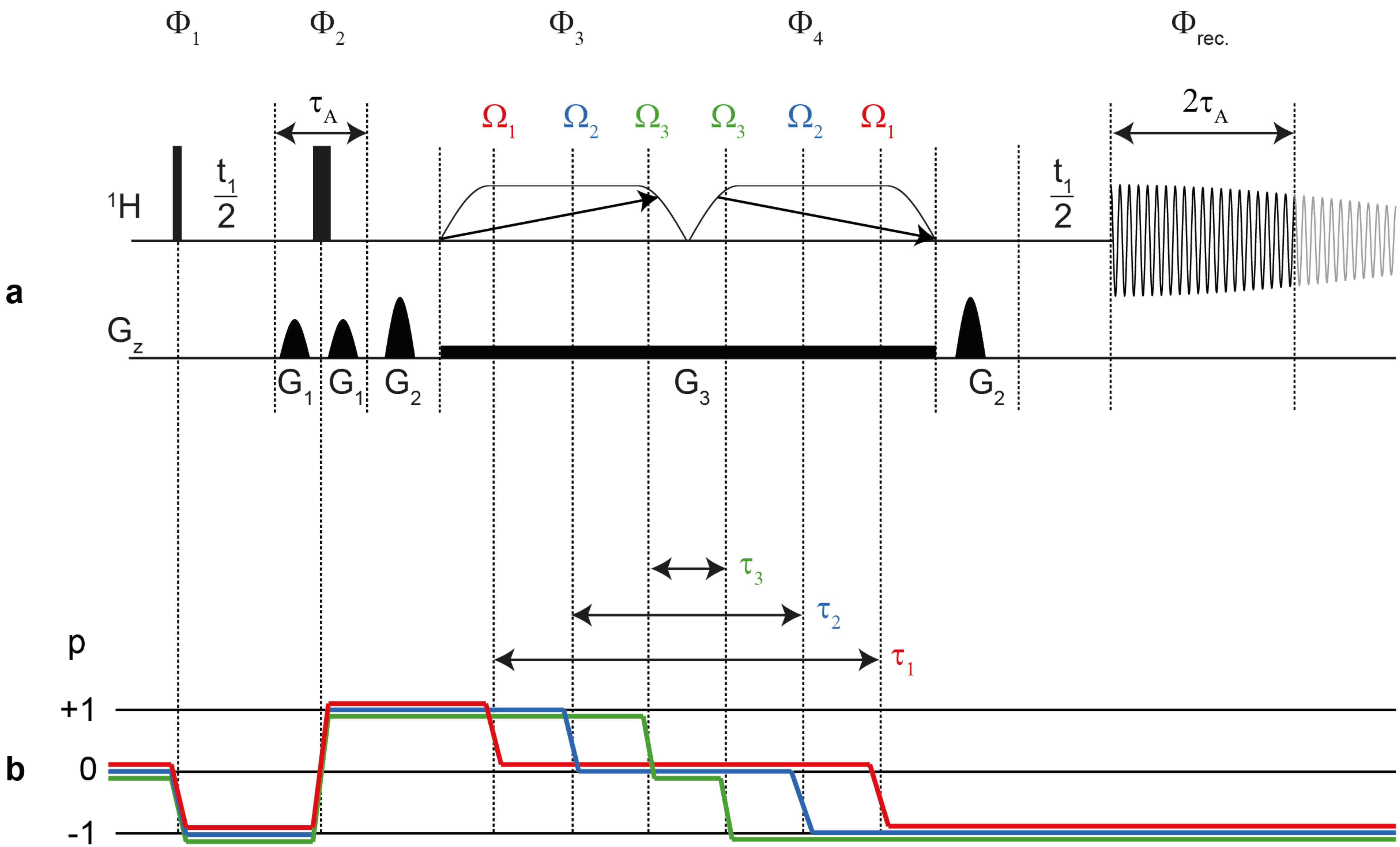
This shows a linear relationship between flip angle and r.f. amplitude of a saltire chirp pulse.

$$A = \left(\frac{\beta}{360}\right) \times \sqrt{\frac{2\Delta F}{\tau_p}}$$





How does PSYCHE work?



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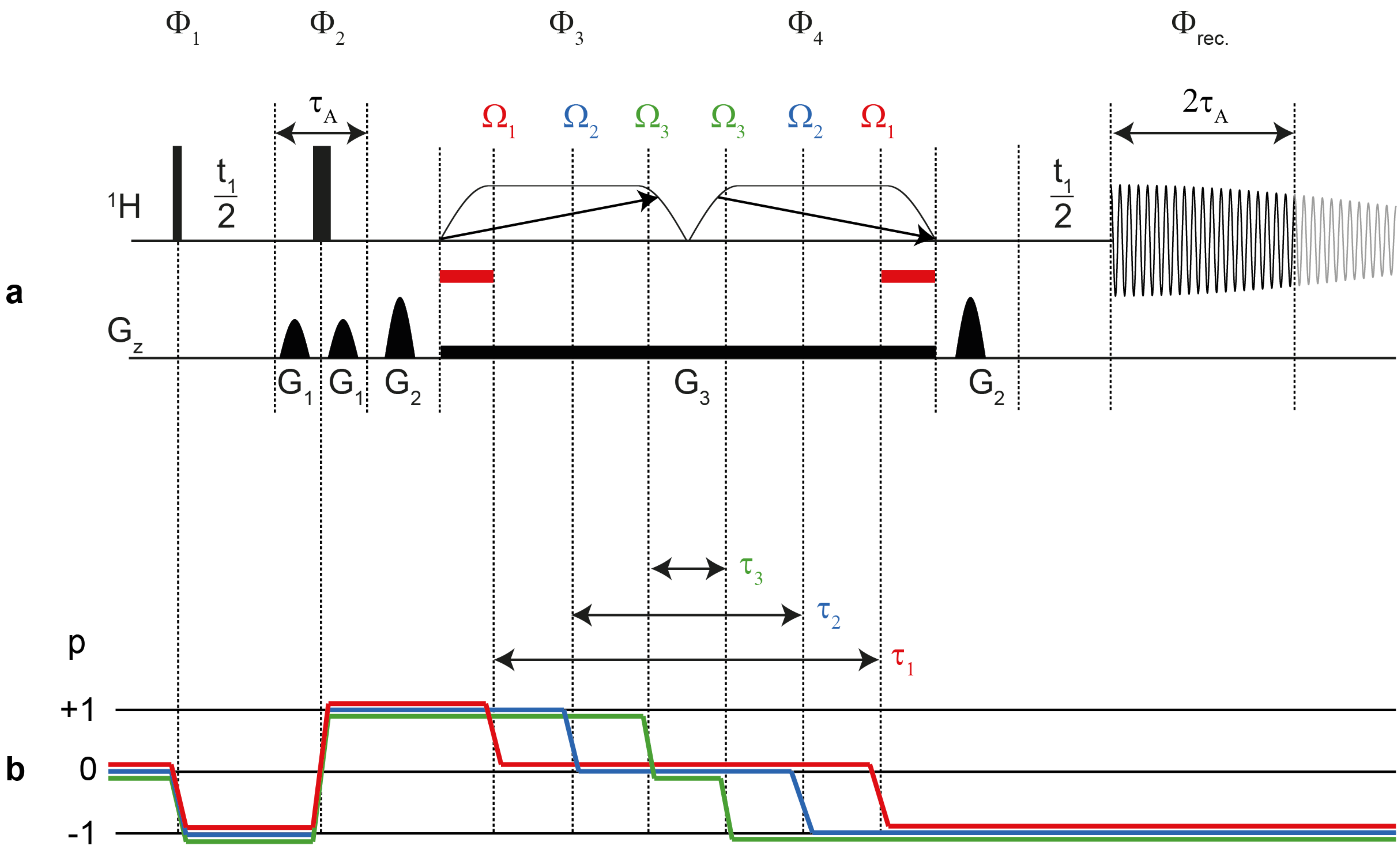

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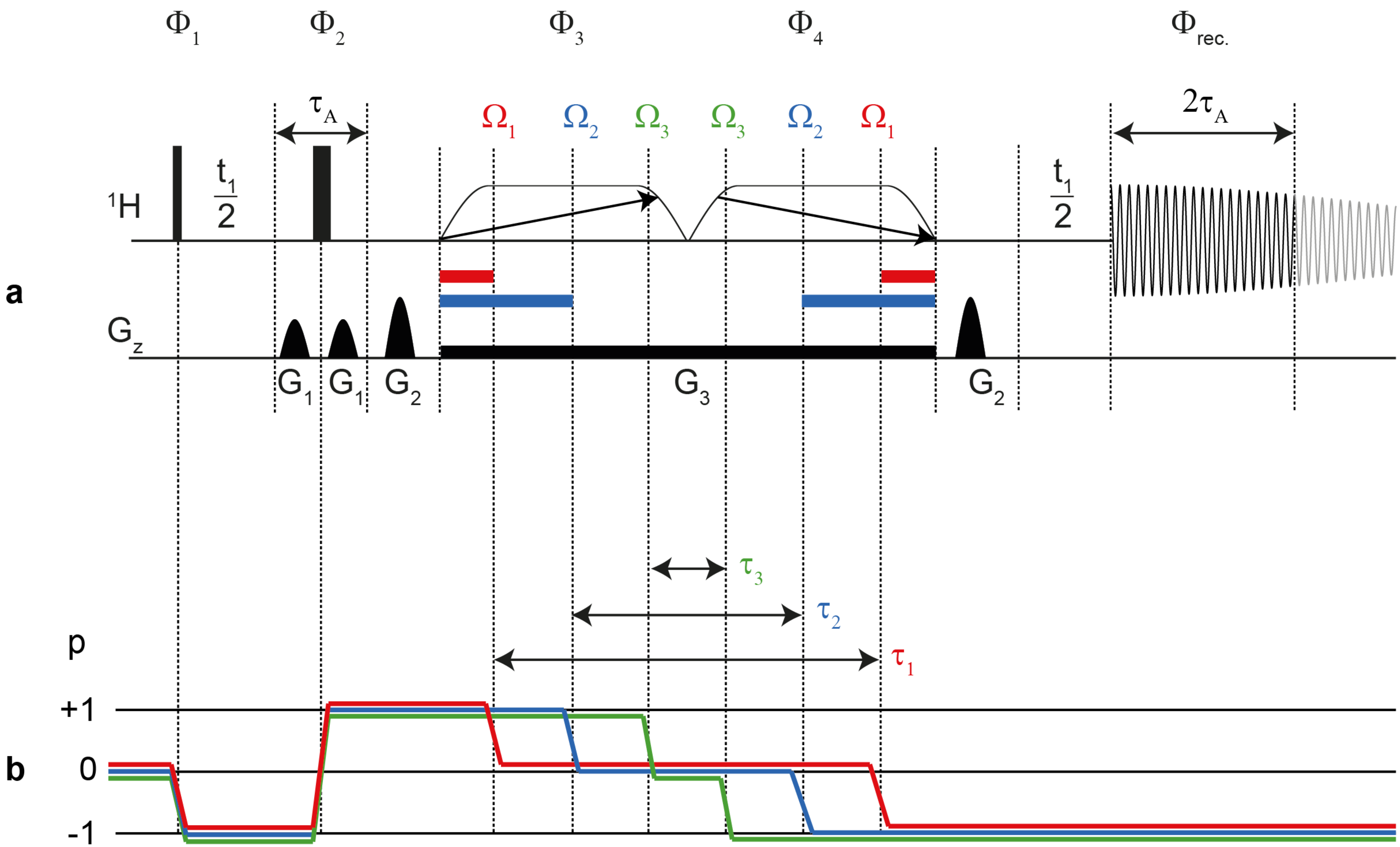

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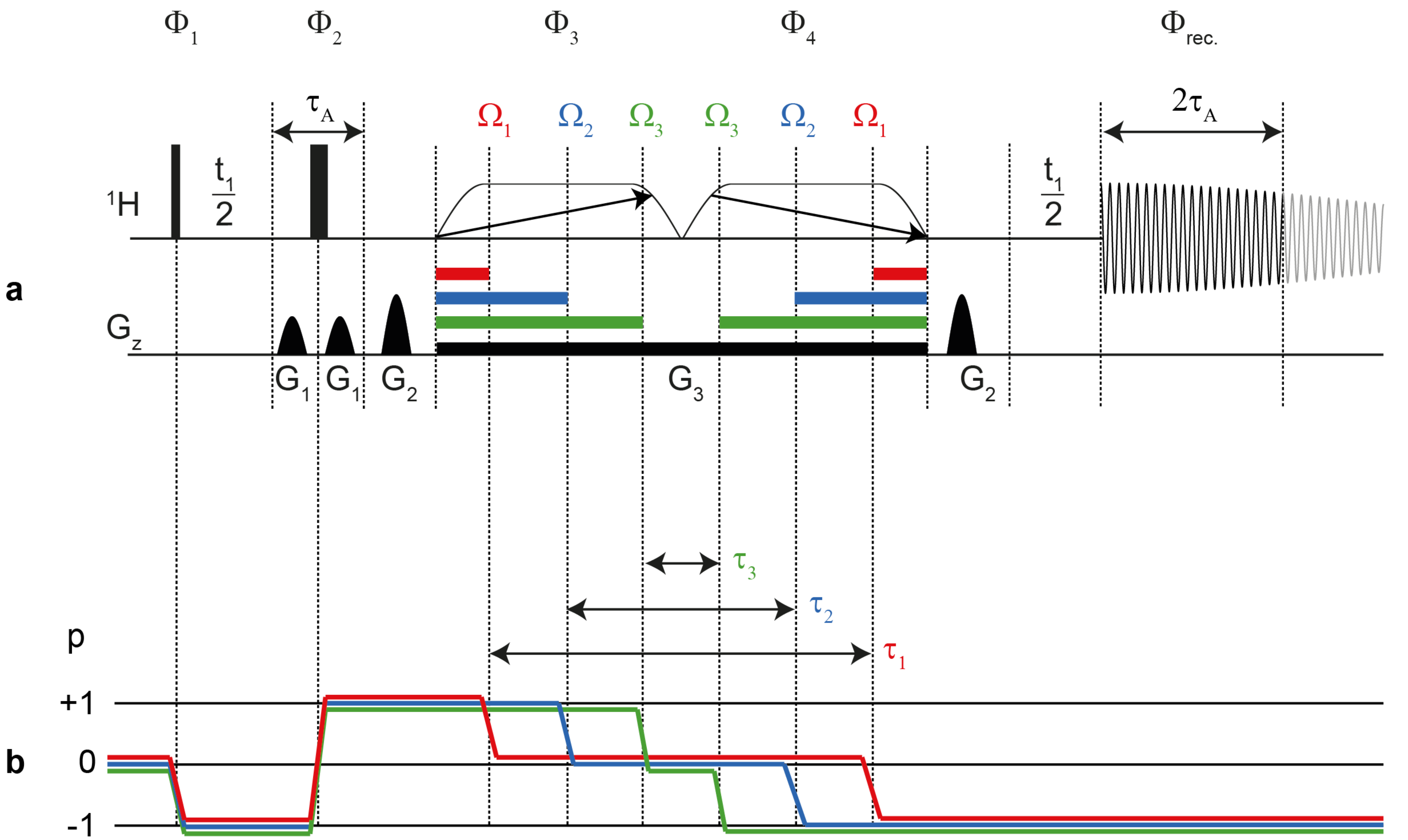
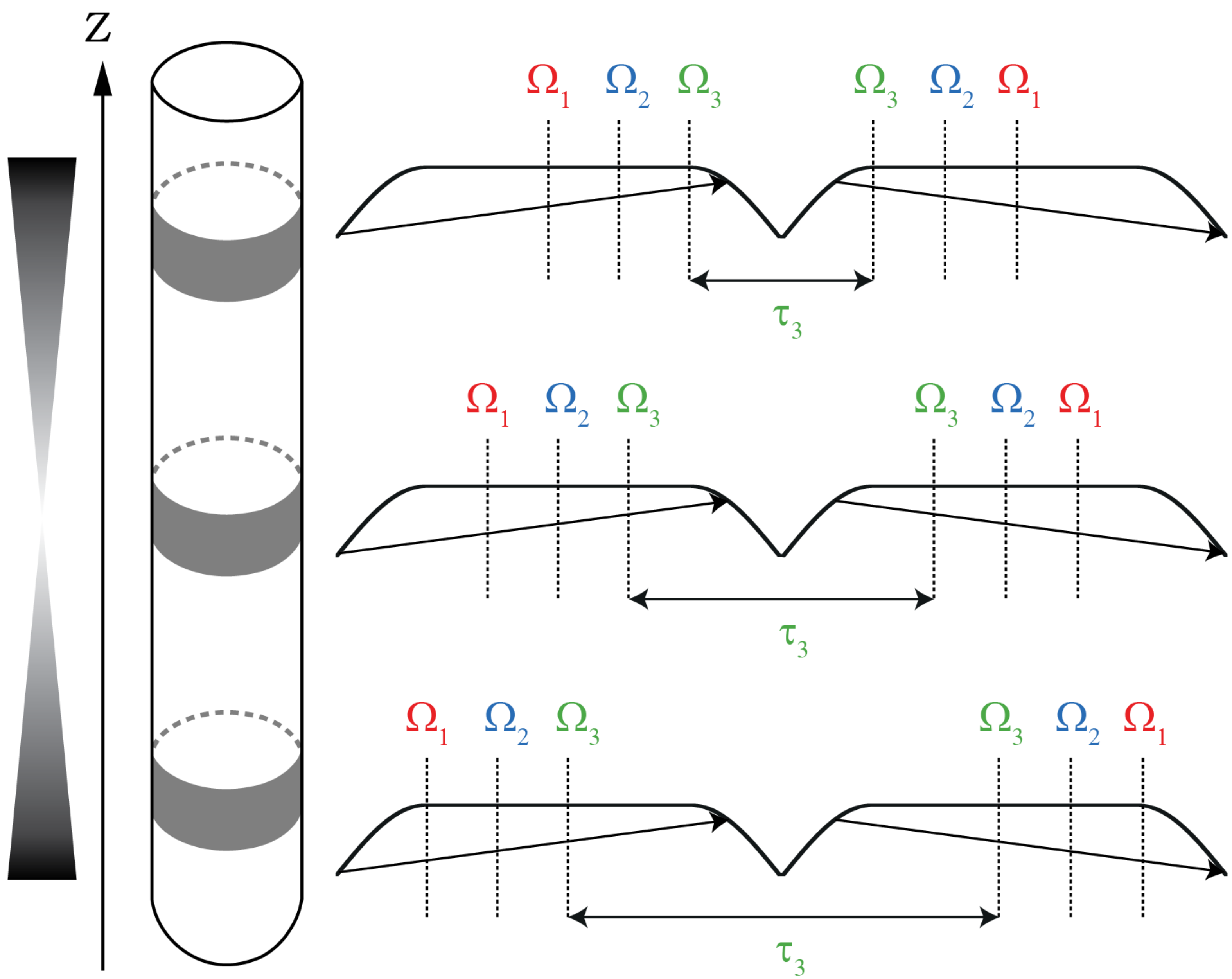


How does PSYCHE work?

$B(z) = B_0 + G_z(z - z_0)$



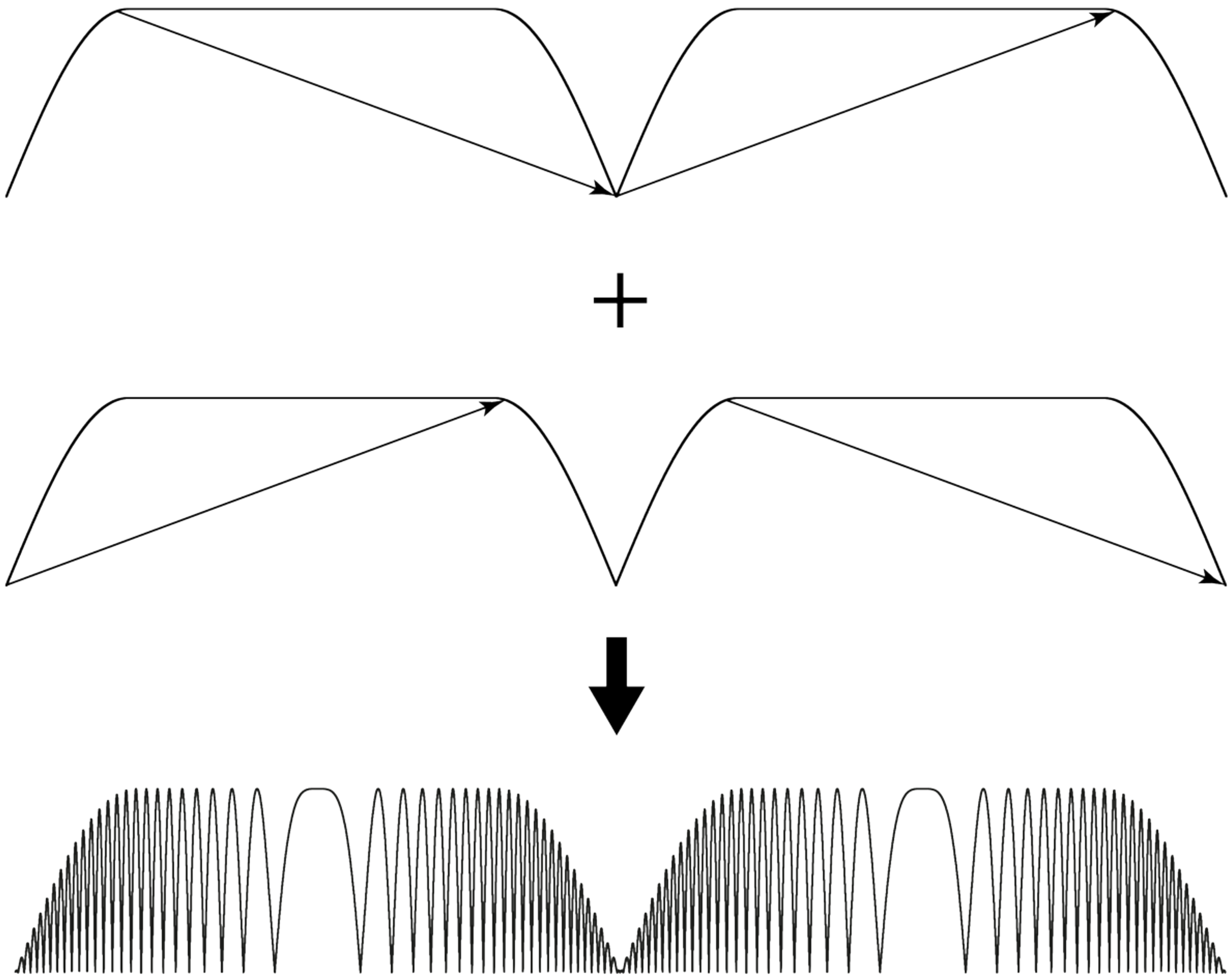
Taking advantage of saltire pulses

Two pairs of counter sweeping unidirectional chirps can be averaged to form a double saltire pulse element.

Two main advantages of saltire pulses:

i) Linear dependence of r.f. on flip angle, which is useful especially when very small r.f. amplitude are needed.

ii) Improved sensitivity compared to unidirectional sweep.



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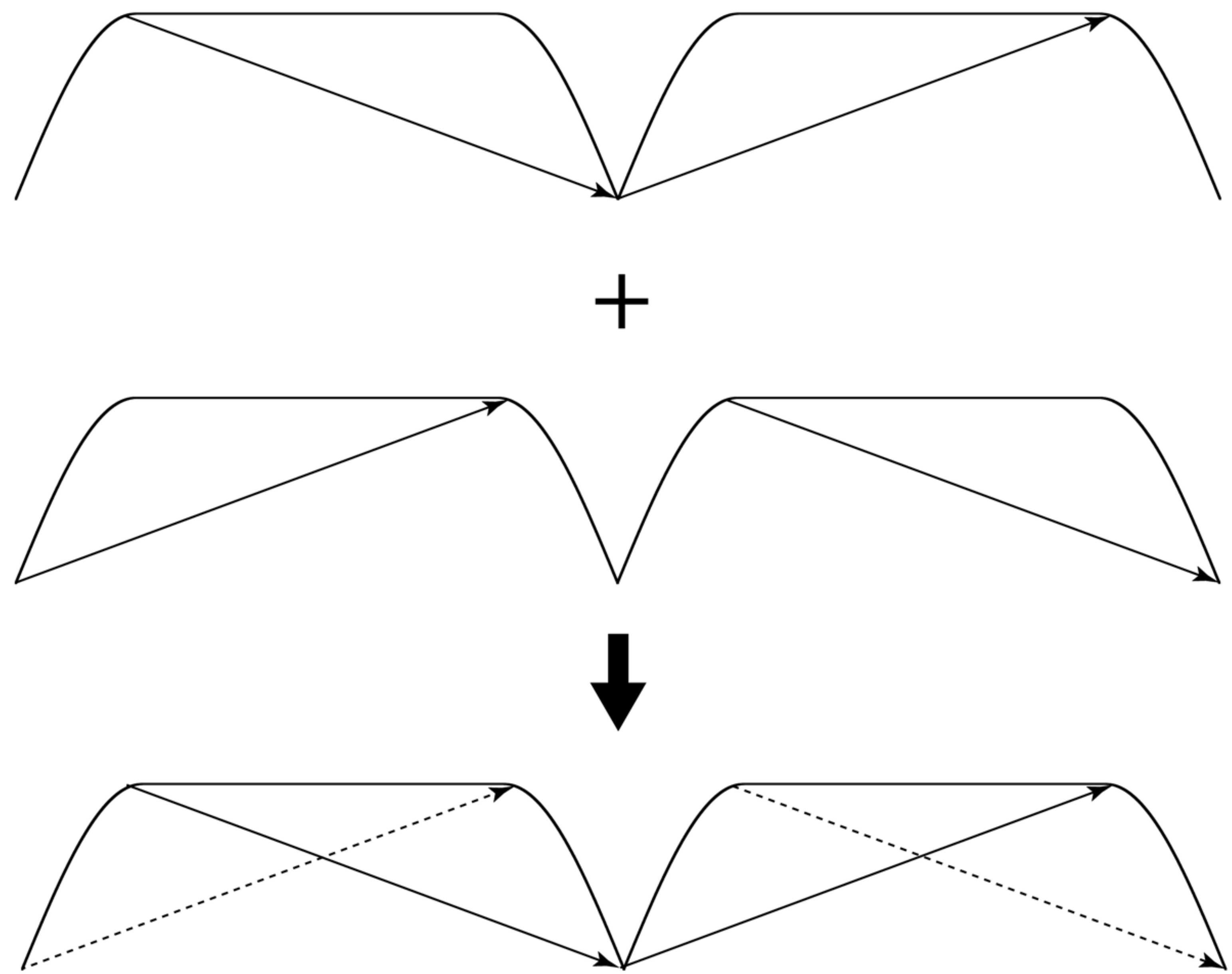
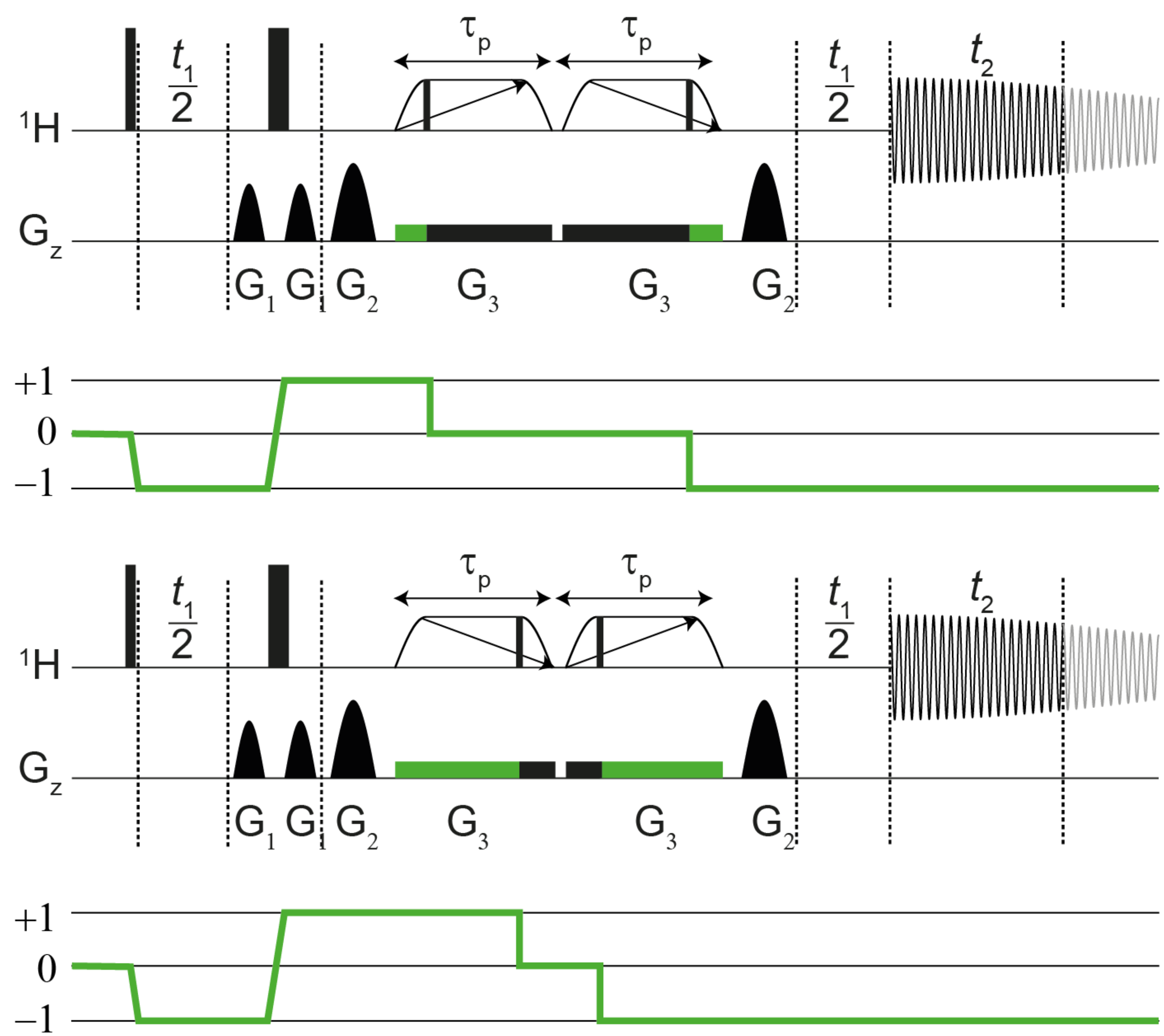


CTP selection during saltire pulses

The evolution of coherences during a saltire PSYCHE element can be represented as the superposition of two independent CTPs being enforced by the presence of the encoding gradient during the pulses.



Some Applications

1D PSYCHE

Angewandte
Communications

NMR Spectroscopy

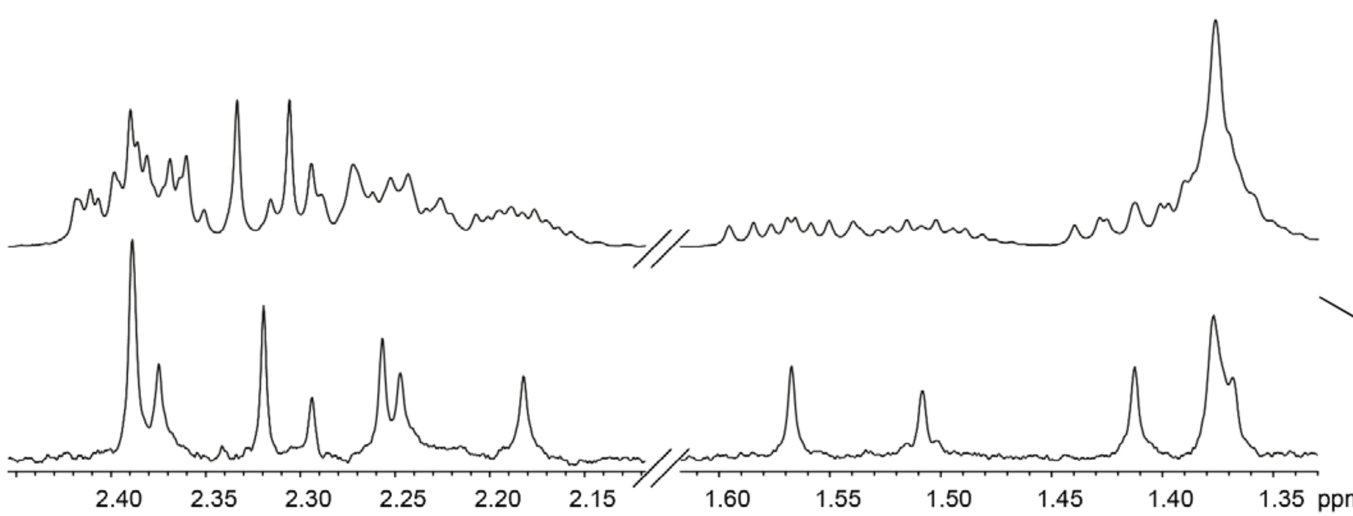
DOI: 10.1002/anie.201404111

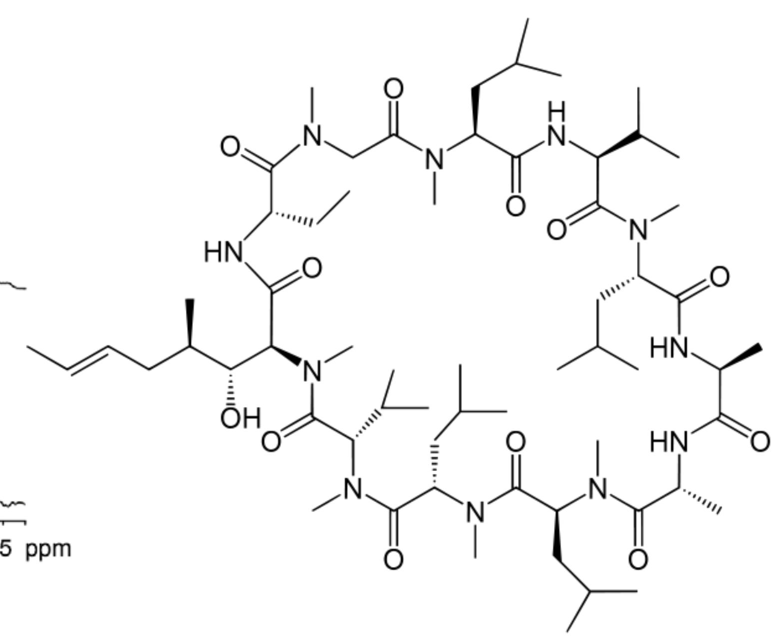
Ultrahigh-Resolution NMR Spectroscopy**

*Mohammadali Foroozandeh, Ralph W. Adams, Nicola J. Meharry, Damien Jeannerat, Mathias Nilsson, and Gareth A. Morris**

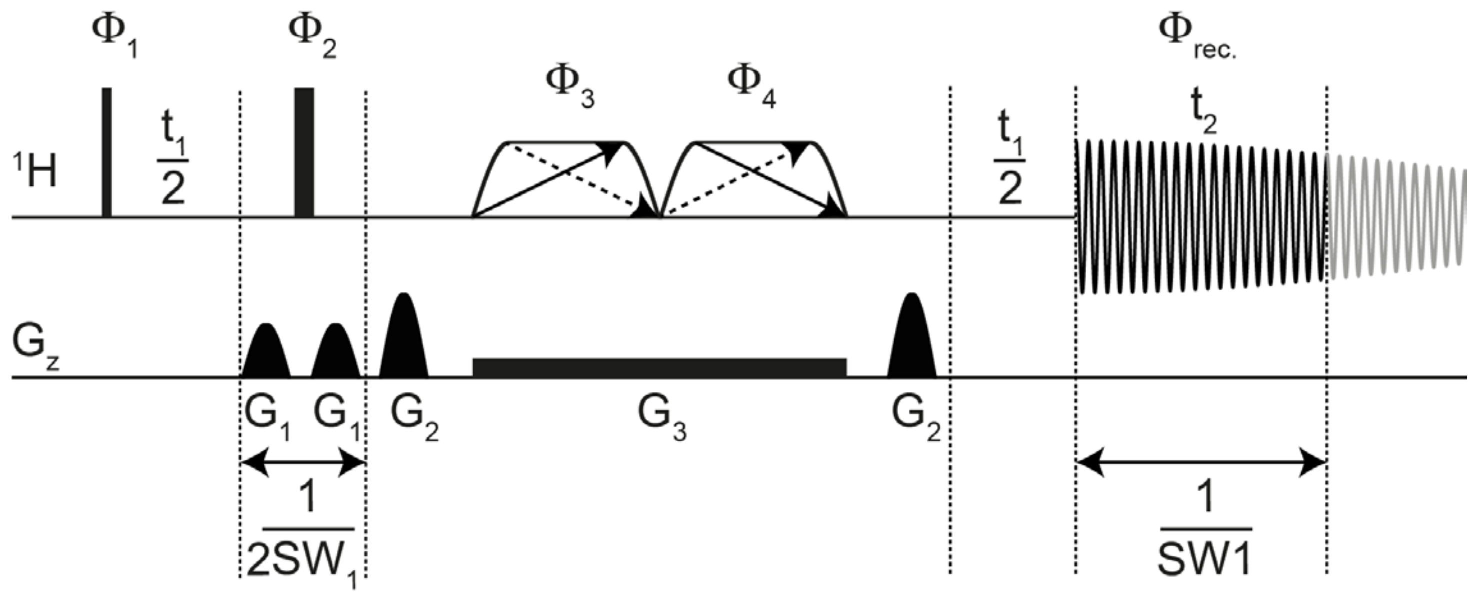
Conventional

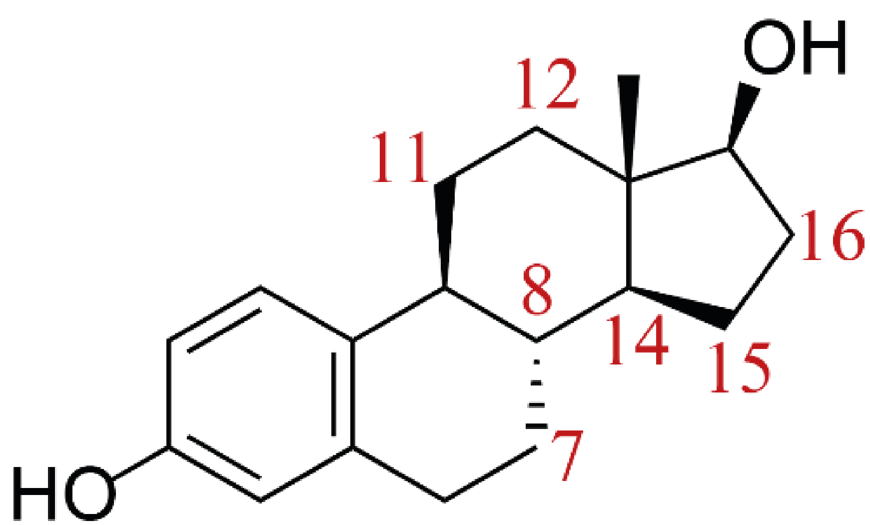
PSYCHE

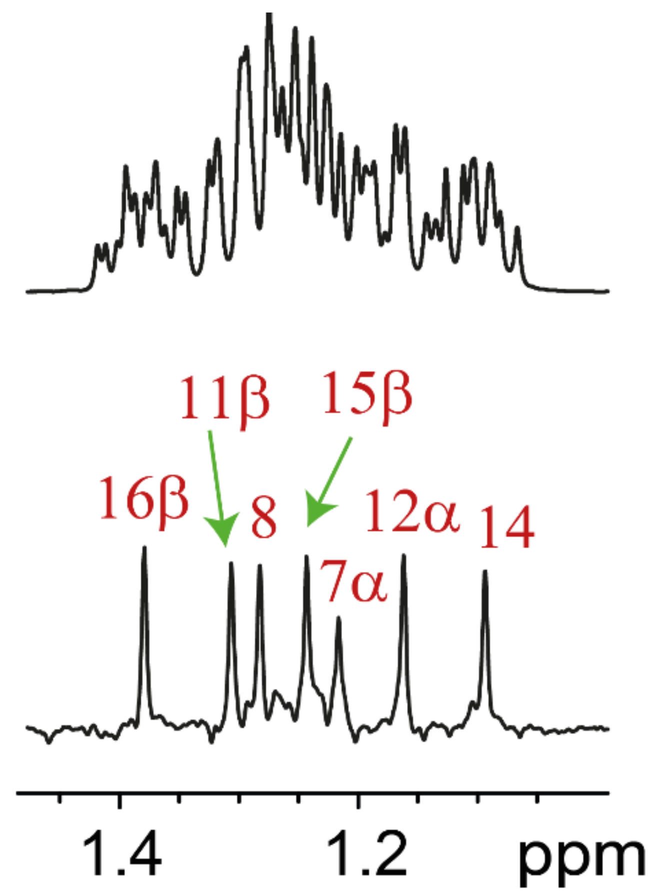




1D PSYCHE





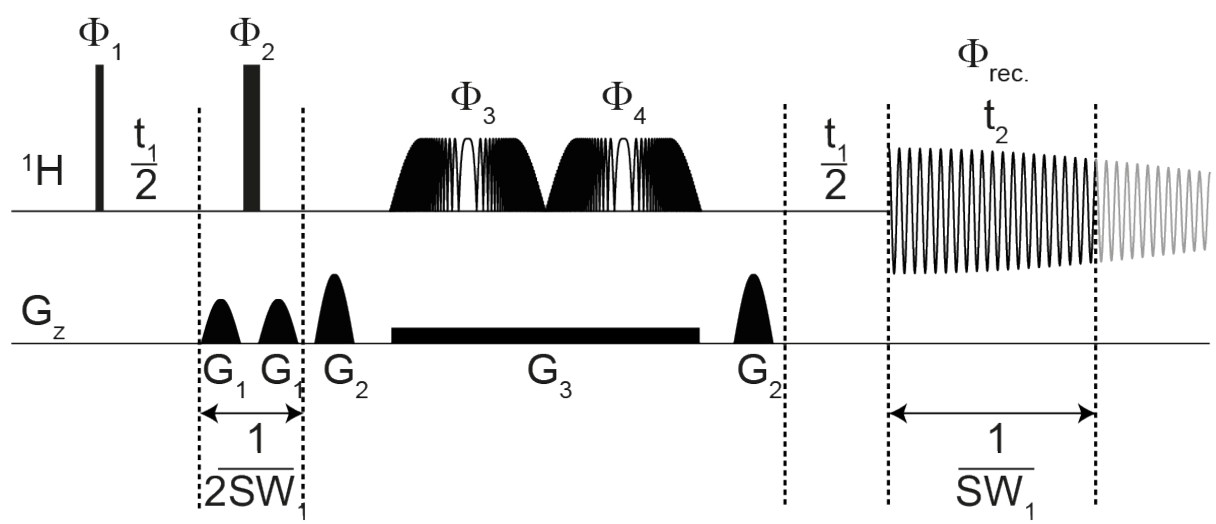


Angew. Chem. Int. Ed., **2014**, *53*, 6990.

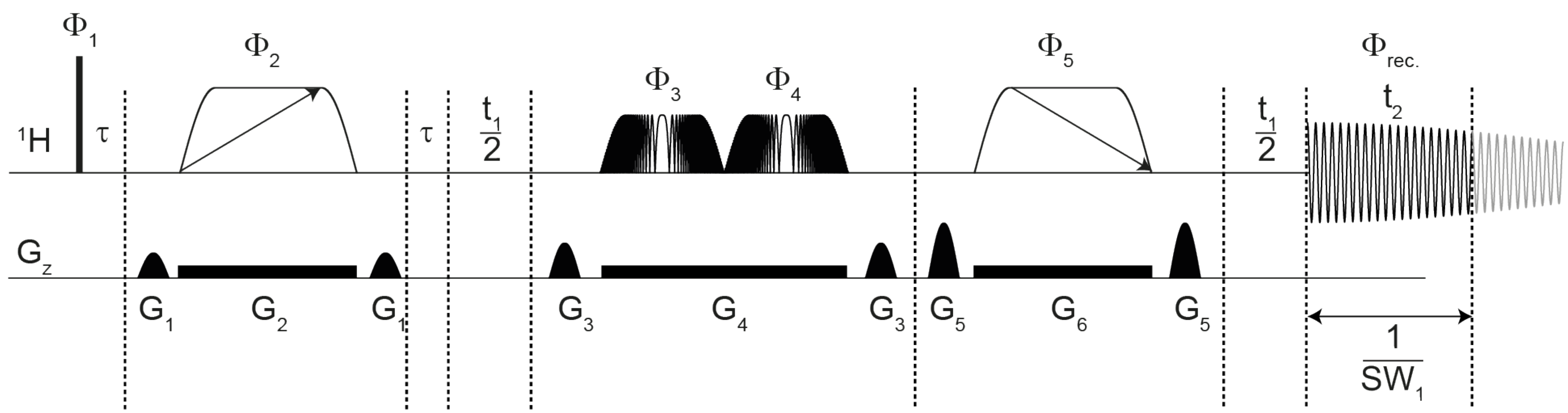
TSE – PSYCHE (Triple Spin Echo PSYCHE)

Addition of two extra 180° chirp pulses in the presence of weak pulsed field gradient instead of a hard 180° pulse results in additional spatio-temporal averaging and significant improvement in spectral quality.

PSYCHE

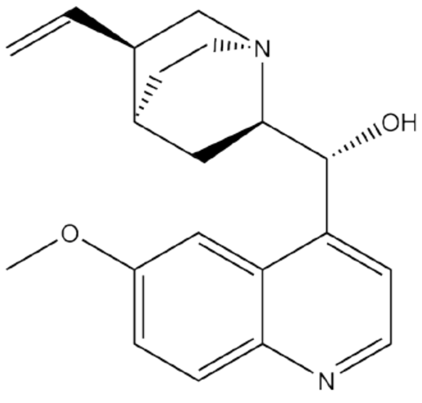


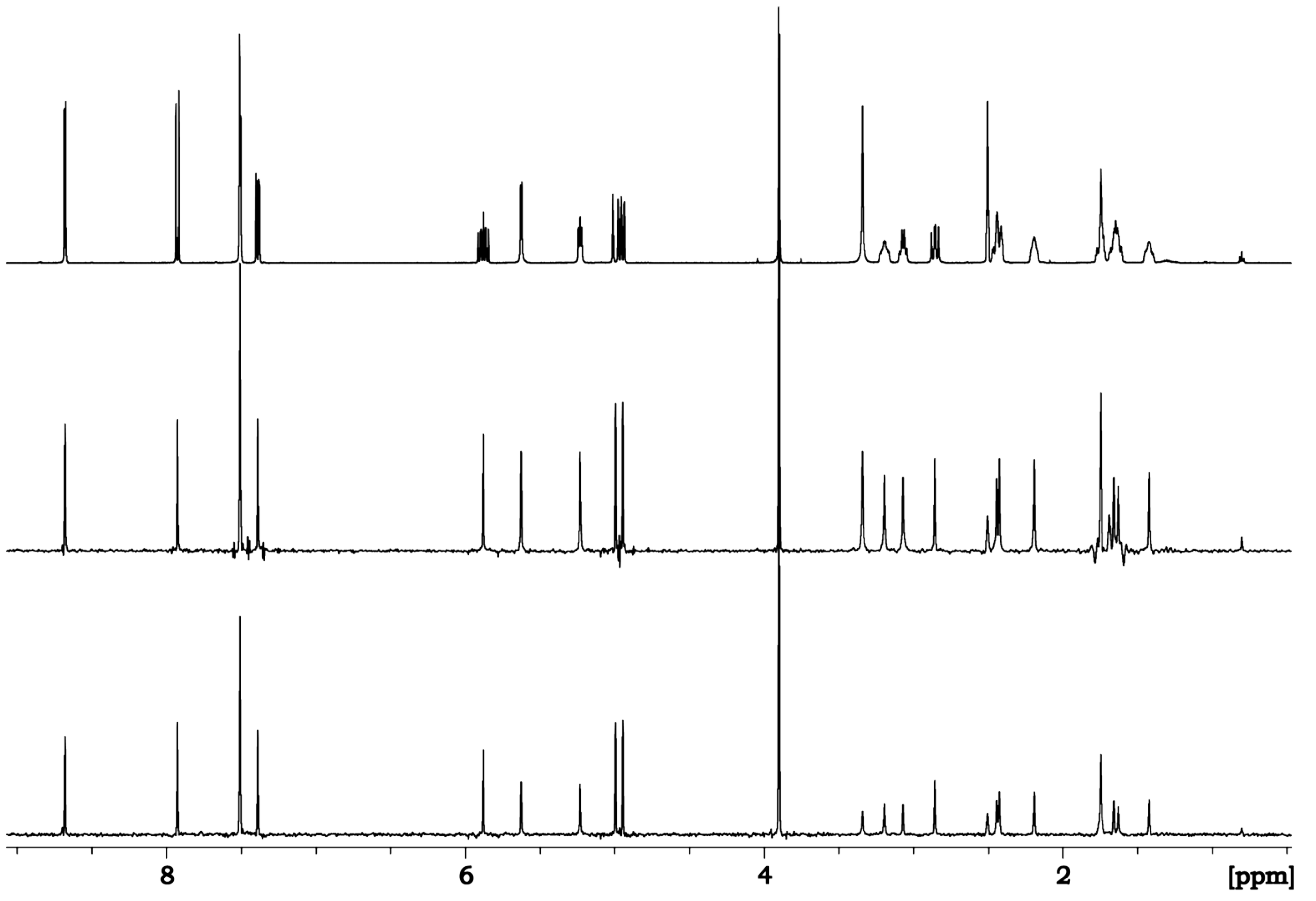
TSE-PSYCHE



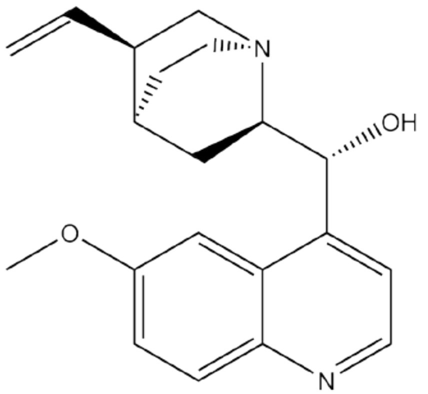
Chem. Commun., **2015**, *51*, 15410.

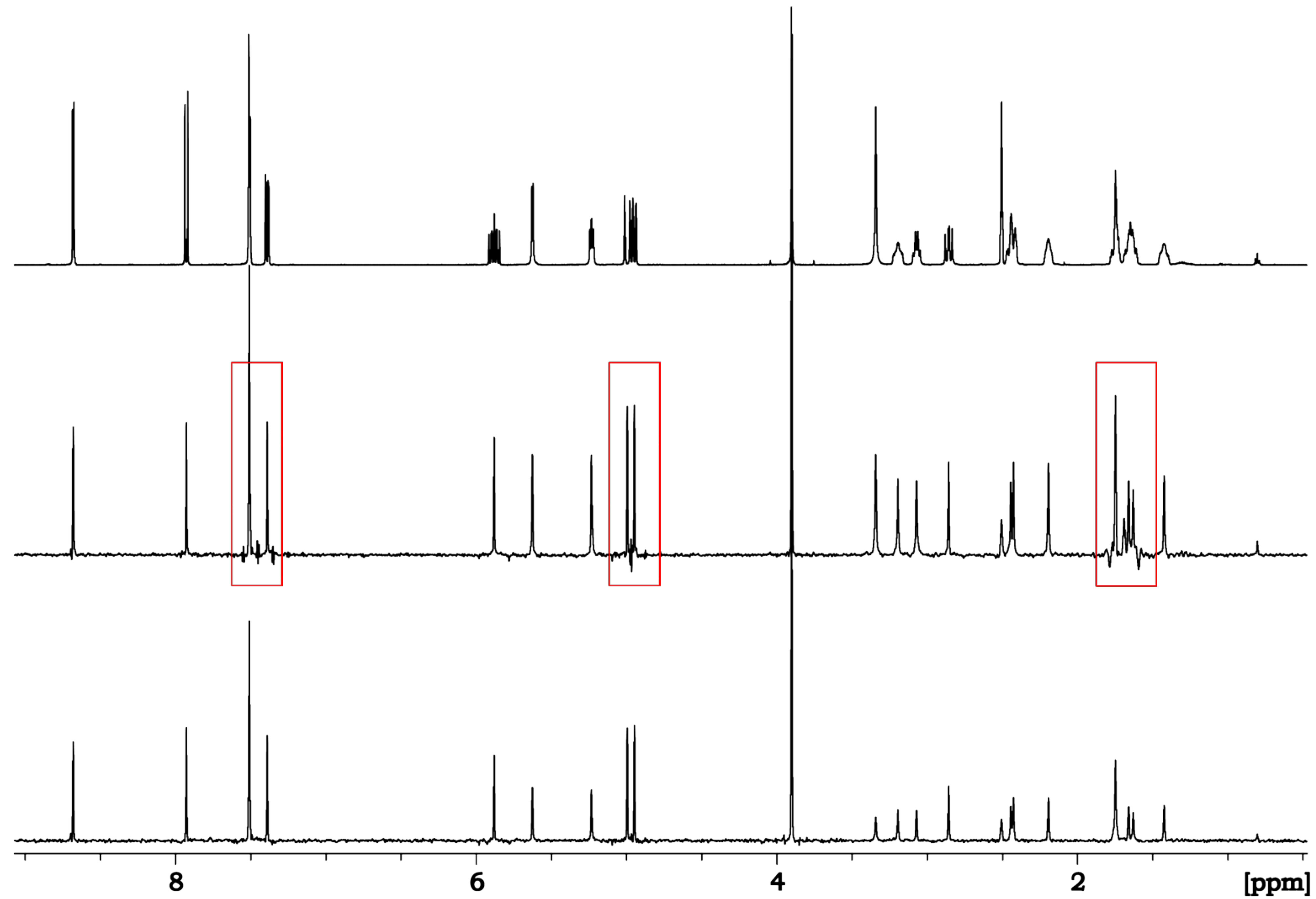
TSE – PSYCHE and strong coupling





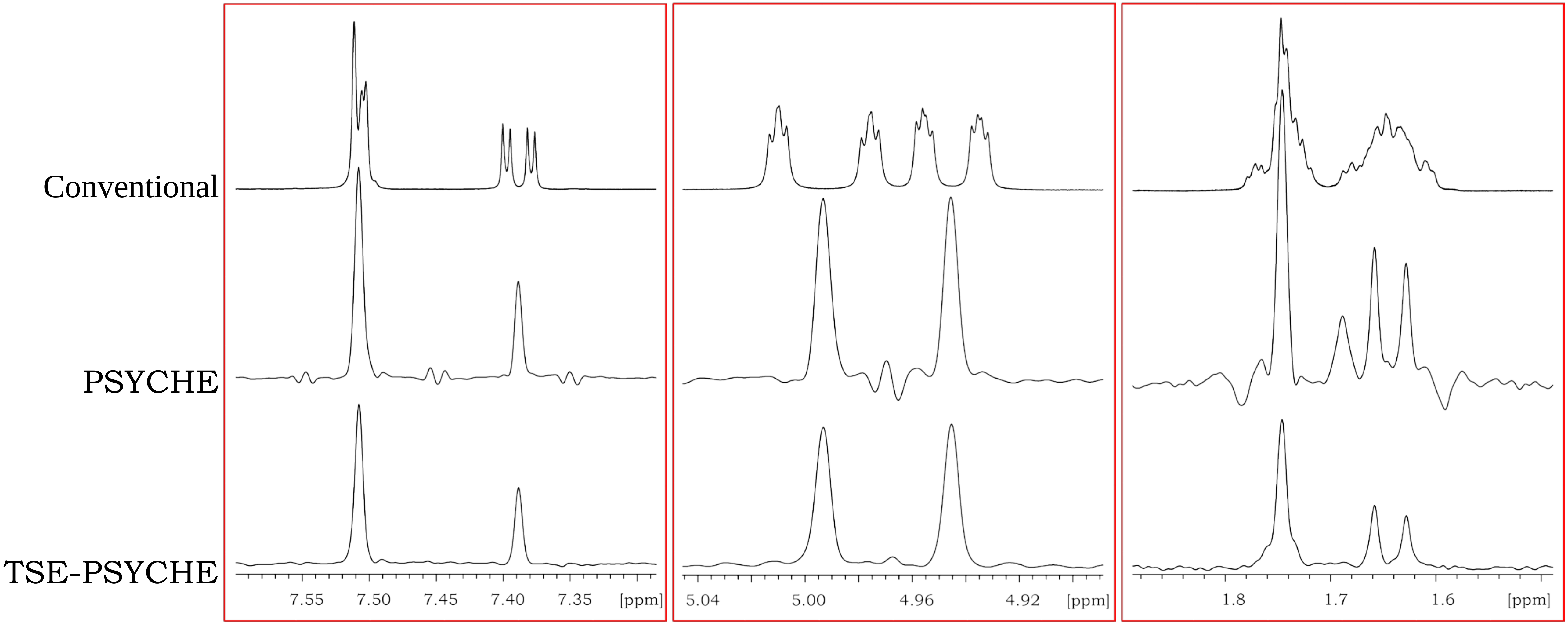
TSE – PSYCHE and strong coupling



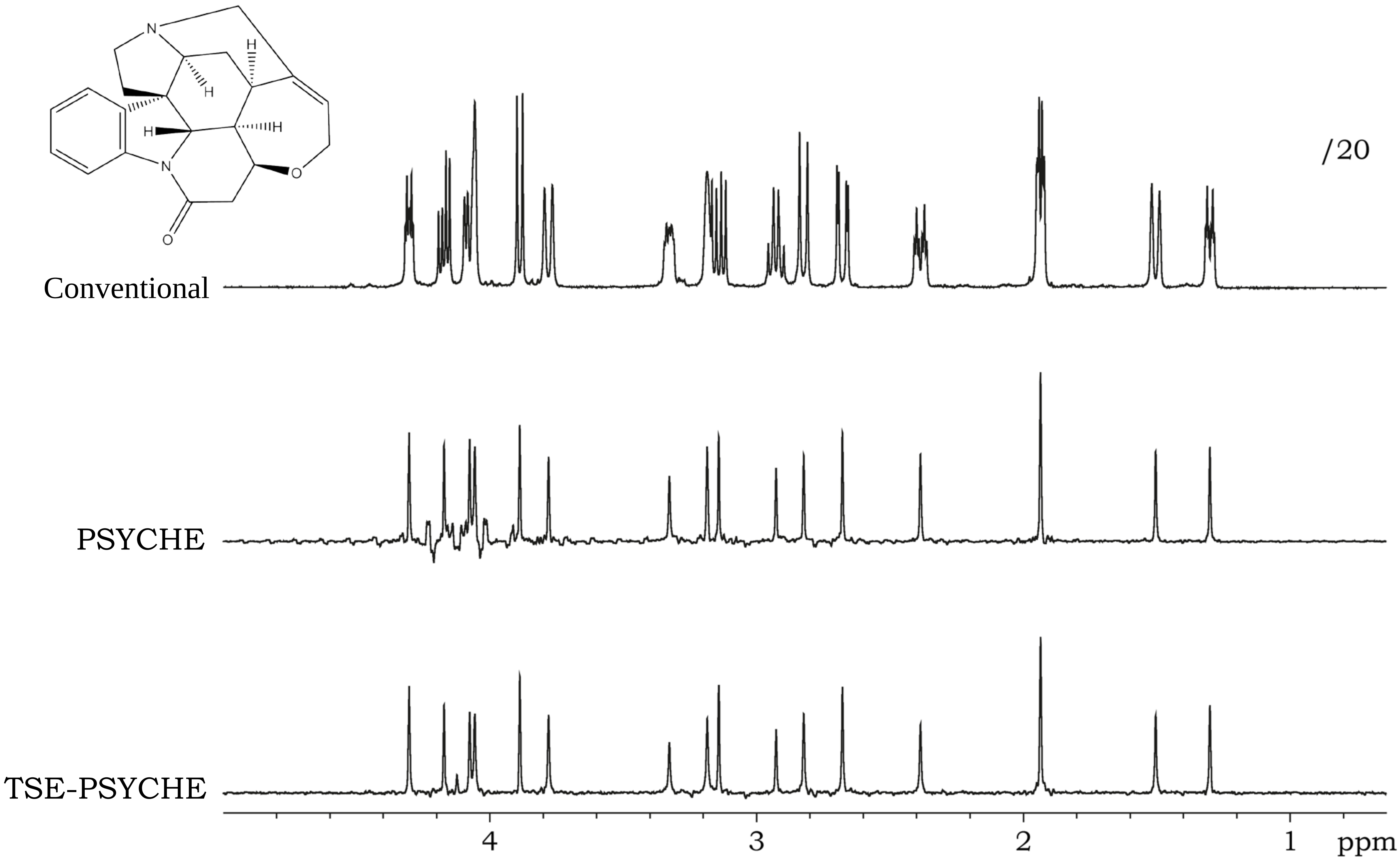


TSE – PSYCHE and strong coupling

Generally the signal-to-noise ratio of TSE-PSYCHE can be less than PSYCHE with hard 180° pulse, due to diffusion and relaxation, but the signal-to-artefact ratio is much higher.

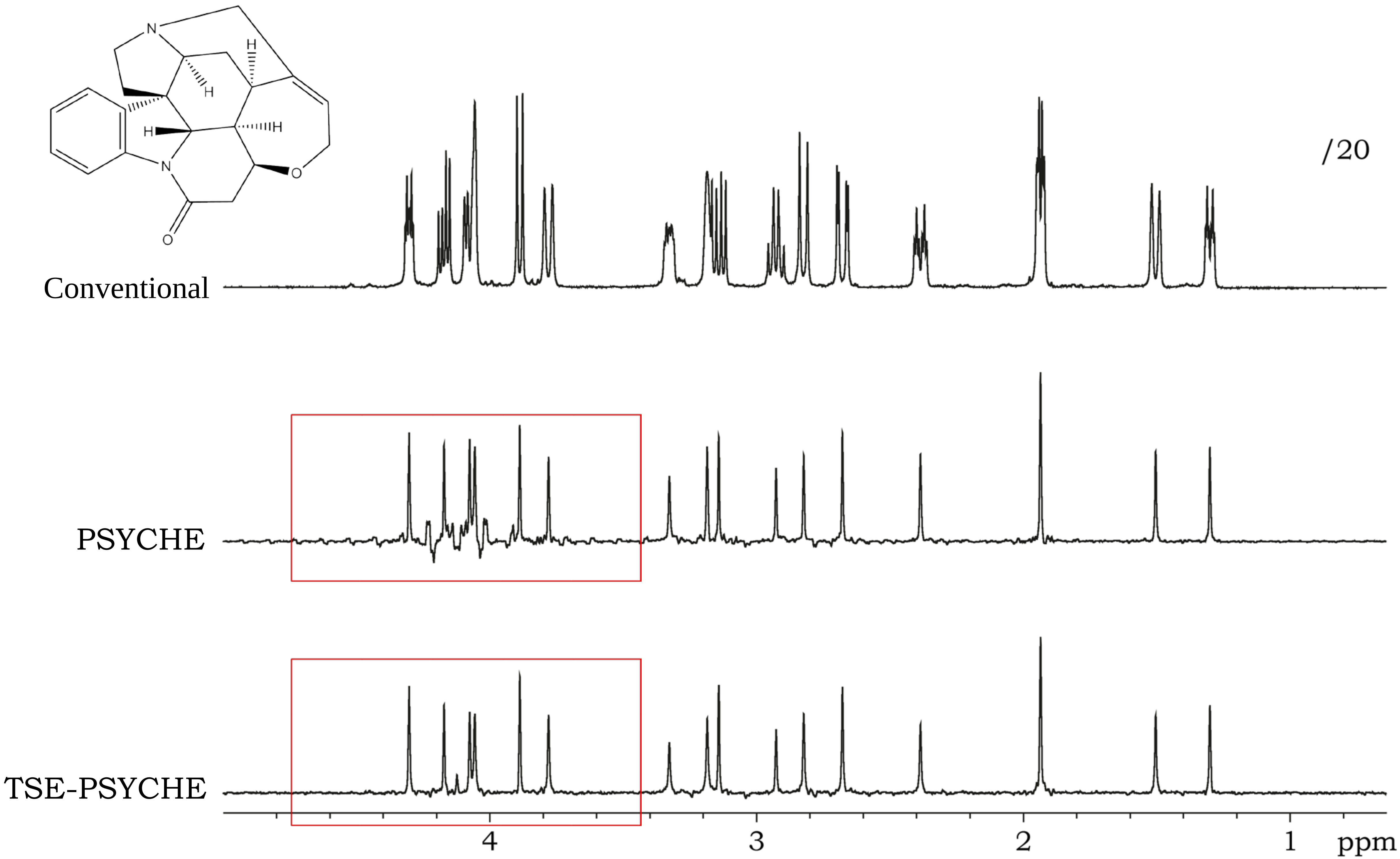


TSE – PSYCHE and strong coupling



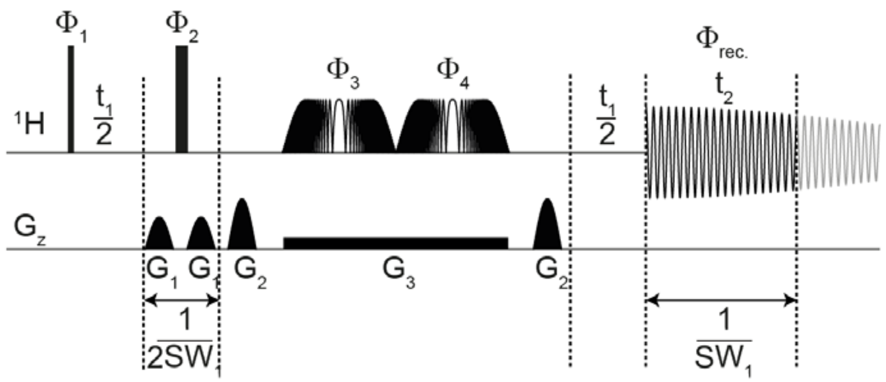
- *Chem. Commun.*, **2015**, *51*, 15410.

TSE – PSYCHE and strong coupling

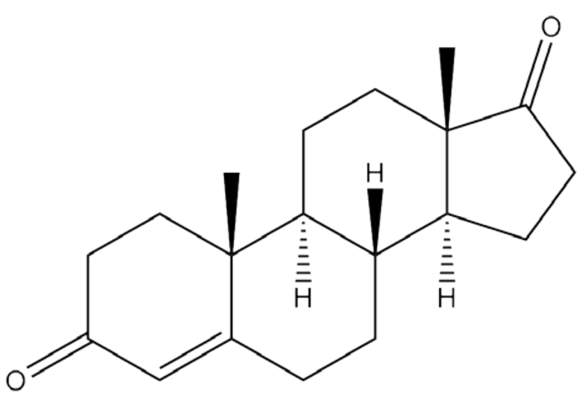


- *Chem. Commun.*, **2015**, *51*, 15410.

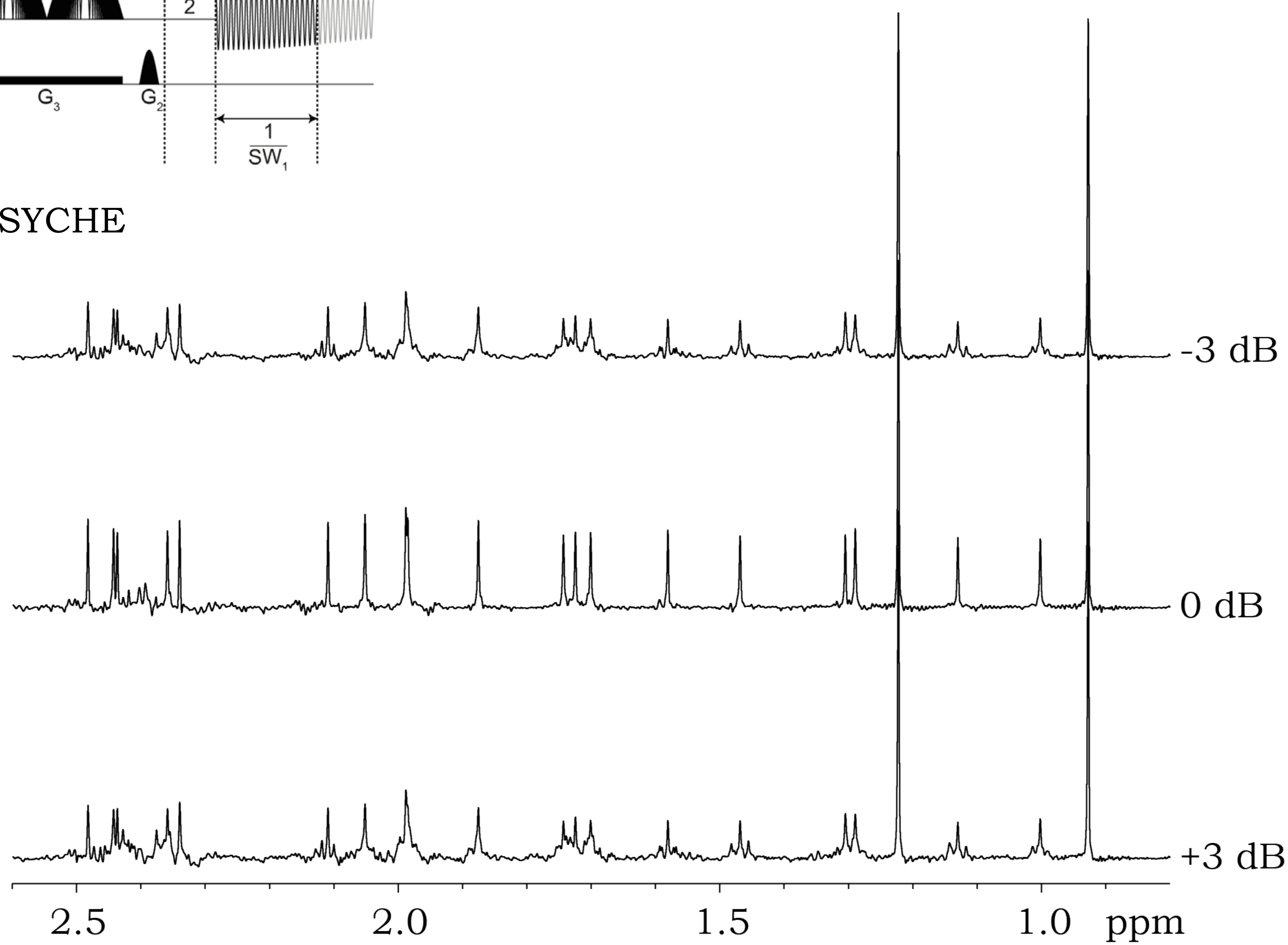
Pulse miscalibration and B_1 inhomogeneity



PSYCHE

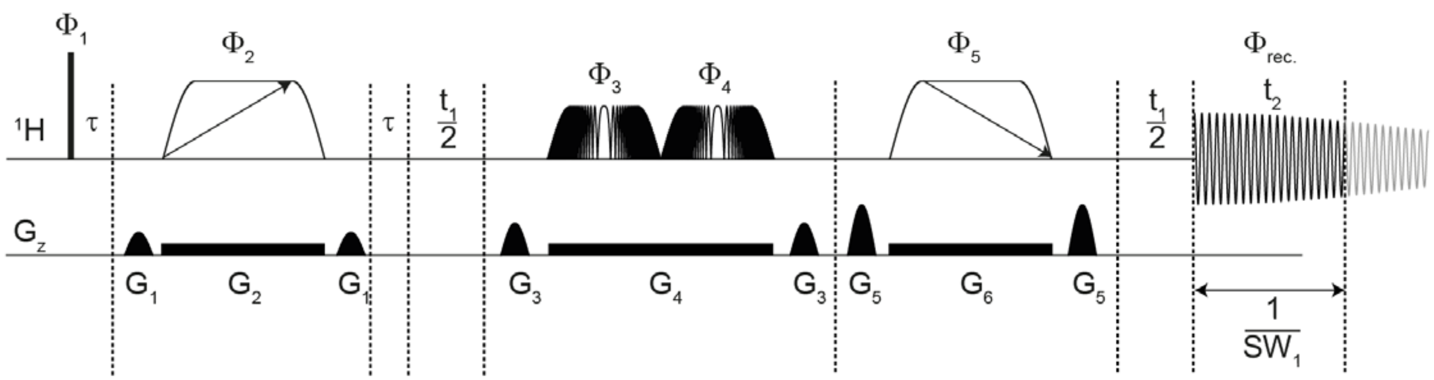


Androstenedione

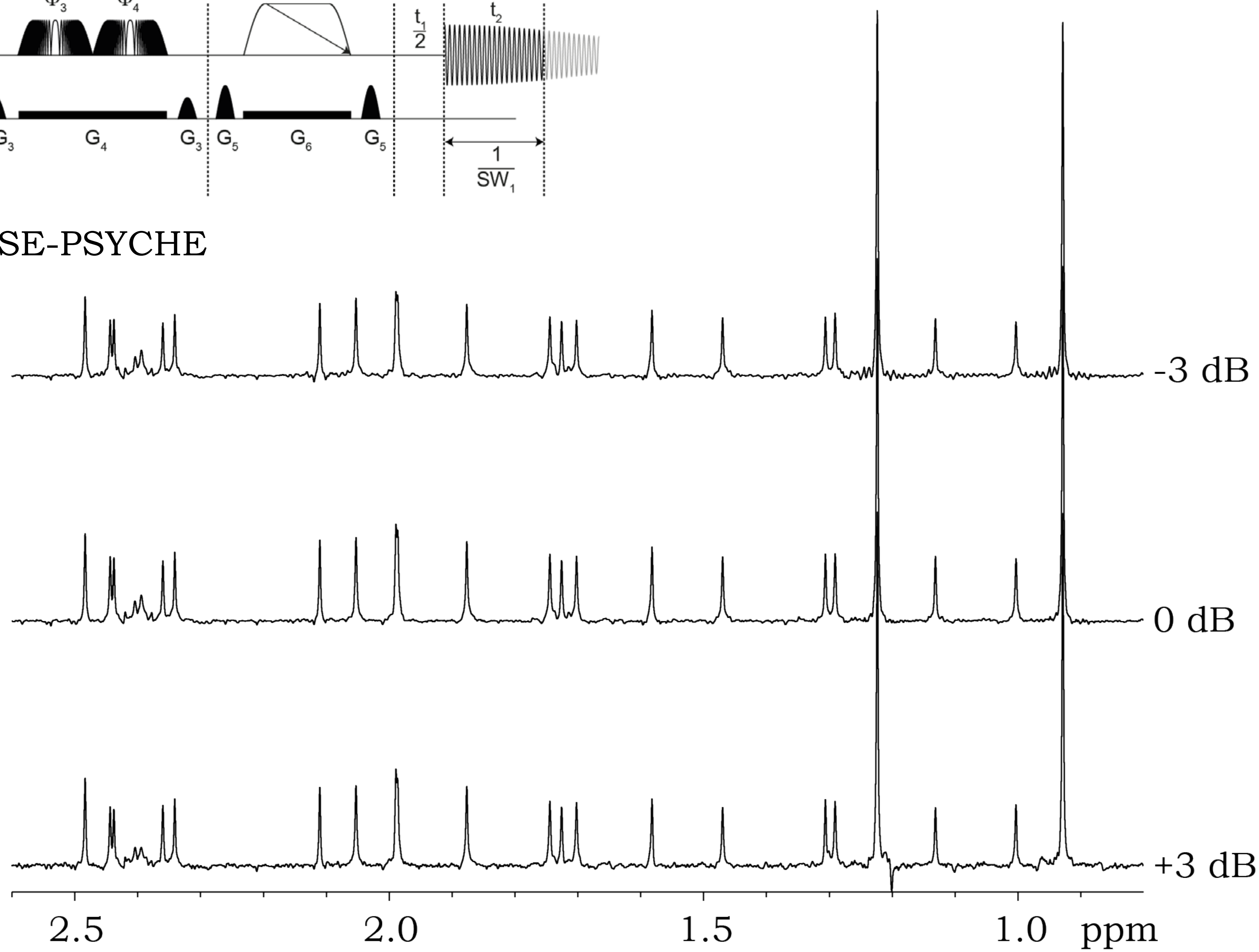


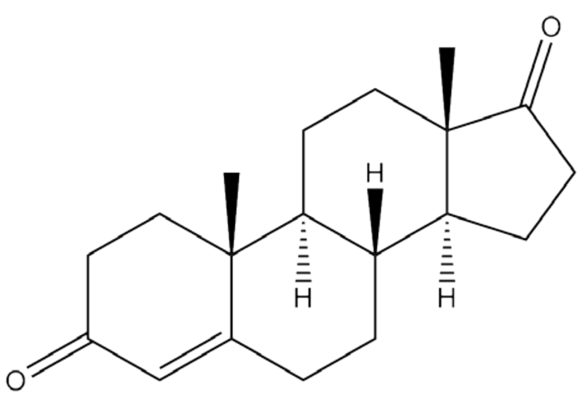
▶ *Chem. Commun.*, **2015**, *51*, 15410.

Pulse miscalibration and B_1 inhomogeneity



TSE-PSYCHE





Androstenedione

Chem. Commun., **2015**, *51*, 15410.

F_1-PSYCHE TOCSY

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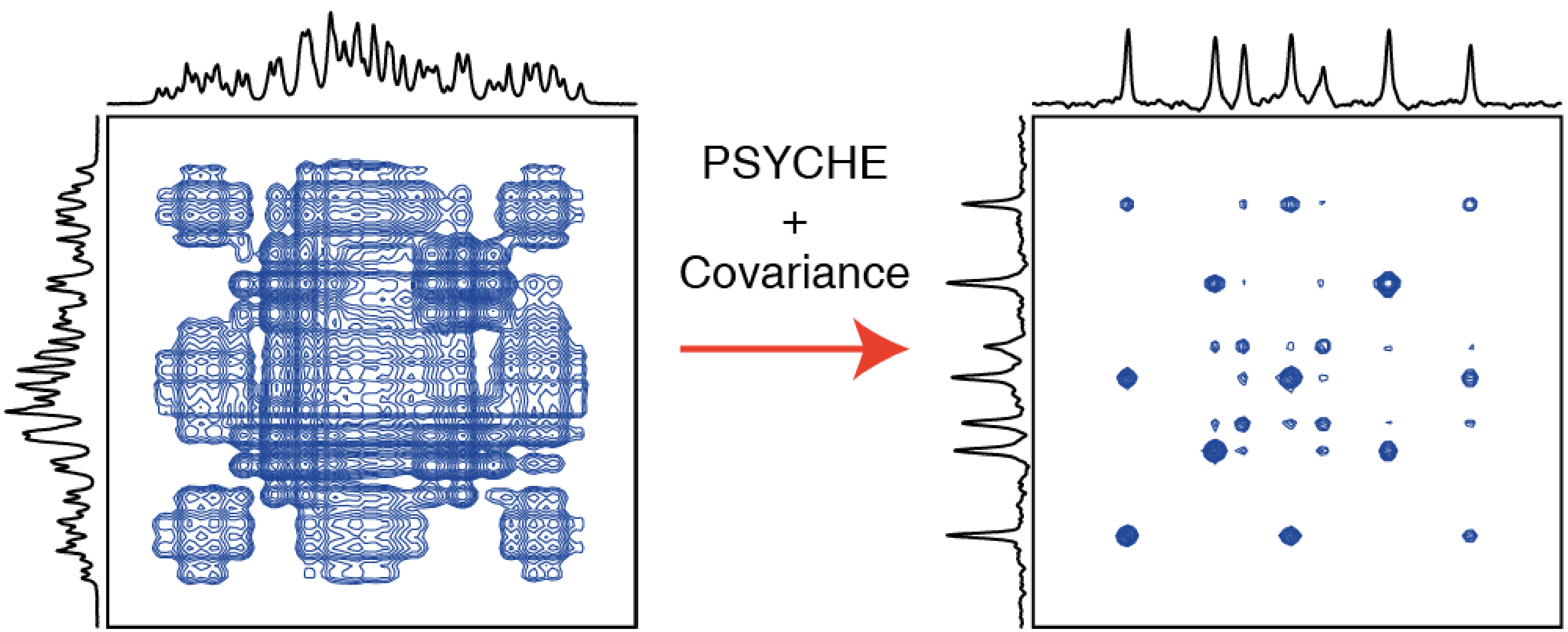
Ultrahigh-Resolution Total Correlation NMR Spectroscopy

Mohammadali Foroozandeh,[†] Ralph W. Adams,[†] Mathias Nilsson,[†,‡] and Gareth A. Morris*[,†]

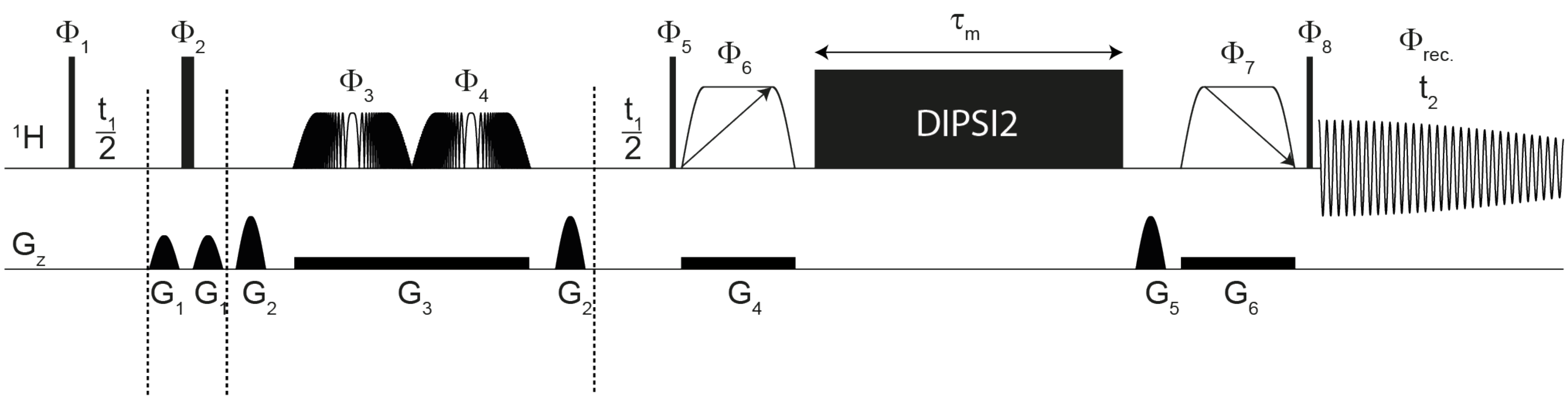


Conventional TOCSY

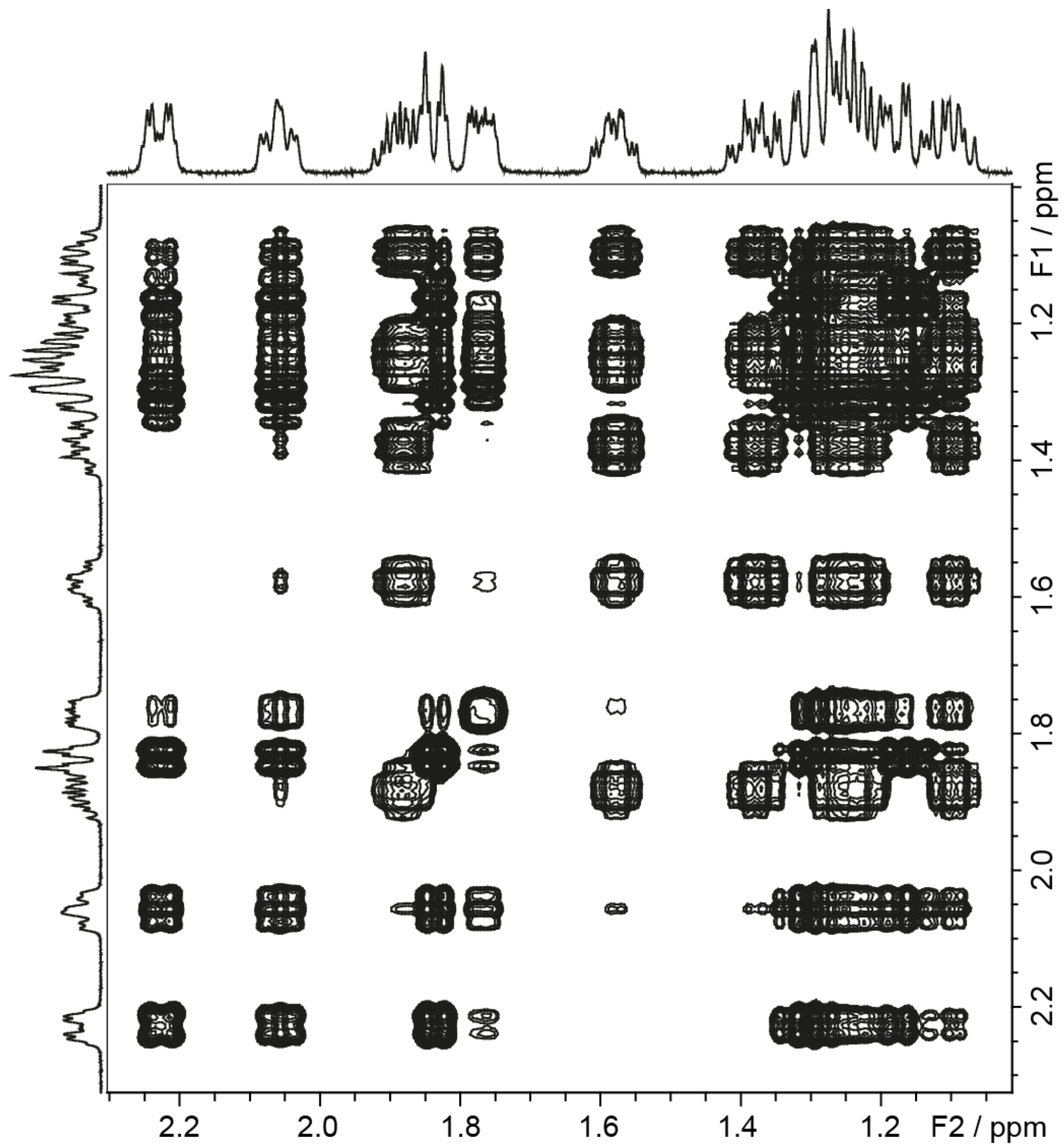
Double pure shift TOCSY

F_1-PSYCHE TOCSY

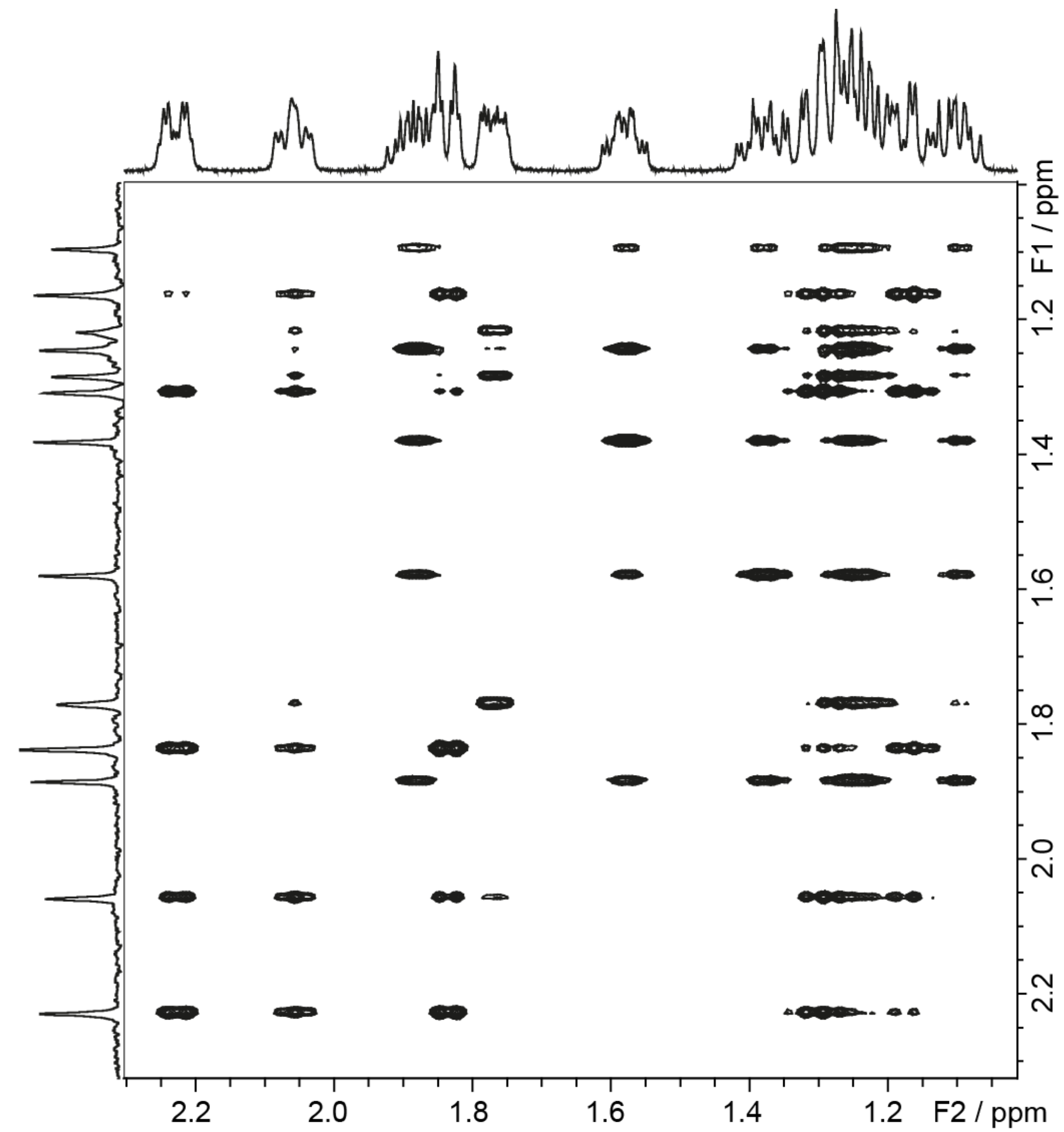
Application of PSYCHE in the indirect dimension of a 2D TOCSY experiment gives pure shift signals along the F_1 dimension. This method is immune to chunking artefacts. Although it requires high digital resolution along the F_1 dimension, compared to the interferogram variant it has no time penalty.



F_1-PSYCHE TOCSY



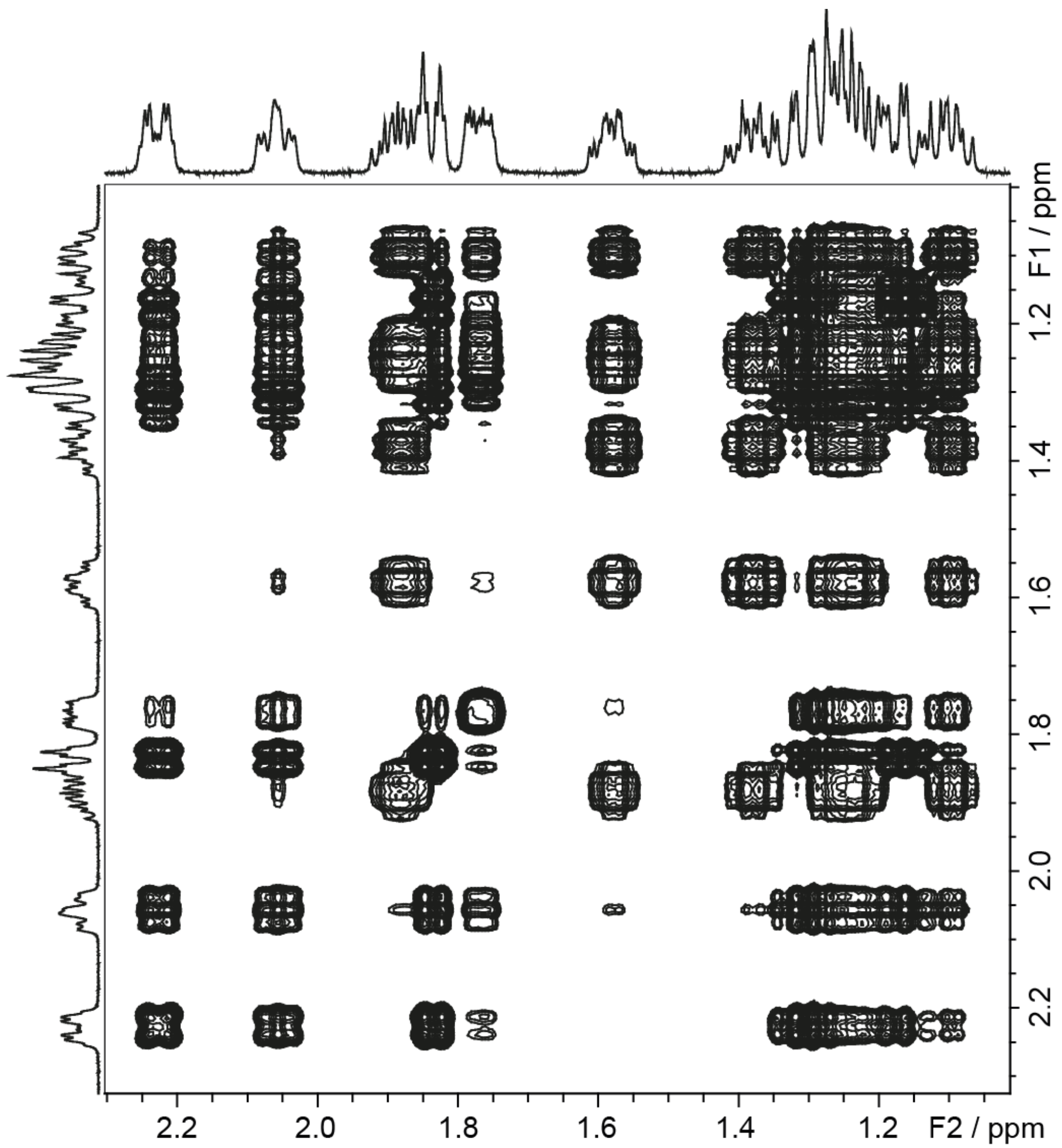
TOCSY



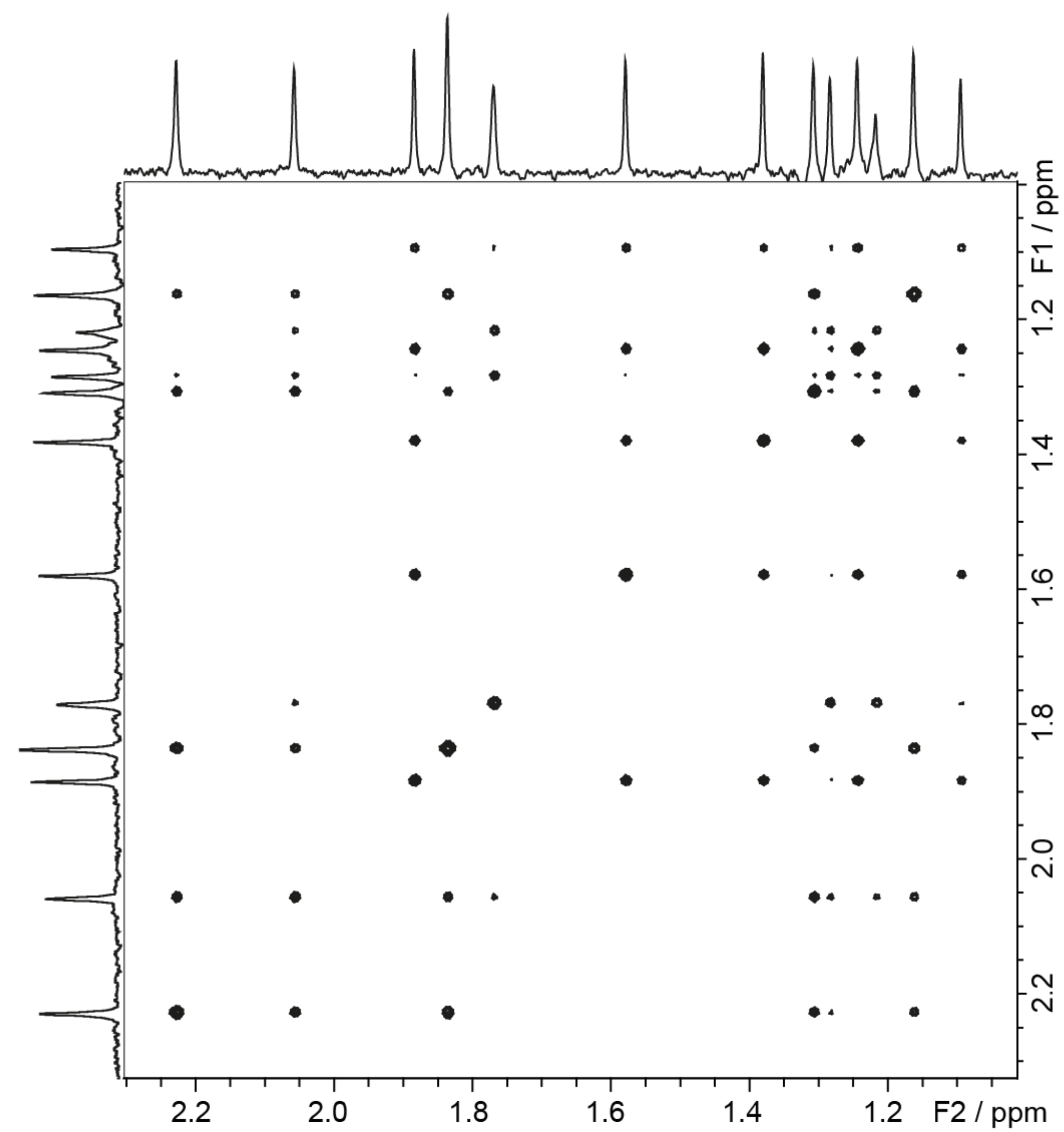
F_1-PSYCHE TOCSY

J. Am. Chem. Soc., **2014**, *136*, 11867.

F_1-PSYCHE TOCSY



TOCSY



F_1-PSYCHE TOCSY
With indirect covariance processing

J. Am. Chem. Soc., **2014**, *136*, 11867.

PSYCHE-2D J

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Received 28th July 2015,
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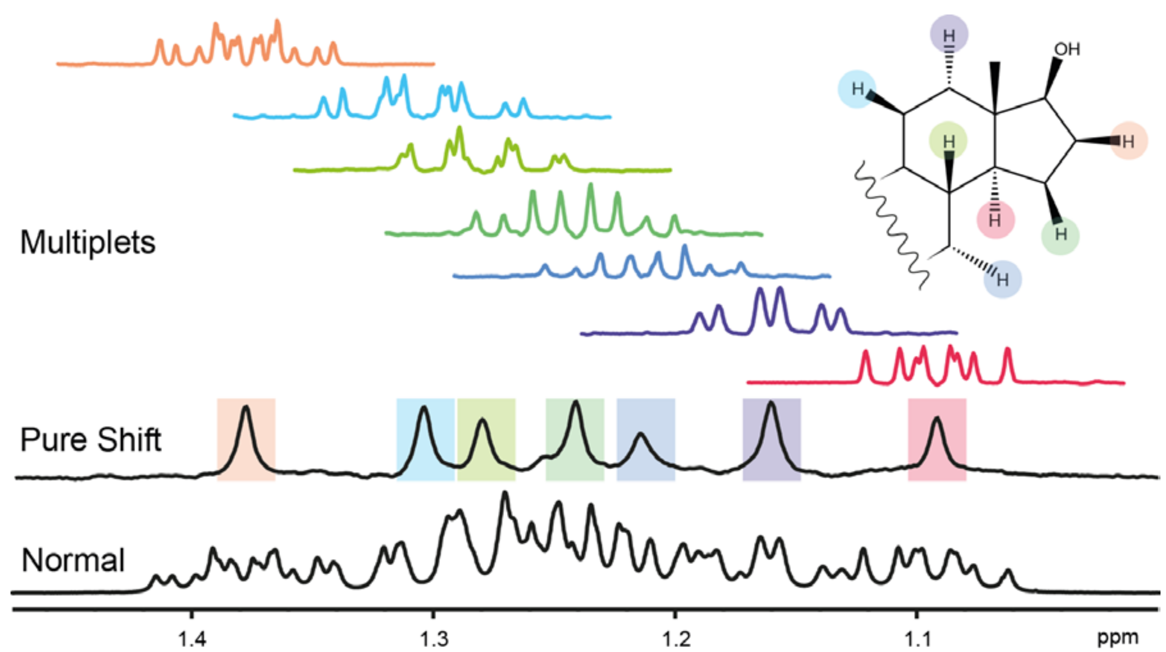
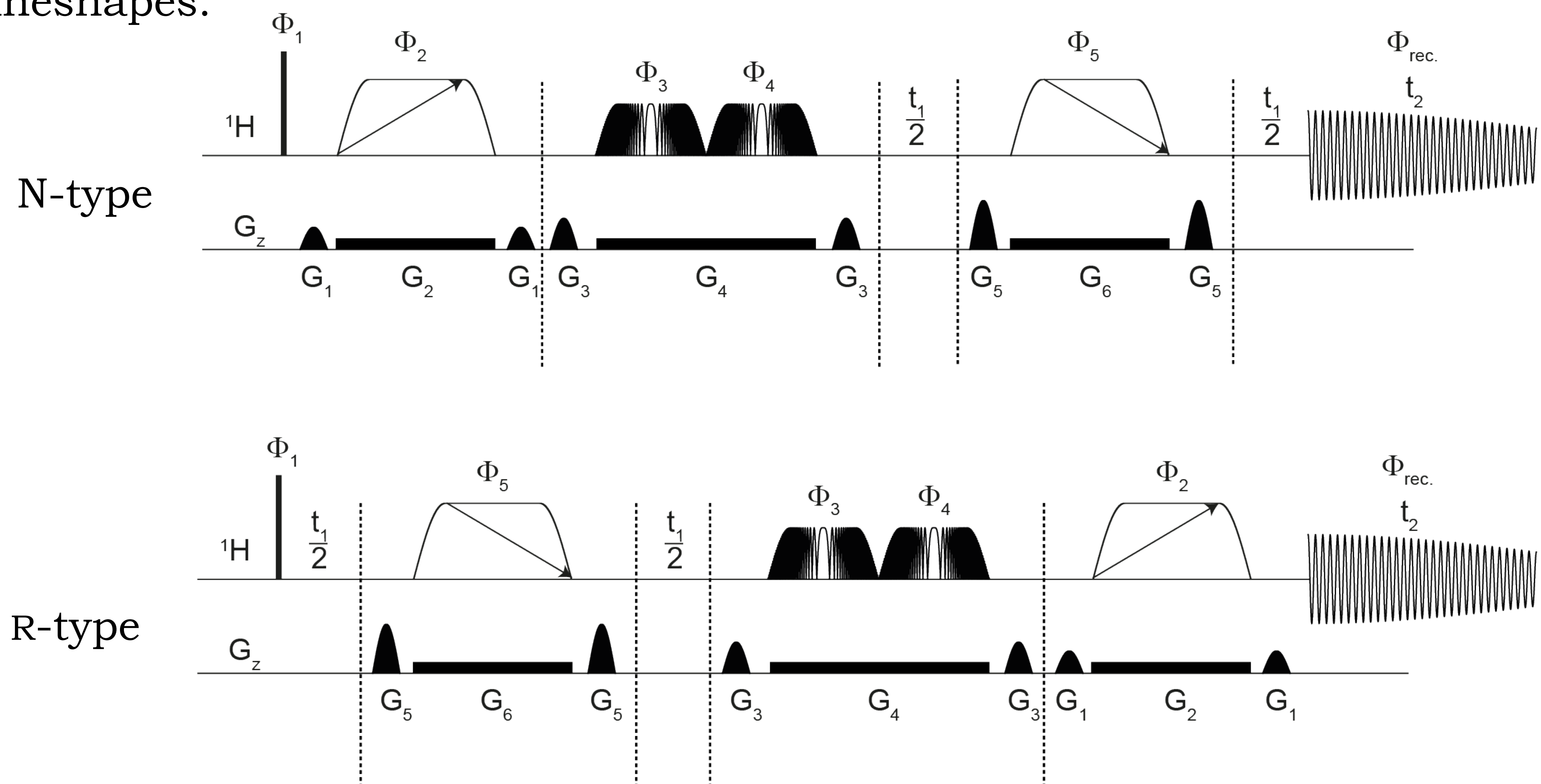
Measuring couplings in crowded NMR spectra: pure shift NMR with multiplet analysis†

M. Foroozandeh,* R. W. Adams, P. Kiraly, M. Nilsson and G. A. Morris

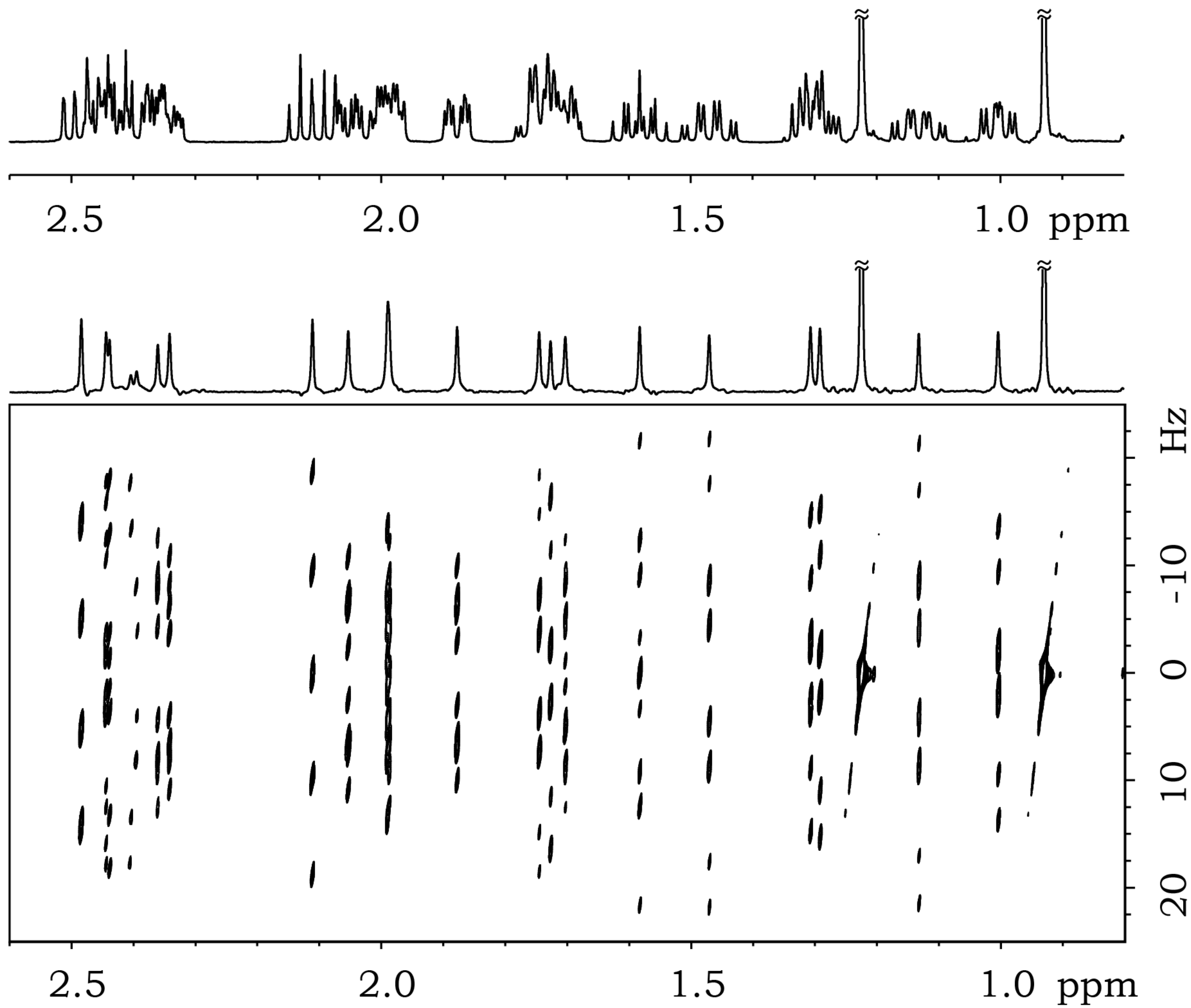


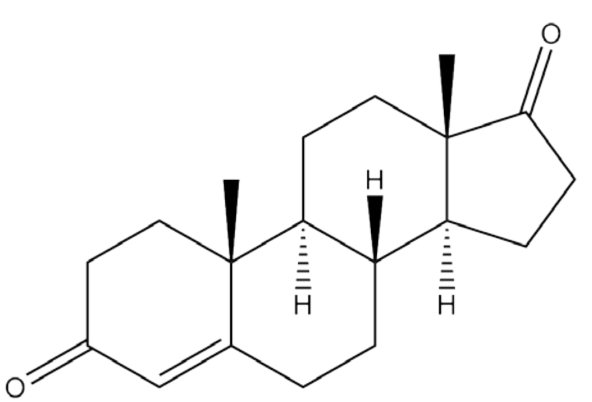
PSYCHE-2D J

The TSE experiment can be combined with the 2D J acquisition scheme introduced by Pell and Keeler to give 2D J spectra with absorption mode lineshapes.



PSYCHE-2D J





Androstenedione

Chem. Commun., **2015**, *51*, 15410.

PSYCHE-*i*DOSY

Communications

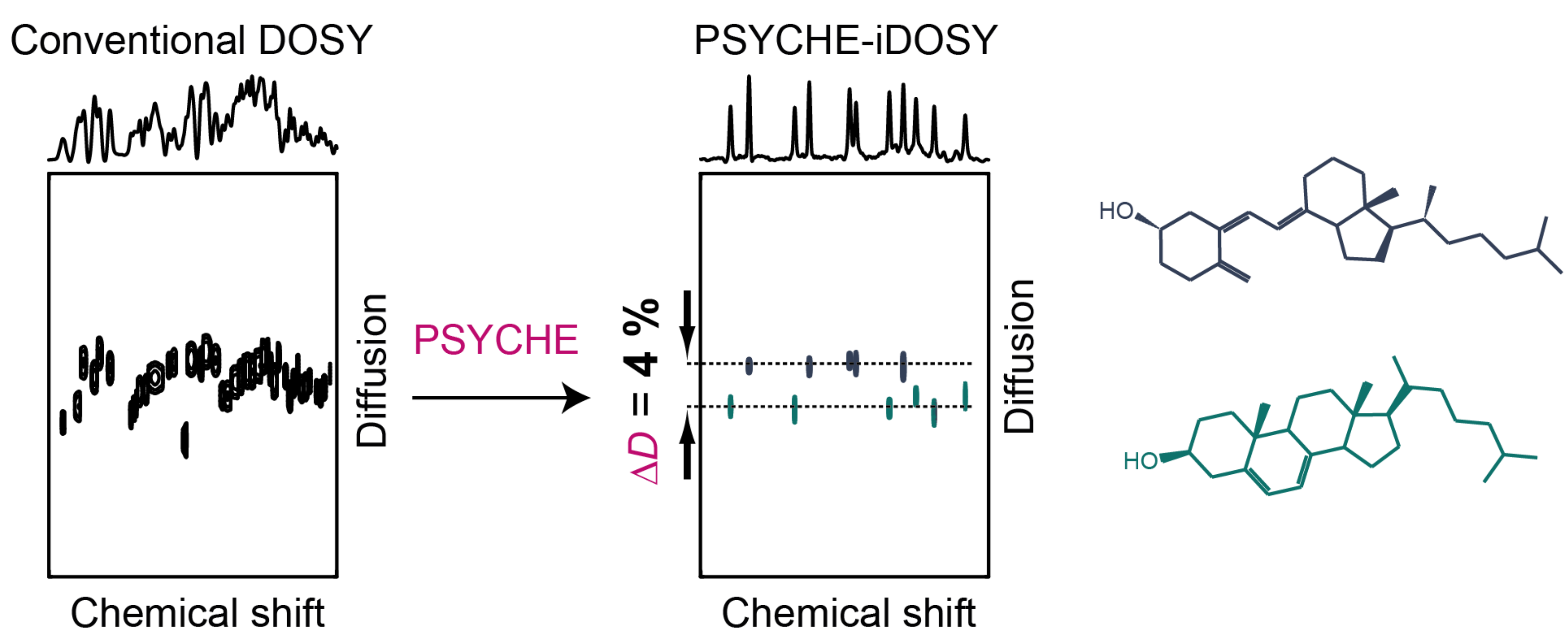
Angewandte Chemie International Edition

NMR Spectroscopy *Hot Paper*

International Edition: DOI: 10.1002/anie.201609676
German Edition: DOI: 10.1002/ange.201609676

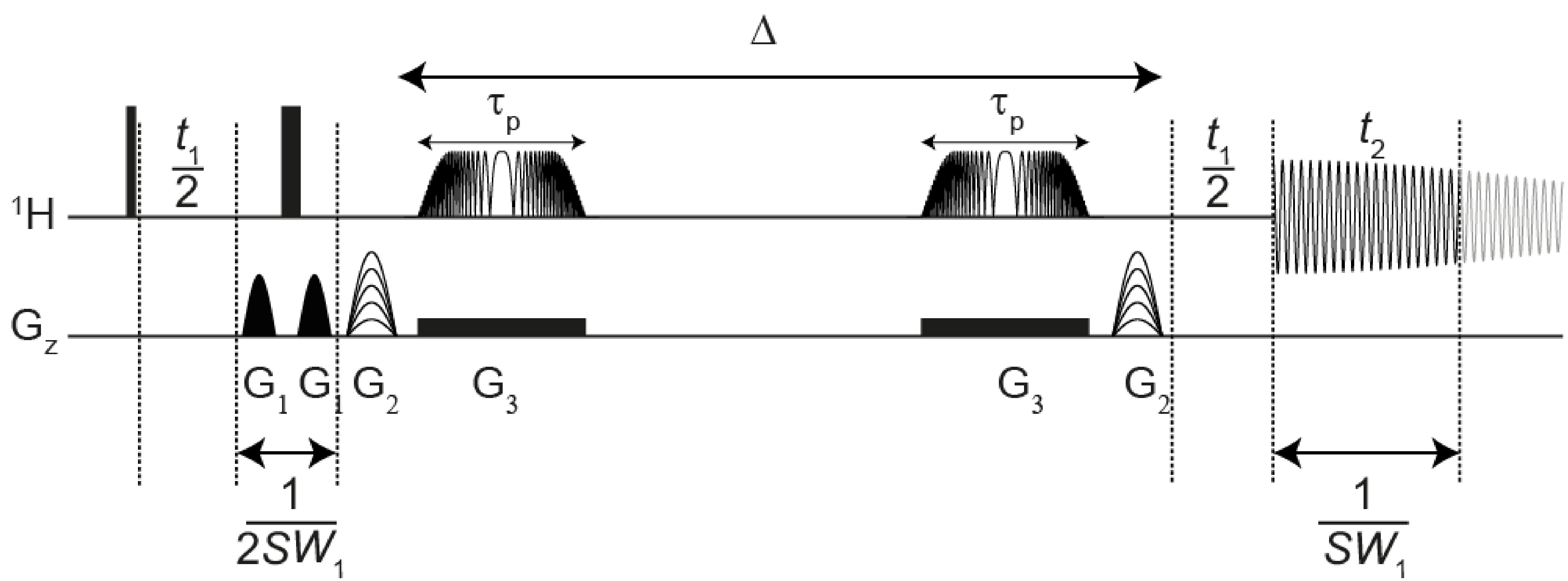
Ultrahigh-Resolution Diffusion-Ordered Spectroscopy

*Mohammadali Foroozandeh, Laura Castañar, Lucas G. Martins, Davy Sinnaeve, Guilherme Dal Poggetto, Claudio F. Tormena, Ralph W. Adams, Gareth A. Morris, and Mathias Nilsson**



PSYCHE-*i*DOSY

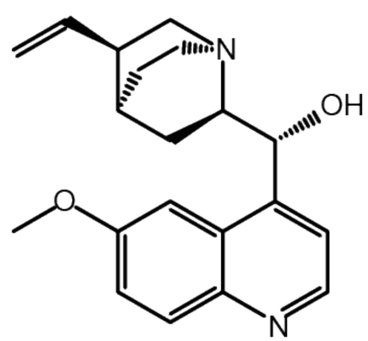
The PSYCHE element made of two saltire pulses can be seen as a stimulated echo, and hence can be used for diffusion measurement by inserting a diffusion delay between the two saltire pulses and incrementing gradients either side of the whole element.



▸ *Angew. Chem. Int. Ed.*, **2016**, *55*, 15579.

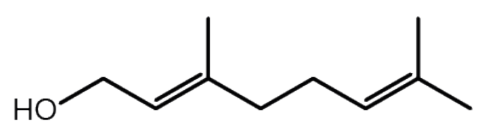
PSYCHE-*i*DOSY

quinine



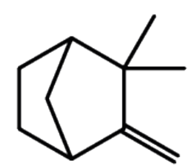
1

geraniol



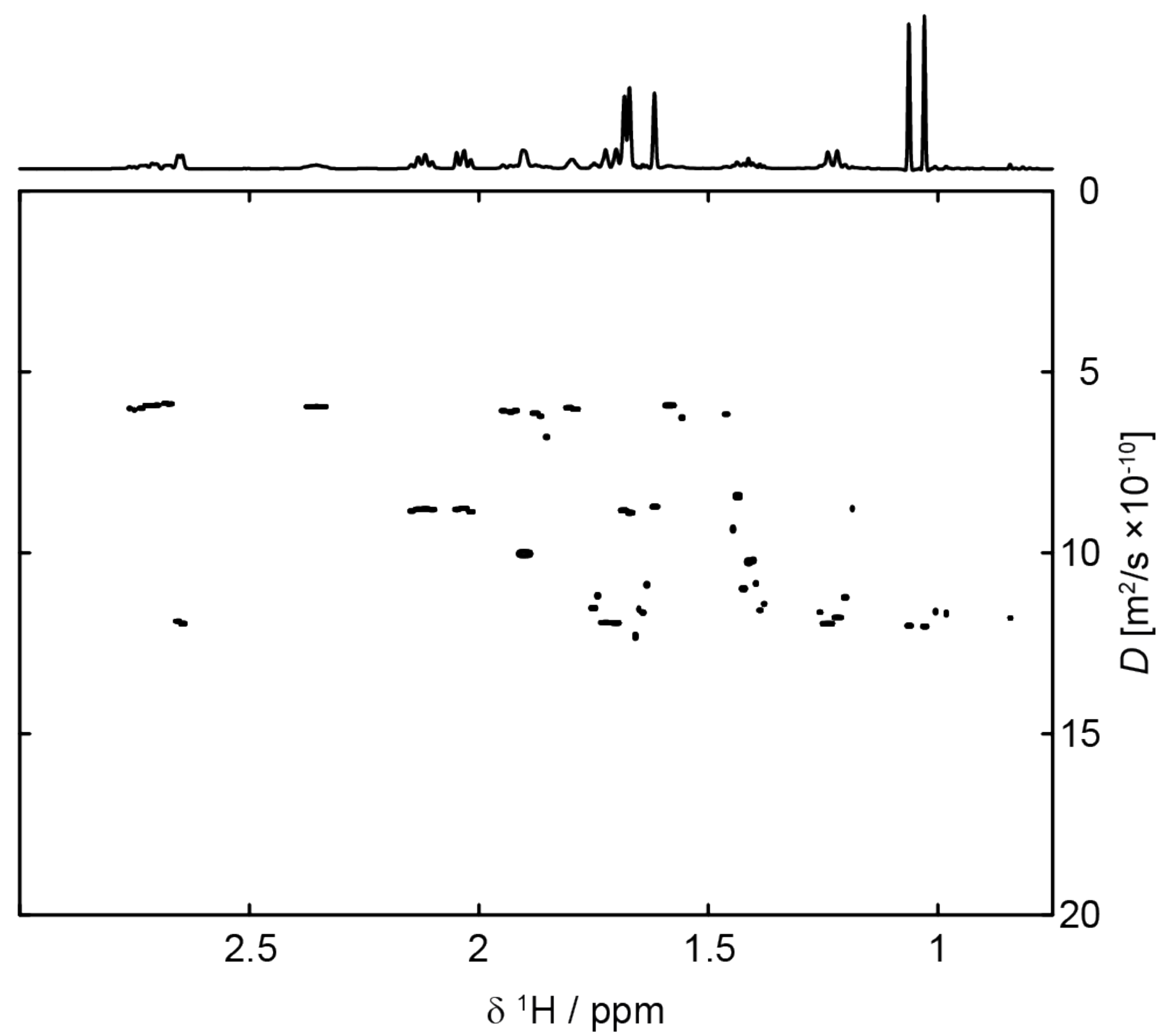
2

camphene



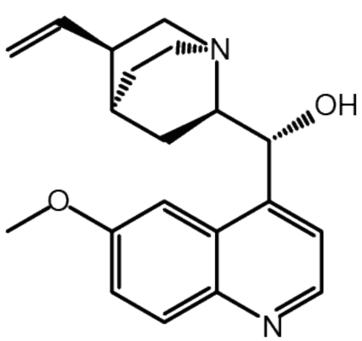
3

Oneshot DOSY



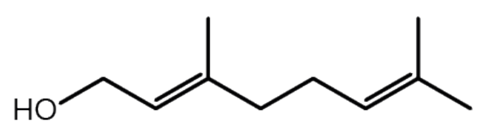
PSYCHE-*i*DOSY

quinine



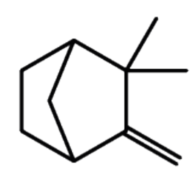
1

geraniol



2

camphene



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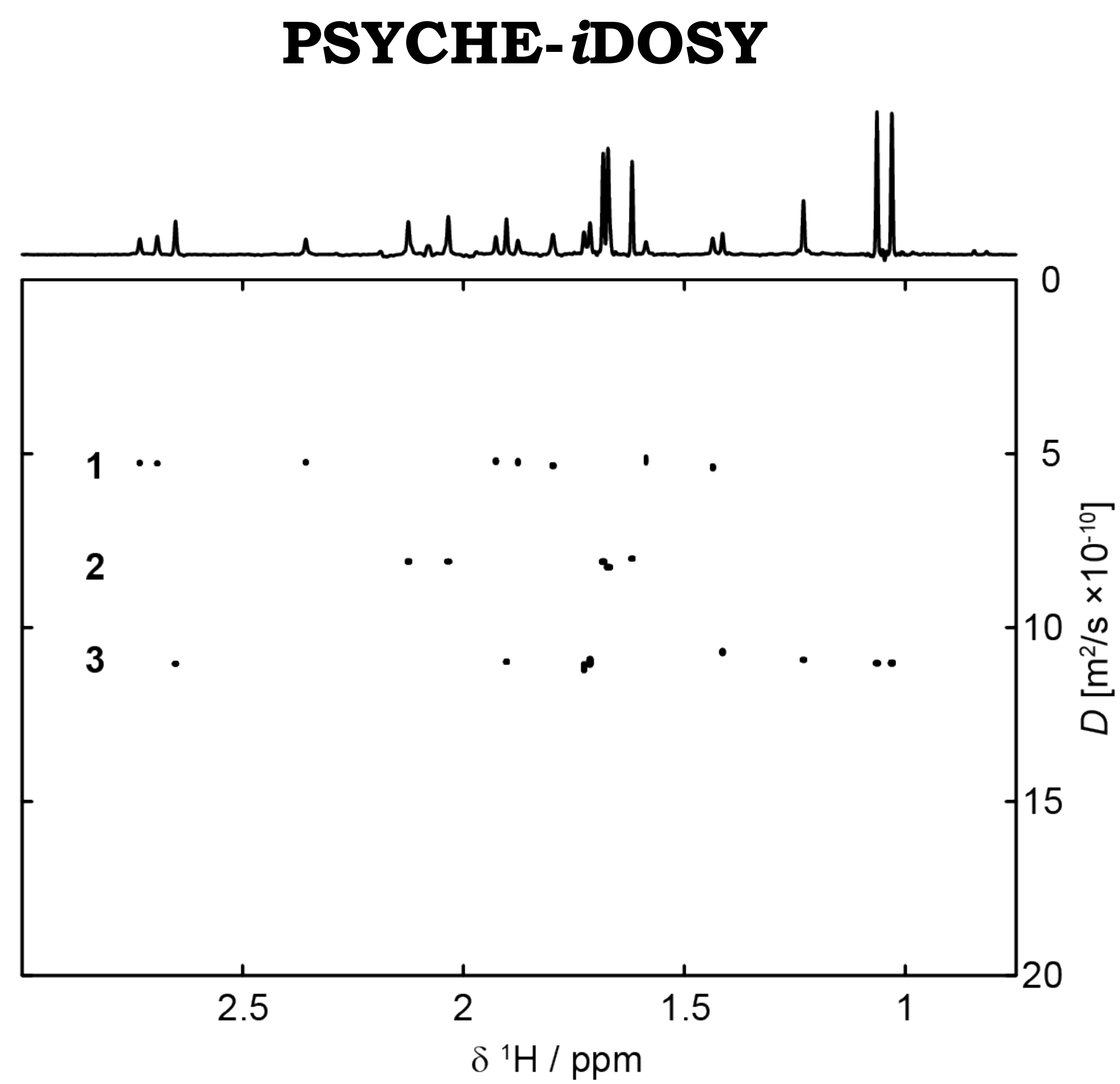

Angew. Chem. Int. Ed., **2016**, *55*, 15579.

PSYCHE-*i*DOSY

Due to the additional diffusion encoding during the PSYCHE pulse element, we need to add a correction term to the Stejskal-Tanner equation.

$$A\left(g_d^2\right) = \exp\left(-\gamma^2 D g_d{}^2\left(\Delta - \frac{\delta}{3}\right)\right)$$

PSYCHE-*i*DOSY

Due to the additional diffusion encoding during the PSYCHE pulse element, we need to add a correction term to the Stejskal-Tanner equation.

$$A\left(g_d^2\right) = \exp\left(-\gamma^2 D g_d{}^2\left(\Delta - \frac{\delta}{3}\right)\right)$$

Fortunately with a good approximation the corrected equation can be simplified to a form very close to the original Stejskal-Tanner equation, in which the only difference is an additional gradient offset added to the values of diffusion gradient in the gradient list.

$$A\left(g_d^2\right) = \exp\left(-\gamma^2 D\left(g_d + \Delta g\right)^2\left(\Delta - \frac{\delta}{3}\right)\right)$$

$$\Delta g = \frac{\pi\tau_p g_p\left(2\delta - 2\Delta + 4\tau_s + \tau_p\right)}{2\delta\left(\delta - 4\Delta\right)}$$

Angew. Chem. Int. Ed., **2016**, *55*, 15579.

Notes and Summary

- **Low-flip angle chirp pulses**: compromises should be made for maximum sensitivity and minimum recoupling signals
- **Sweep-rate of the pulse ($\Delta F/\tau_p$)**: for suppression of ZQ signals, COSY-type responses and strong coupling signals. Compromises should be made to maximize spectral purity and minimize signal loss due to relaxation and diffusion.
- **Gradient during pulse:** is used for spatial averaging and should be matched to the bandwidth of the PSYCHE pulse for the best performance.
- **TSE-PSYCHE** and **PSYCHE-2DJ** generally outperform original 1D PSYCHE experiment and are recommended as default experiments.

Thank you!

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