

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		<i>Lunch and poster session</i>
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		<i>Question and answer session</i>

A Pure Shift NMR Workshop

11.00 Gareth Morris **Welcome, introduction and history**

What ?

Why ?

Who ?

When ?

How ?

What *Is* Pure Shift NMR?

A pure shift spectrum is one in which peak positions are determined solely by chemical shifts, but ...

... in spectra of systems with homonuclear couplings, a perfect pure shift spectrum is an unattainable ideal: all we can do is to approximate it as closely as possible. Strong coupling sets fundamental limits on our ability to distinguish between coupled spins; and practicalities usually force us to compromise between sensitivity and spectral purity.

A Pure Shift NMR Workshop

What ?

Why ?

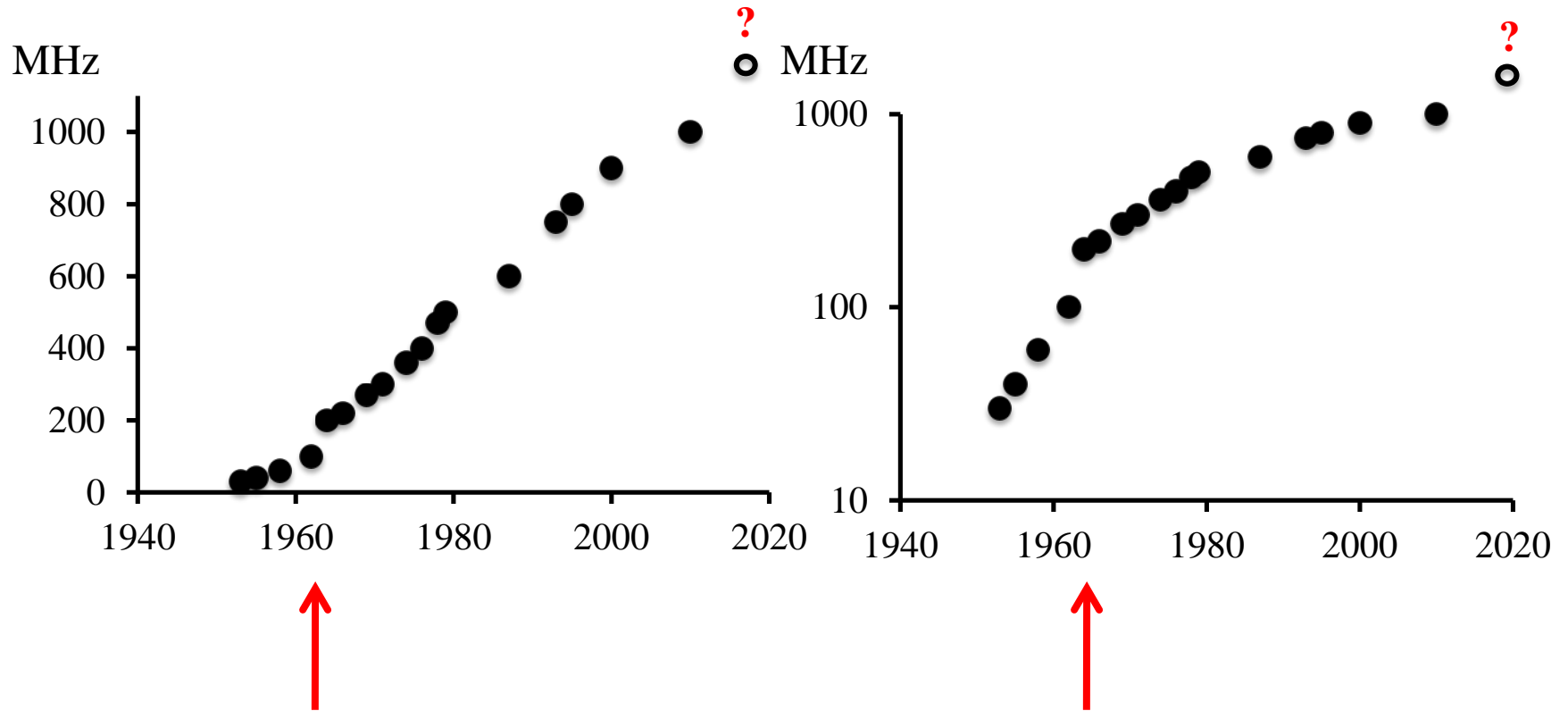
Who ?

When ?

How ?

Magnet Development: Proton Resonance Frequency by Year

Maximum commercially available spectrometer field as a function of year, on linear (left) and log (right) scale



Introduction of superconducting magnets

Is High Temperature Superconductivity the Answer?



A Pure Shift NMR Workshop

What ?

Why ?

Who?

When ?

How?

1962

... My own work dealt with the construction of high sensitivity radio frequency preamplifiers ... on the theoretical side, I was concerned with stochastic resonance ... **I tried in particular to design a scheme of homonuclear broadband decoupling to simplify proton resonance spectra. By applying a stochastic sequence with a shaped power spectral density that has a hole at the observation frequency, all extraneous protons should be decoupled without perturbing the observed proton spin.** The theoretical difficulties were mainly concerned with the computation of the response to nonwhite noise. Experiments were not attempted at that time, we did not believe in the usefulness of the concept anyway, and I finished my thesis in 1962 with a feeling like an artist balancing on a high rope without any interested spectators.

Richard Ernst, Nobel autobiography (1991)

1976 : 45° Projection of a 2D J Spectrum

Homonuclear broad band decoupling and two-dimensional J -resolved NMR spectroscopy*

W. P. Aue, J. Karhan, and R. R. Ernst

Laboratorium für Physikalische Chemie, Eidgenössische Technische Hochschule, 8006 Zürich, Switzerland
(Received 2 March 1976)

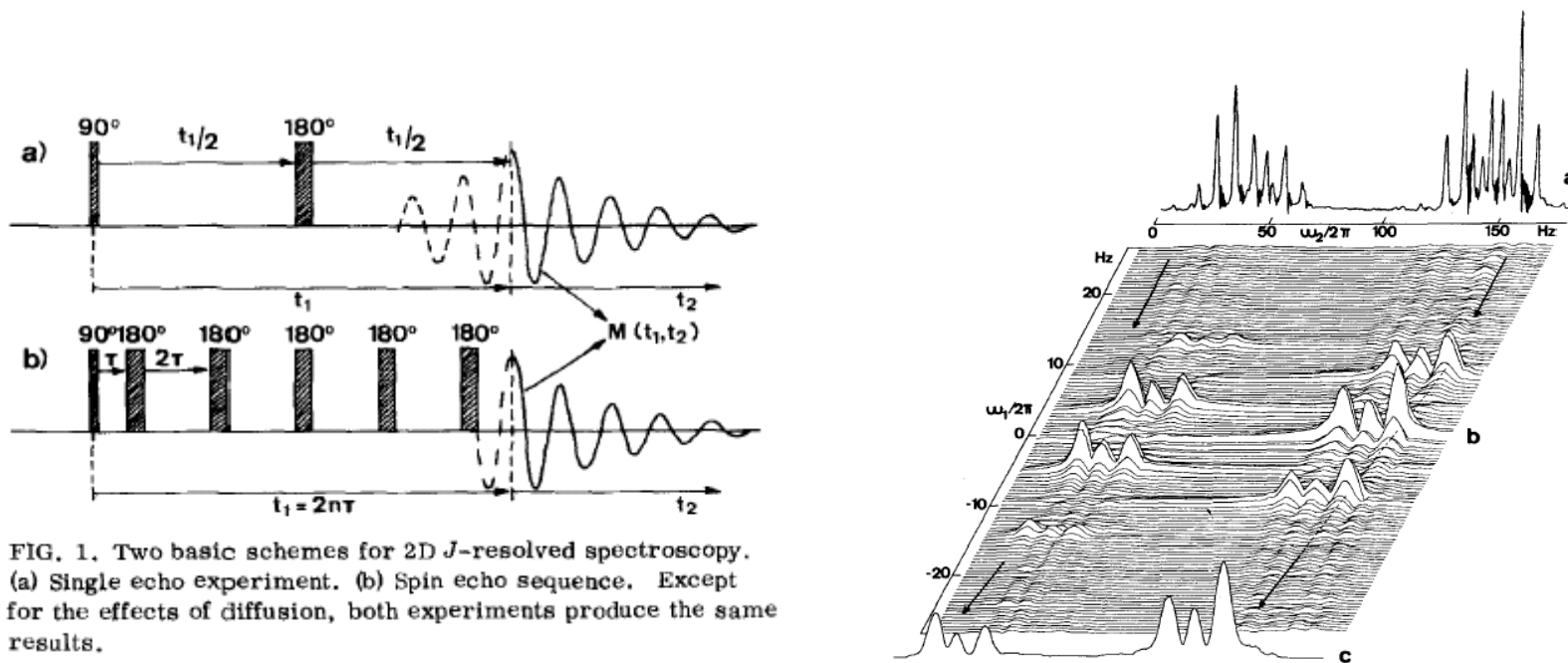


FIG. 1. Two basic schemes for 2D J -resolved spectroscopy. (a) Single echo experiment. (b) Spin echo sequence. Except for the effects of diffusion, both experiments produce the same results.

1978 : the Cross-Section – Projection Theorem in NMR

The Use of Cross-Sections and of Projections in Two-dimensional NMR Spectroscopy

K. NAGAYAMA,* P. BACHMANN,† K. WÜTHRICH,* AND R. R. ERNST†

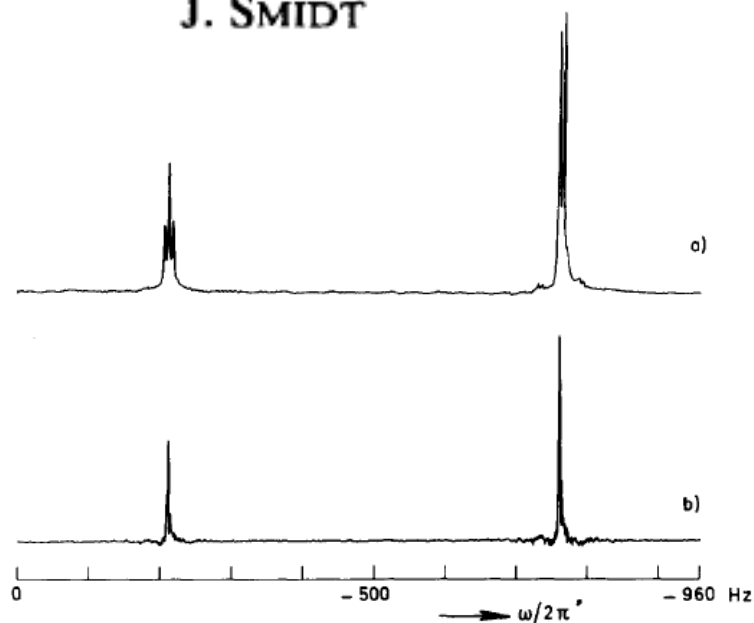
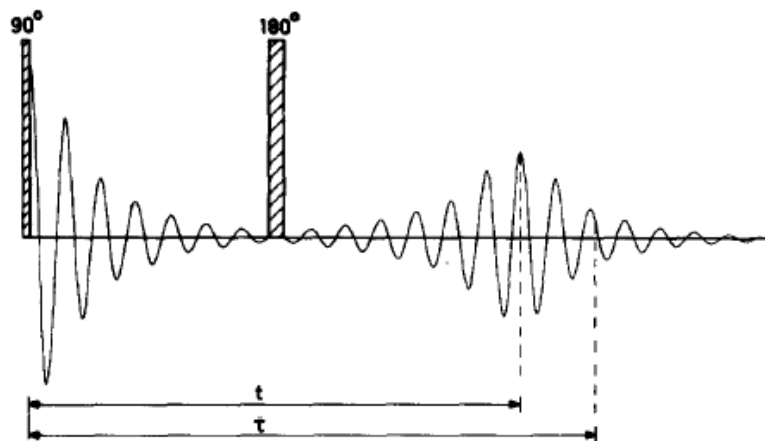
... This shows that the projections for $\pi/2 < \phi < \pi$ of the spectrum of any 2D physical response must be equal to zero.² This has important consequences for the projection of 2D *J*-resolved proton NMR spectra. The multiplet lines of a 2D *J*-resolved proton spectrum are aligned along straight lines with $\phi = \pi/4$. To obtain a completely decoupled proton spectrum, it is necessary to project the 2D spectrum $S(\omega_1, \omega_2)$ along lines with $\phi = \pi/4$ onto a line with $\phi = 3\pi/4$. This leads immediately to the conclusion that this projection is identical to zero and cannot be used in practice. ...

... An obvious remedy for saving the idea of complete decoupling of proton spectra by projection is to project an absolute-value spectrum. Here, cancellation of the intensities does not occur because the spectrum takes only positive values.

1979 : Constant-Time Evolution

Homonuclear Broadband-Decoupled Absorption Spectra, with Linewidths Which Are Independent of the Transverse Relaxation Rate

A. BAX
A. F. MEHLKOPF
J. SMIDT



1982 : BIRD

BILINEAR ROTATION DECOUPLING OF HOMONUCLEAR SCALAR INTERACTIONS

J.R. GARBOW, D.P. WEITEKAMP and A. PINES

Department of Chemistry and Lawrence Berkeley Laboratory, University of California, Berkeley, California 94720, USA

Received 1 September 1982; in final form 5 October 1982

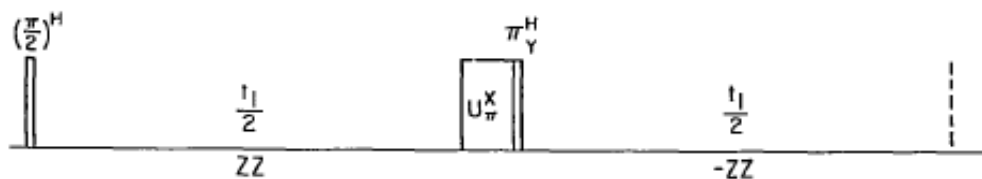
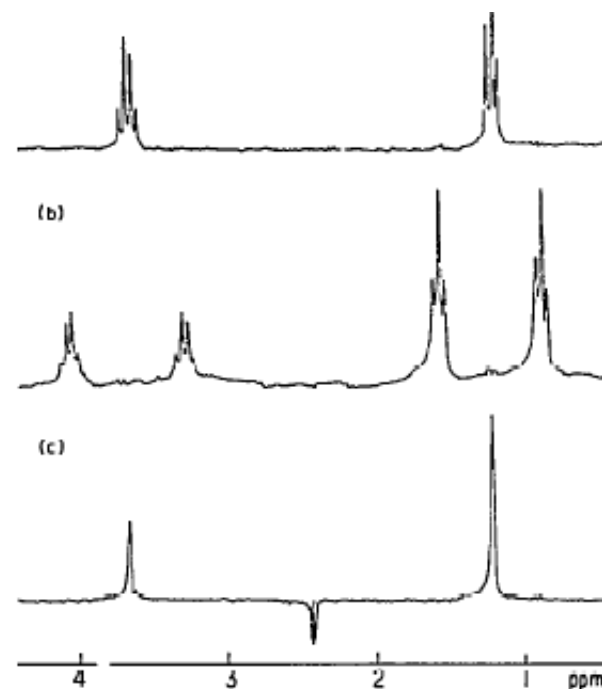


Fig. 1. Proton NMR spectra at 182 MHz of ethanol illustrating removal of J -couplings by BIRD. Samples were spun horizontally at 60–80 Hz in a vertical superconducting magnet with a horizontal solenoid r.f. coil.



1997 : Pattern Recognition in 2D J Spectra

Proton Chemical-Shift Spectra

SVETLANA SIMOVA,* HELMUT SENGSTSCHMID,† AND RAY FREEMAN

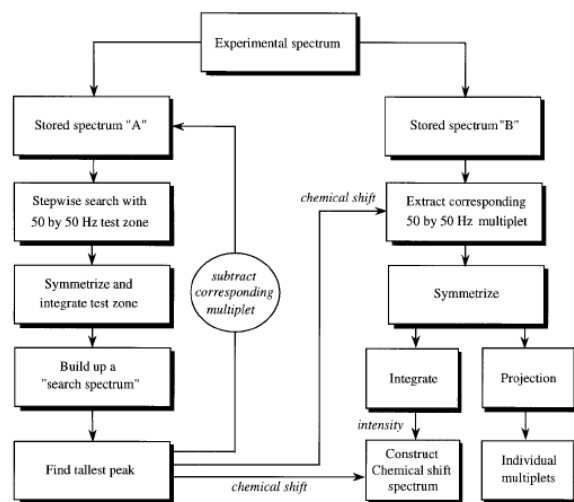


FIG. 5. Schematic flow chart of the program to extract chemical shifts and individual spin-multiplet patterns. Note that a second copy "B" of the experimental spectrum is used for the final processing stage; this avoids cumulative errors arising from repeated subtraction.

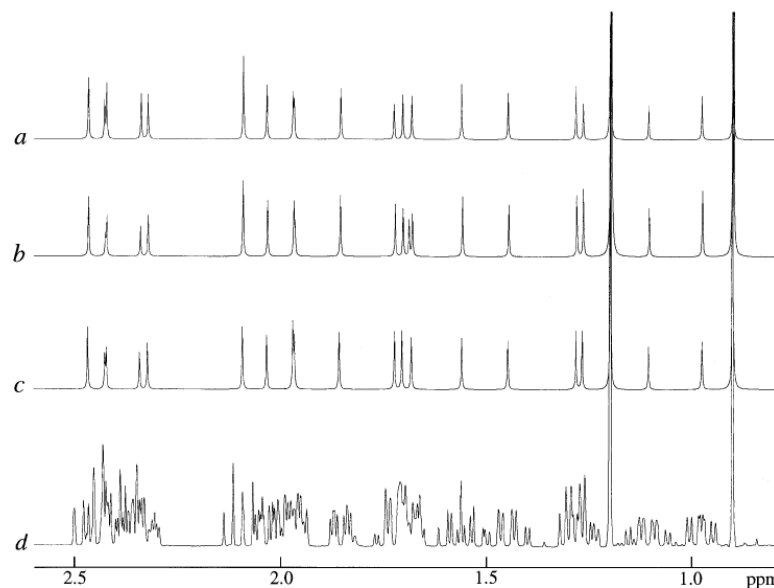


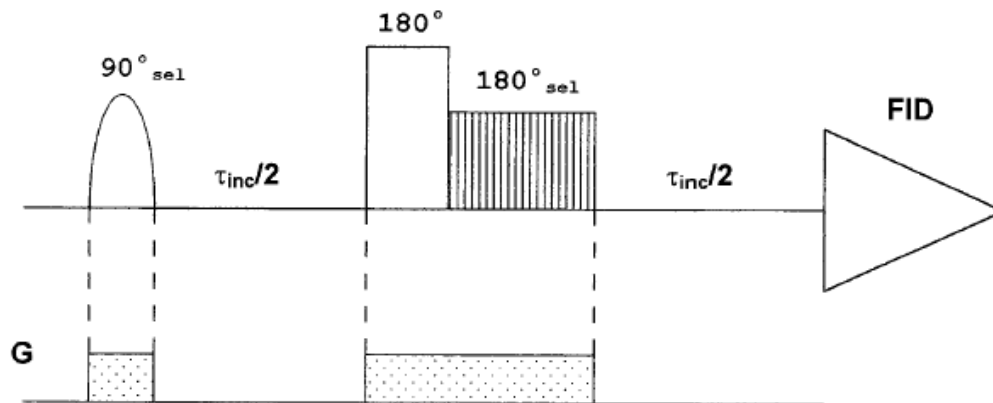
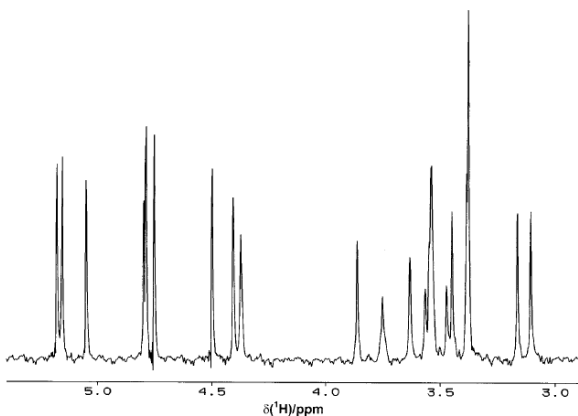
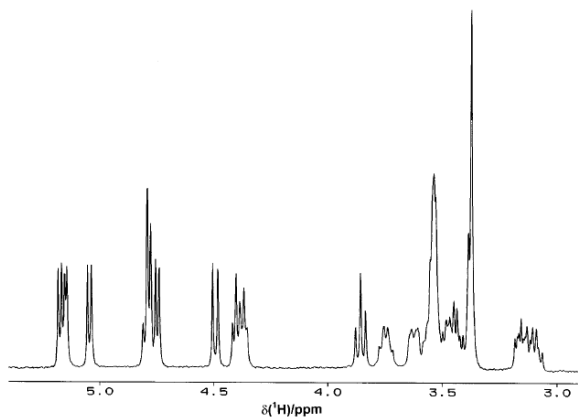
FIG. 15. Chemical-shift spectra of 4-androsten-3,17-dione obtained (a) from the reflected J spectrum, (b) from the purged J spectrum, and (c) from the z-filtered J spectrum. There is an additional response in (b) near 1.7 ppm from the residual water signal. The conventional spectrum (d) is included for comparison.

1997 : the Zangger-Sterk Method

Homonuclear Broadband-Decoupled NMR Spectra

KLAUS ZANGGER AND HEINZ STERK *

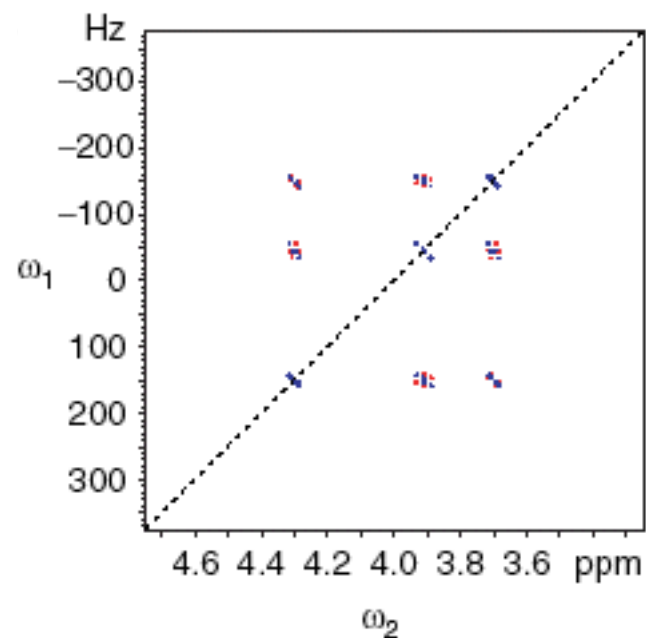
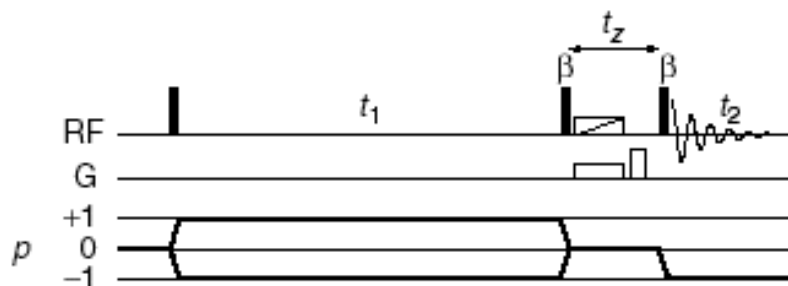
Institut für Organische Chemie, Karl-Franzens-Universität Graz, Heinrichstraße 28, 8010 Graz, Austria



2007 : Anti-z-COSY

Broadband proton-decoupled proton spectra[†]

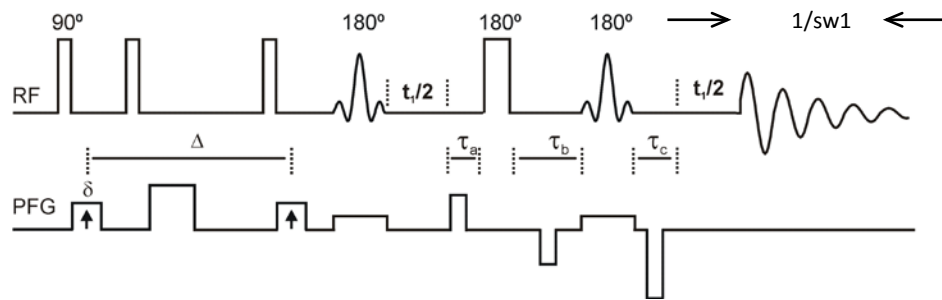
Andrew J. Pell,¹ Richard A. E. Edden² and James Keeler^{1*}



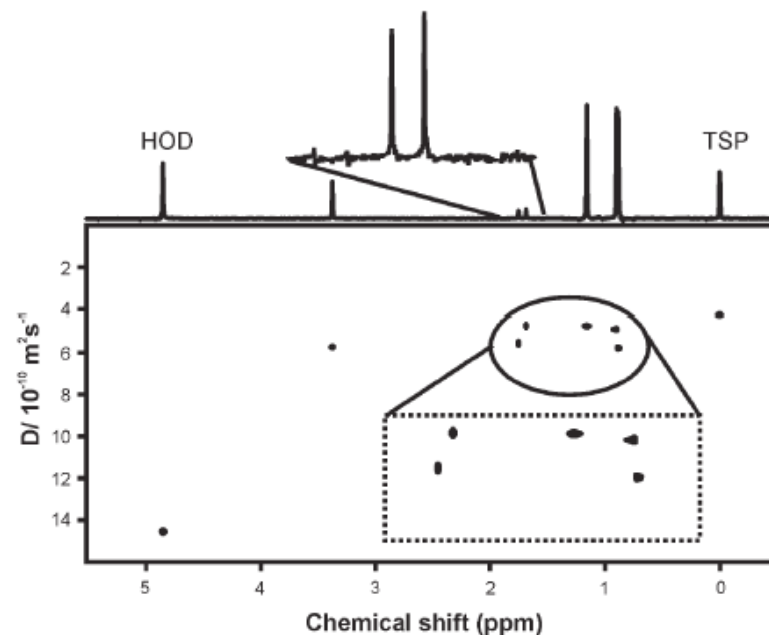
2007 : Zangger-Sterk Revisited / Pure Shift DOSY

Pure shift proton DOSY: diffusion-ordered ^1H spectra without multiplet structure

Mathias Nilsson and Gareth A. Morris*



PFGSTE ZS sequence for DOSY



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Pure Shift NMR: Broadband Homonuclear Decoupling

$$\hat{\mathcal{H}} = -\sum_i \nu_i \hat{I}_z^i + \sum_{i<j} J_{ij} \hat{I}^i \cdot \hat{I}^j \simeq -\sum_i \nu_i \hat{I}_z^i + \sum_{i<j} J_{ij} \hat{I}_z^i \hat{I}_z^j$$

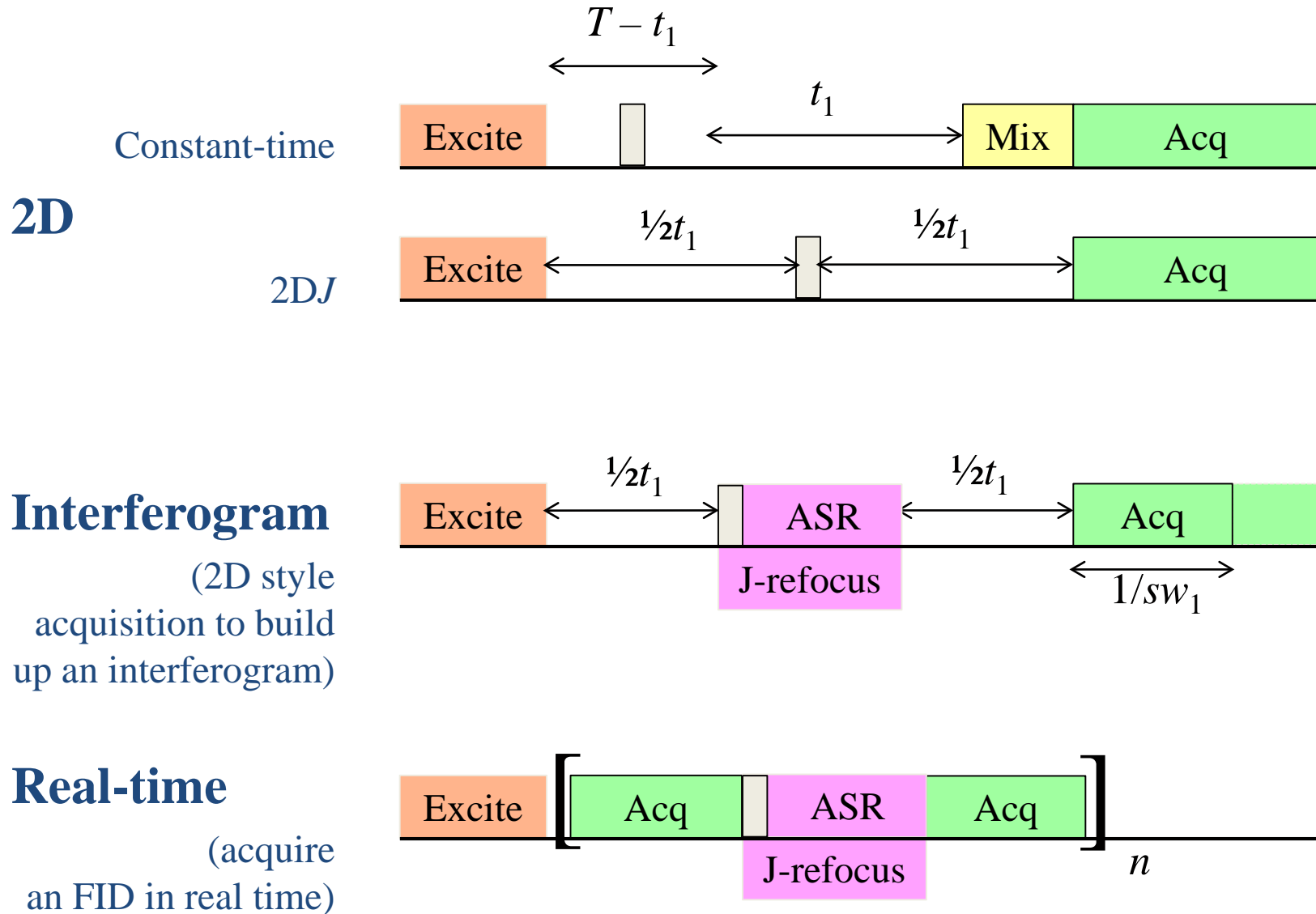
Shifts

Couplings

Need a general method for separating the effects of shifts (δ) and couplings (J), e.g.

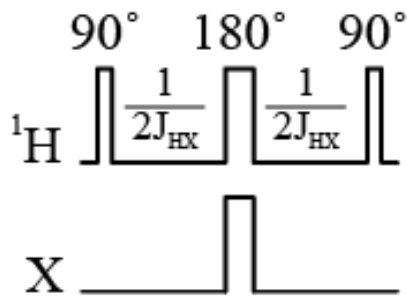
- hard 180° pulse
 - reverses effects of δ but not of J
- “active spin refocusing”
 - reverses both δ and J , but for active spin only, leaving passive spins unperturbed

Pure Shift NMR: Acquisition Methods



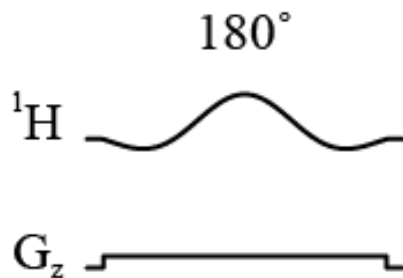
“Active Spin Refocusing” Methods

Divide the available spins into *active* spins that we observe, and *passive* spins that we manipulate to suppress the effects of couplings



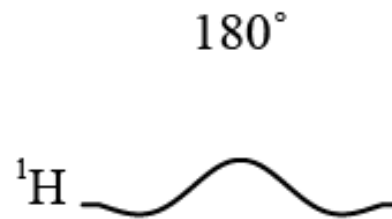
BIRD

Bilinear Rotation Decoupling:
 π rotation of protons coupled to ^{13}C



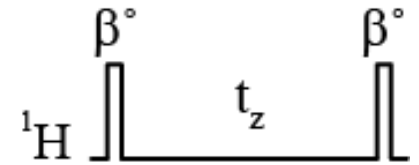
ZS

Zangger-Sterk:
 slice- / shift-selective π rotation



BS

Band-Selective homonuclear decoupling:
 shift-selective π rotation



“double β ”
 (PSYCHE)

PSYCHE / anti-z-COSY:
 π rotation of a fraction $\sin^2\beta$ of spins

Classifying Pure Shift Methods: Acquisition Modes

2D 2D *J* spectroscopy (with 45° projection; absolute value)
Filtered 2D *J* spectroscopy (with post-processing)
Pell-Keeler 2D *J* spectroscopy (with 45° projection)
Constant-time (CT) evolution

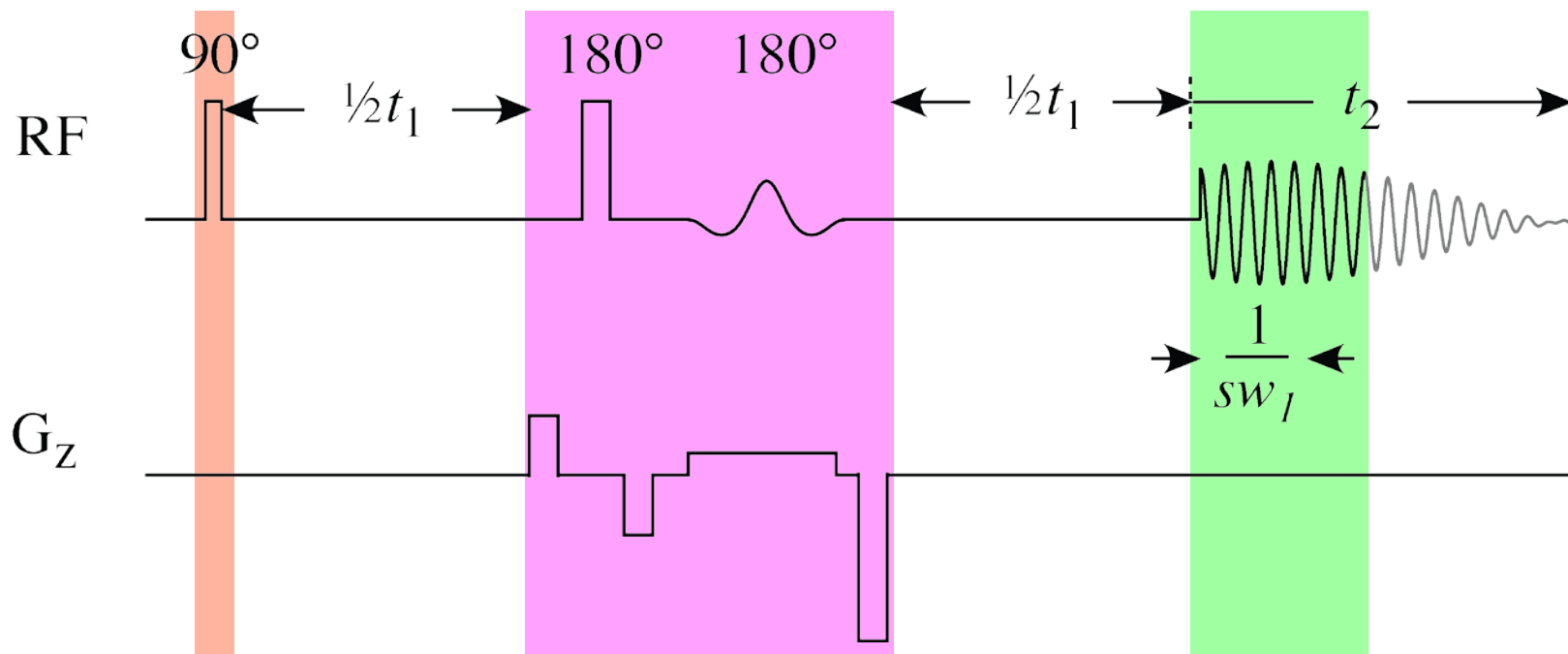
Interferogram Zangger-Sterk
BS
BIRD
PSYCHE
R-type Pell-Keeler 2D *J* spectroscopy

Real-time BIRD
BASHD
Zangger-Sterk

Classifying Pure Shift Methods: Pulse Sequence Types

Hard 180°	2D J spectroscopy with 45° projection (absolute value)
	Filtered 2D J spectroscopy (with post-processing)
	Constant-time (CT) evolution in nD NMR
Active Spin Refocusing	Band-selective homodecoupling (BS) (shift selection)
	Zangger-Sterk method (spatial and shift selection)
	Bilinear Rotation Decoupling (BIRD, isotopic selection)
	PSYCHE (statistical selection)
Hybrid	Pell-Keeler 2D J spectroscopy (using ZS, BIRD, BS or PSYCHE) with 45° projection (phase sensitive)
	Anti-z-COSY (statistical selection)

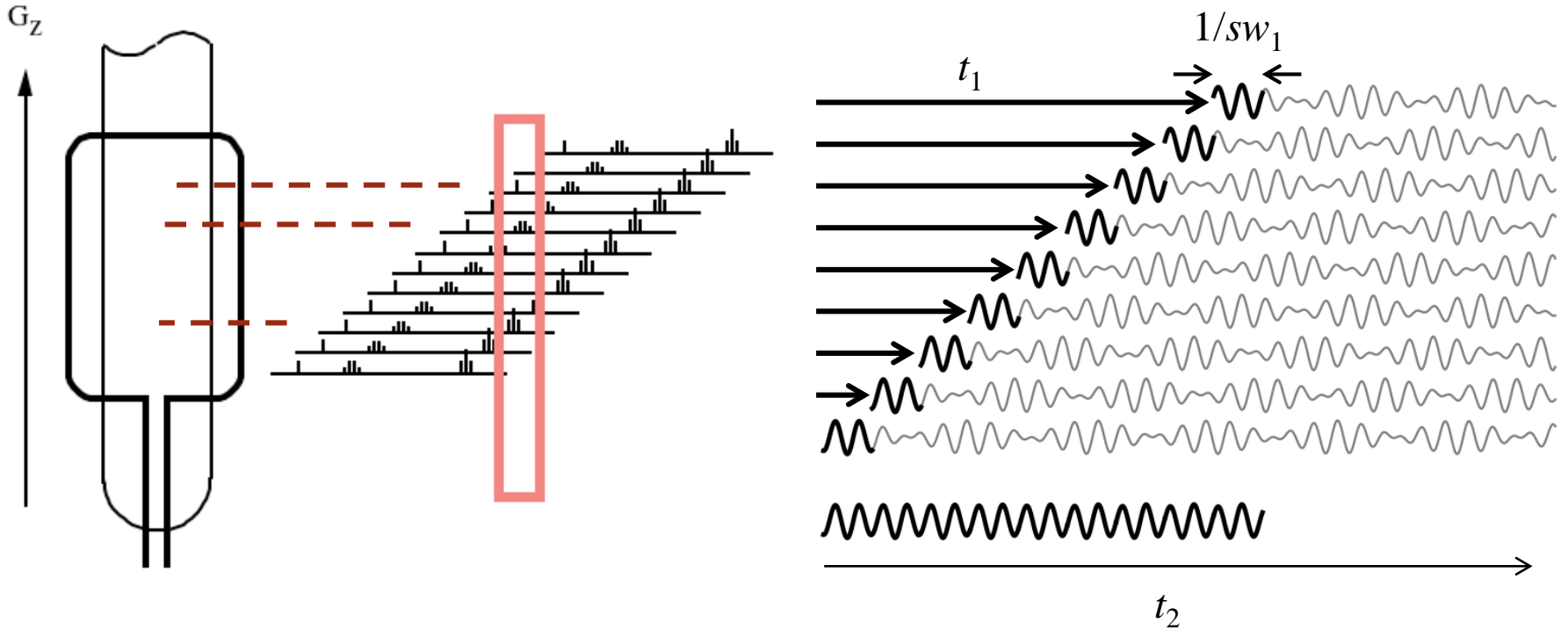
Zangger-Sterk Pure Shift NMR



δ	+	+	+
J	-	+	+

The combination of a hard 180° pulse and a slice- and shift-selective 180° pulse leaves the active spins (within the slice) unperturbed and the passive (outside the slice or at a different shift) inverted, refocusing the J modulation of the active spins.

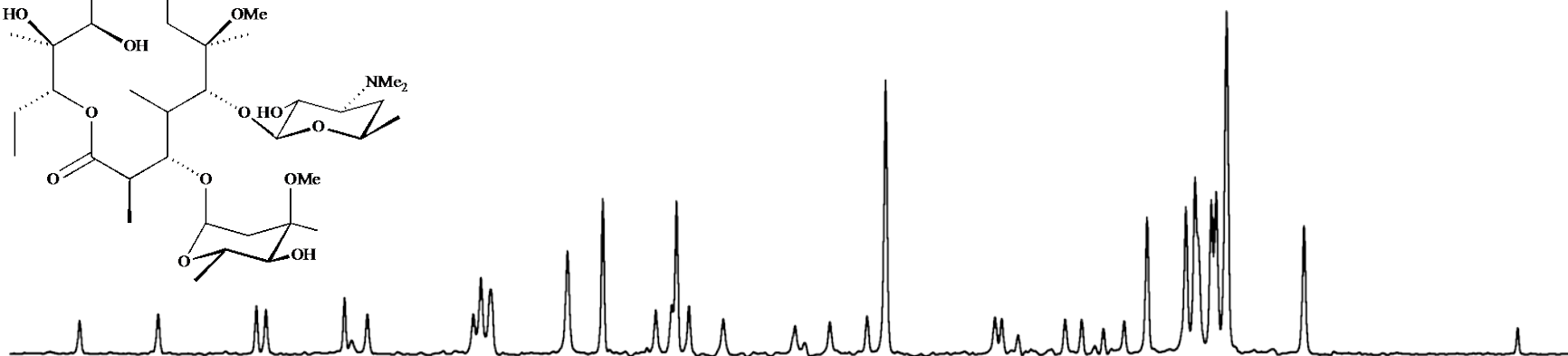
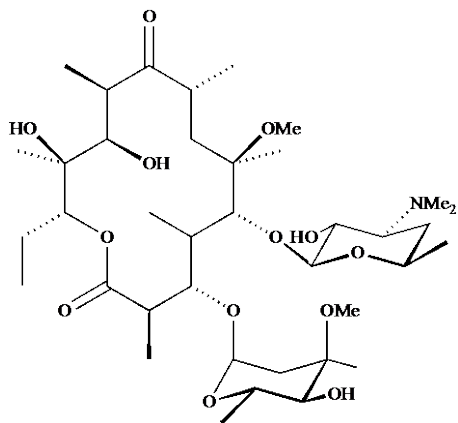
Mechanics of the Zangger-Sterk Experiment



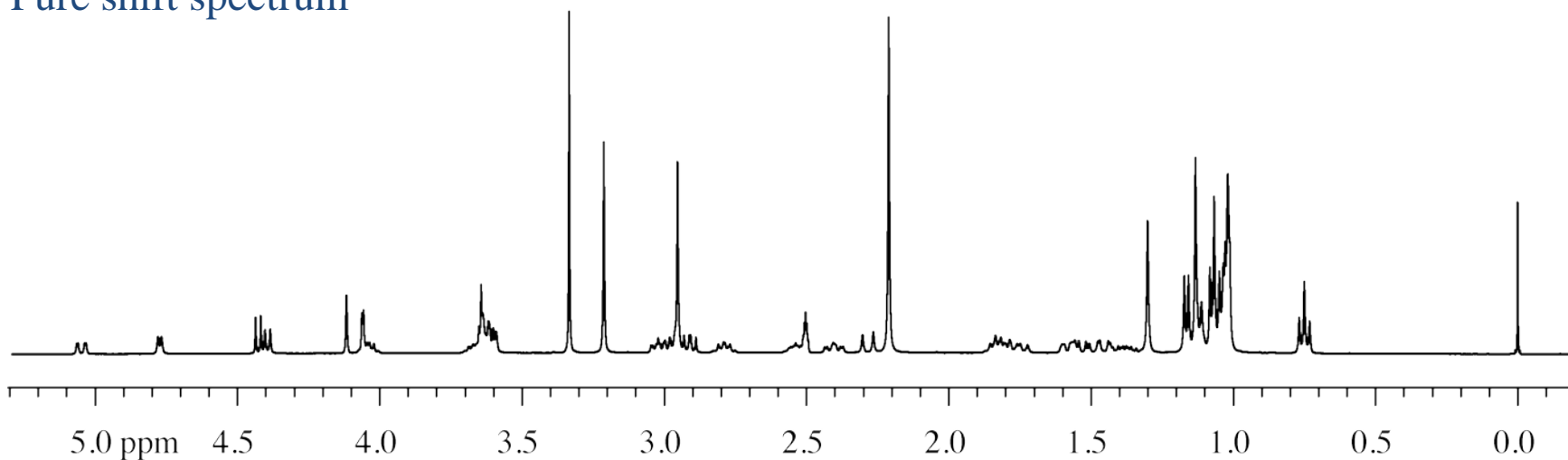
Soft and hard 180° pulses invert passive spins, refocusing J modulation *but leaving shift evolution intact*

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 residual effect of J is to cause weak sidebands at multiples of sw_1 .

400 MHz ZS Pure Shift ^1H Spectrum of Clarithromycin



Pure shift spectrum



Conventional spectrum

Acknowledgments - Manchester

Ralph Adams, Juan Aguilar, Adolfo Botana, Liam Byrne, Laura Castañar, Yingxian Chen, Matt Cliff, Adam Colbourne, Guilherme Dal Poggetto, Rob Evans, **Steve Faulkner**, Mohammadali Foroozandeh, Saidul Islam, Peter Kiraly, Andy McLachlan, Nicola Meharry, Pinelopi Moutzouri, **Mathias Nilsson**, Liladhar Paudel, Matthew Powner, **John Sutherland**, Iain Swan, **Jon Waltho**

Acknowledgments - Funding



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