Interferogram and real-time acquisition methods

Peter Kiraly

NMR Methodology Group,
School of Chemistry, University of Manchester

Workshop on Pure Shift NMR
12th Sep 2017
Outline

• Why are we interested in decoupling?

• Basic concepts in pure shift NMR
  • Active and passive spins
  • Active spin refocusing elements: BS / Zangger-Sterk / PSYCHE / BIRD

• The interferogram acquisition method
  • Theory and pulse sequences
  • Illustrative examples

• The real-time acquisition method
  • Theory and pulse sequences
  • Illustrative examples

• Summary
Partial $^{13}$C NMR spectrum of estradiol in DMSO-d$_6$ with (bottom) and without (top) proton decoupling.
Suppressing multiplet structure – homonuclear decoupling

Partial $^1$H NMR spectrum of glucose in D$_2$O

$^1$H NMR of glucose in D$_2$O

conventional $^1$H

pure shift
The concepts of spin decoupling

Heteronuclear decoupling
WALTZ / GARP / adiabatic bi-level

Homonuclear decoupling

1. time management
2. selectivity problem

pure shift

?
Active and passive spins in pure shift NMR

50 mM quinine in dmsø-d₆

pure shift

conventional $^1$H

50 mM quinine in dmsø-d₆
all work by differentially manipulating active and passive subpopulations of protons
all work by differentially manipulating **active** and **passive** subpopulations of protons
Double spin echo experiment with an ASR element

- **Excitation 90° pulse**
- **Broadband 180° pulse**
- **Active spin refocusing 180° pulse**
- **Chunk 4τ₁**
- **Acquisition**

Chemical shift is refocused at the beginning of acquisition, but …

... homonuclear coupling (J) is refocused 2τ₁ later

J-evolution is negligible during the first few data points (period 4τ₁) delivering a small chunk of the desired pure shift FID.
Interferogram pure shift experiment – 2D acquisition

Analogous to 2D NMR

J << \( \delta \) allows data acquisition in ‘chunks’ of duration 1/sw1
The interferogram pure shift pulse sequence

- Chemical shift is refocused $\Delta = \text{[integer]} / \text{sw}$ later than the beginning of acquisition
- $J$ is refocused at the midpoint of each chunk ($4\tau_1$)
- Incremented delay allows recording all chunks of pure shift FID (during $t_1$ $\delta$ evolves, but $J$ is refocused)
- Phase cycle and/or PFG pairs can enforce CTP selection
The triple spin echo analogue with an ASR element

- Frequency-swept broadband pulses can be implemented
- Useful to deal with strong coupling artefacts e.g. in TSE-PSYCHE
- Duration of the chunk is not limited by duration of gradient pulses, but more relaxation loss
Resolution in interferogram pure shift experiments

Interferogram band-selective pure shift spectra of an AX spin system calculated in Matlab/Spinach.

(20 ms chunk duration; $J_{AX} = 10$ Hz)
Effect of duration of chunk (SW₁)

Interferogram band-selective pure shift spectra of an AX spin system calculated in Matlab/Spinach. (AQ = 1.3 s; J_{AX} = 10 Hz)
Effect of RF phase instability (scan-to-scan)

Interferogram band-selective pure shift spectra of an AX spin system calculated in Matlab/Spinach. 
(AQ = 1.3 s; $J_{AX} = 10$ Hz; $SW_1 = 50$ Hz)

Phase irreproducibility

± 0°

± 1°

± 3°

± 5°

Analagous to $t_1$-noise in 2D NMR

Interleaved 2D data acquisition is advisable for long experiments
Speeding things up

interferogram approach

*J. Magn. Reson.*

**124**, 486 (1997)

a set of experiments

1st experiment

2nd experiment

3rd experiment

4th experiment

Pure shift FID

real-time approach

1 single experiment

*J. Magn. Reson.*

**218**, 141 (2012)
Chunks are collected from a single scan.

Resolution is worse compared to interferogram experiment, because of relaxation, diffusion/convection, and cumulative errors of pulse imperfection.
Relaxation losses in real-time experiments

Selected traces of real-time pure shift HSQC BIRD. The total echo time ($\tau_r$) of the $J$-refocusing element was incremented.

Broadening here is due to proton $T_2$ relaxation.
Effect of BIRD timing error

If $\tau = 1 / (2 \times J_{\text{CH}})$, then BIRD element refocuses the $^{13}\text{C}$-attached protons.

Selected traces of real-time pure shift HSQC BIRD ($^{1}\text{CH} = 190 \text{ Hz}$). The echo time ($\tau$) of the BIRD element was varied (HSQC sequence element was kept constant).

Broadening here is due to BIRD timing error.
Effect of pulse imperfection in real-time pure shift HSQC using BIRD

Gradient pulses omitted, basic phase cycle, and no supercycle...

2nd carbon 180 pulse is omitted in BIRD...

G_{1-4} varied chunk-to-chunk extended phase cycle (*2), and MLEV-16 supercycle...

... extra signals next to the pure shift signal and $F_1$ mirror images

... extra signals appear due to heteronuclear $J$-evolution during $\tau_2$

... clean
$^{15}\text{N HSQC}$ of L80C mutant N-PGK protein in water (90\%H$_2$O / 10\%D$_2$O)

N-terminal domain of PGK

10 mg amikacin in D$_2$O
Mixture of glucose, trehalose, raffinose, and α-cyclodextrin

13C HSQC

$\delta_{13c}$

ppm

pure shift $^{13}$C HSQC

$\delta_{1H}/$ ppm
Interferogram vs real-time pure shift NMR

50 mM quinine in dmso-d$_6$

conventional $^1$H

interferogram Zangger-Sterk

real-time Zangger-Sterk

experiment time

0.5 min

5 min 30 s

0.5 min
Summary

Interferogram experiments

- Resolution enhancement requires extended experiment time
- There is a trade-off between experiment time and quality of spectrum
- Many kinds of active spin refocusing element are available
- System instability may affect very high resolution experiments

Real-time acquisition

- Experiment times of parent and pure shift methods are practically identical
- Simultaneous sensitivity and resolution enhancement in real-time HSQC using BIRD
- Resolution enhancement is limited by relaxation, diffusion/convection, and pulse imperfection
- Lock disturbance can be a problem in high resolution experiments
Acknowledgements

Gareth Morris, Mathias Nilsson
and the NMR Methodology Group

http://nmr.chemistry.manchester.ac.uk/

Funding
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 Ėriks Kupčė  Bruker shaped pulse implementation
15.30  Question and answer session

University of Manchester, 12th September 2017