Introduction

Speeding-up NMR molecular analysis is an important research field which has been continuously advancing since NMR early days. The relevant benefits are clear and evident:

- Reduce analysis time per sample ➔ reduce analysis cost.
- Gain Spectrometer time to analyze new samples ➔ improve spectrometer efficiency.

Multiple FID Acquisition (MFA) strategy consists in the design of a pulse sequence experiment accommodating N acquisition windows, each registering different relevant structural information. This strategy is faster than performing a traditional sequential acquisition of N separated experiments. Mainly, time savings come from skipping long 1st recovery delay. Several design strategies are possible:

Orthogonal CTP Acquisition (Coherence Transfer Pathways) was firstly described in the COCONOSY experiments[1], were COSY and NOESY experiments where combined in one (COSY was acquired during NOESY mixing time).

Afterglow Acquisition, that is the application of a mixing sequence after the FID, transforming signal to new information which is then acquired again. Typical mixings are COSY, RELAY and TOCSY transfers. Applications have been demonstrated successfully in the obtention of up to 4 experiments in a single 1, in both, homonuclear and heteronuclear experiments[2].

NODA (NMR Ordered Acquisition with 1H-detection)[3]. This strategy nest independent experiments ordered from low to higher sensitive and waits for a single recovery delay. Table below summarize its properties in a two

Orthogonal CTP Acquisition

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exp1 embedded in Exp2</td>
<td>Exp1 and Exp2 are nested</td>
</tr>
<tr>
<td>Exp1 and Exp2 shares d1 and t1</td>
<td>Exp1 and Exp2 have a single common d1 but independent t1</td>
</tr>
<tr>
<td>Orthogonal CTP acquired</td>
<td>Continuous CTP acquired</td>
</tr>
<tr>
<td>2nd Magnetization stored in z-axis during 1st FID</td>
<td>2nd Magnetization comes from acquired 1st FID</td>
</tr>
<tr>
<td>Diffusion dependency in FID</td>
<td>Signal Saturation dependency (recovery between experiments)</td>
</tr>
<tr>
<td>Standard FID allowed</td>
<td>Truncated FID (moderate resolution)</td>
</tr>
<tr>
<td>Typically 2 FID recorded</td>
<td>Up to 4 FID are plausible</td>
</tr>
</tbody>
</table>

MFA TOCSY/TOCSY experiment where two equivalent CTPs components are acquired in interleaved mode. Sequence incorporates gradient-enhanced CTP selection based on the well-known echo-anti-echo acquisition and processing protocols to provide pure absorption line shapes.

FID1 is designed to observe exclusively transverse $I_z$ components generated during the $T_1$ mixing time, whereas the other $I_z$ component remains non-observable. After that, the purging G2 gradient is applied to remove any residual transverse magnetization, and a subsequent 90° pulse flips the unexploited $I_z$ component to the transverse plane to be acquired during a second acquisition period FID2 inserted after another TOCSY transfer. This method allowed the single-shot dual acquisition of two different TOCSY experiments sharing the same variable $t_1$ period but recorded with two different mixing times ($T_1$ and $T_2$, respectively). It is important to comment that a slight reduction in sensitivity is observed in FID2 due to diffusion. Nevertheless, the benefits of sensitivity per time unit are demonstrated to be favorable using MFA compared to sequential acquisition.

MFA TOCSY/TOCSY pulse sequence scheme

MFA offers a time-efficient strategy, recording equivalent pathways in a dual interleaved mode.

Interleaved Dual NMR Acquisition of Equivalent Transfer Pathways in TOCSY

Spectral Aliasing in Dually Acquired HSQC (SADA-HSQC)

In SADA-HSQC experiment two equivalent CTPs components are acquired in interleaved mode, allowing to obtain two HSQC with different spectral widths simultaneously. The key point is the differential $T_1$ evolution for each orthogonal magnetization component. While term I and term II evolves equally during $T_1$, there is an extra period $(1-1)/T_1$ where term I continues to evolve, while term II is stored as zz-magnetization. Thus, the SADA-HSQC experiment yields a 2D HSQC spectrum with its full spectral width (SW1++) in FID2 whereas an aliased HSQC spectrum showing a reduced SW1 aliased according to the $k$ factor is obtained in FID1:

$$\text{SADAaliased = SWINormal}/k$$

It is important to remark, that such designs are not incompatible one each other and can be combined between them. For instance, a triple COSY/TOCSY/TOCSY experiments can be designed in many different ways[4]. Another example is a zz-filter NOAH-2BS[5] design where first experiment HMBC stores Z-magnetization to be used for the second HSQC therefore minimizing saturation losses on it.

In this poster is presented the design of the Interleaved (orthogonal) CTP acquisition of Equivalent Transfer Pathways in Sensitivity Enhanced (SE) version of TOCSY and HSQC. Due to poster space requirements only two of the possible applications are shown[6].

References


Summary

- MFA offers a time-efficient strategy, recording equivalent pathways in a dual interleaved mode.
- Acquiring two TOCSY with different mixing time in a single experiment is shown.
- Acquiring conventional and aliased HSQC spectra in a single experiment is demonstrated.