Two-dimensional NMR spectroscopy on a desktop NMR system

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Desktop NMR system

Two-dimensional (2D) NMR spectroscopy is a general concept that enables chemical information to be encoded into a second dimension making use of spin-spin interactions like the *J*-coupling. It is particularly useful to simplify 1D spectra with overlapping signals and to identify coupled chemical groups. While 2D techniques are routinely used at high field they are not exploited on desktop spectrometers. One of the main reasons for this is the high stability required to sample the data along the indirect dimension. To keep the frequency stable with the accuracy required by these methods, conventional spectrometers are equipped with a lock system that eliminates any drift or fluctuation of the magnetic field. Furthermore, the acquisition of meaningful 2D spectra is only possible if the spectrometer provides enough resolution and high signal-to-noise, otherwise the acquisition time for a 2D spectrum can become excessively long.

In this work we demonstrate the performance of 2D NMR on a 1 Tesla permanent magnet. The magnetic field homogeneity of the magnet can be finely shimmed to achieve sub Hertz resolution by means of shim coils up to order three (see Fig. 1), and high field stability is achieved by means of an external lock system. The results presented here demonstrate that 2D NMR is of great assistance at low field where the spectrum of small molecules may appear crowded due to the strong coupling limit.

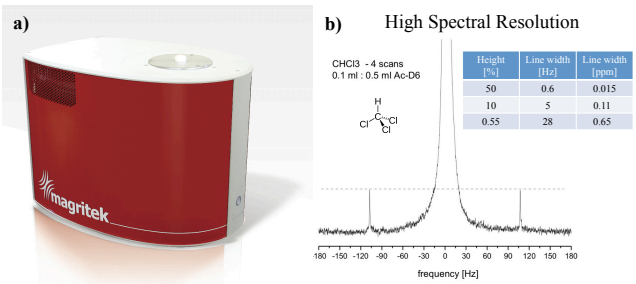
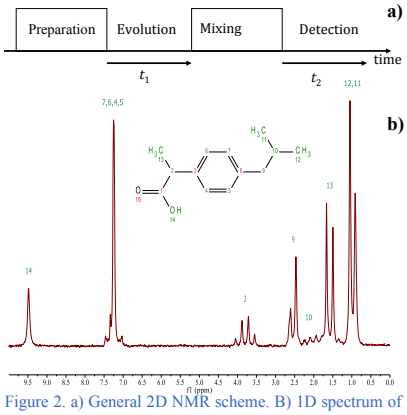


Figure 1: a) Desktop High-resolution NMR system. b) Spectrum of chloroform illustrating the high resolution and sensitivity of the NMR spectrometer.

Methods and sample

The basic scheme of 2D NMR consists of four intervals (Figure 2a). The spin system is prepared to a non-equilibrium state during the *preparation* period. During the *evolution* period, the spin system evolves under the influence of certain couplings. In order to obtain a two-dimensional spectrum, a series of spectra is obtained where the duration t_1 of the evolution delay is incremented. The *mixing* process selects the type of spin coherence to be observed during the detection period. Usually, the duration of the mixing period is fixed in a 2D experiment. During the *detection* period, the transverse magnetization is measured as a function of t_2 in the same way as it is measured in 1D spectroscopy. Since the signal is detected directly along the t_2 dimension, this dimension is usually referred to as the direct dimension, whilst the t_1 dimension is called the indirect dimension. From the large variety of available 2D pulse sequences we tested the performance of *J*-resolved spectroscopy, correlation spectroscopy (COSY), and double quantum filtered COSY.



The example molecule used in this work is Ibuprofen (Fig. 2b). This fairly small molecule (M = 206 g mol^{-1}) exhibits a 1D proton spectrum which has some overlapping multiplets, particularly in the region between 0.50 and 3.00 ppm. To the untrained eye, it may not be clear whether the multiplicities of these peaks are multiplet splittings belonging to the *same* functional group, or result from the chemical shifts of *different* functional groups.

Figure 2. a) General 2D NMR scheme. B) 1D spectrum of 200 mM Ibuprofen in $CDCl_3$. The spectrum was acquired with a single 10 second scan

Correlation spectroscopy

One of the most common 2D experiment used by organic chemists is the homonuclear correlation spectroscopy (COSY) experiment. A COSY spectrum identifies the proton signals from magnetically coupled chemical groups, which in many cases can be directly related to carbon skeleton connectivity in molecules. In this work we implemented a phase sensitive COSY (a) and a phase sensitive double quantum filtered (DQF) COSY sequence (b).

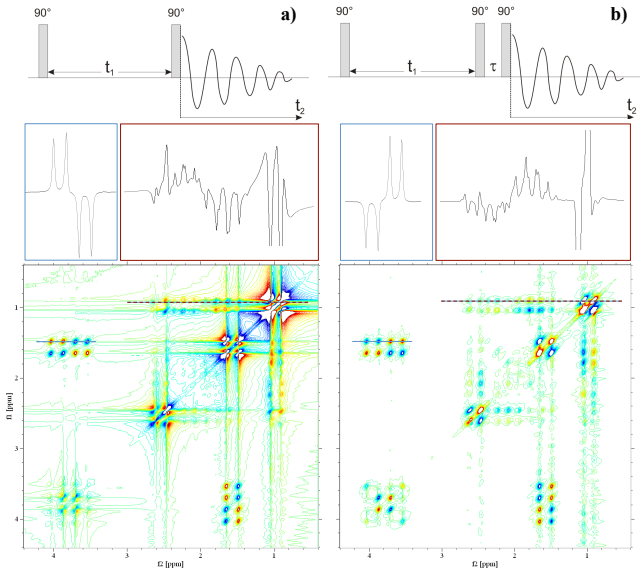


Figure 3. COSY (a) and DQF-COSY (b) of Ibuprofen. The 2D experiments were measured with 256 steps along the indirect dimension with a dwell time of 2 ms. Along the direct dimension 2 sec were acquired using a dwell time of 1 ms. Four and eight scans were used respectively with the phases required to apply the States method to produce pure absorptive 2D spectra. While the COSY spectrum has dispersive diagonal peaks, the DQF version produce pure absorptive cross and diagonal peaks. This is particularly advantageous at low field where J couplings are comparable to chemical shifts.

J-resolved 2D spectroscopy

The homonuclear *J*-resolved 2D experiment is used to resolve proton mutiplets in instances where resonance overlap in a 1D spectrum makes the assignment difficult. A schematic of the pulse sequence consists of a spin-echo sequence, where the echo time is stepped as evolution delay t_1 (Figure 4a). The chemical shift and multiplet splitting of each group are displayed in the direct f2 domain, while the indirect f1 domain only contains proton-proton coupling information (in Hz). Following a simple shear operation, the *J*-multiplets appear in the indirect dimension and the homonuclear decoupled ^{1}H spectrum in the direct dimension.

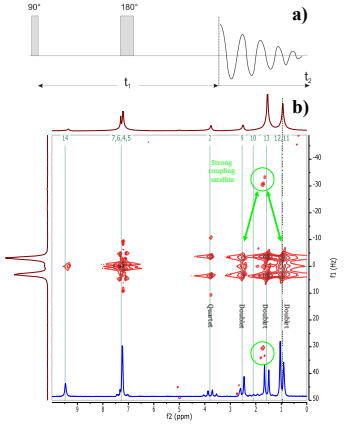


Figure 4: J-resolved 2D spectra can be measured with a comparatively small number of scans in the indirect dimension and tremendously simplify the analysis of low-field spectra in precisely determining *J*-coupling constants and identifying chemical shifts. This is shown using the example of 200 mM Ibuprofen in $CDCl_3$. For comparison, the 1D spectrum with peak assignments is shown as the blue curve. The projection along f1, corresponding to the "decoupled" 1D spectrum is displayed above the 2D spectrum. All multiplets collapse into a single peak at the centre frequency, resulting in a single peak per functional group. The vertical spectrum is a vertical slice along the dotted line through the 2D spectrum at the position of the most upfield peak (1.0 ppm). It clearly shows a doublet with a splitting of 6.4 Hz.

1. J. Perlo, F. Casanova, and B. Blümich, *Science*, 315, 1110-1112 **(2007)**.
2. E. Danieli, J.Perlo, B. Blümich, and F. Casanova, *Angew. Chem. Int. Ed.*, 49, 4133-4135 **(2010)**.
3. K. Kobzar, H. Kessler, and B. Luy, *Angew. Chem. Int. Ed.*, 44, 3145 –3147 **(2005)**.