Ultrafast multiple-quantum and diffusion-ordered NMR spectroscopy

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Nuclear magnetic resonance (NMR) spectroscopy provides a variety of techniques to disentangle the complexity of solution mixtures of small molecules, such as biofluids or extracts. The most powerful of these methods involve the acquisition of multidimensional (ND) data sets. However, the conventional implementation of ND NMR typically results in experiment durations of minutes to hours, and this is a limitation for the analysis of time-evolving or hyperpolarised samples. Using the concept of "ultrafast 2D NMR",[1] we describe the acceleration of two classes of experiments that are particularly useful for mixture analysis: 2D maximum quantum (MaxQ) and 3D diffusion ordered (DOSY) NMR spectroscopy.[2,3]

We first show that multiple quantum (MQ) coherences of coherence orders of up to 5 can be encoded spatially, using, as for single-quantum coherences (SQ), a pair of frequency swept pulses with bipolar gradient pulses.[4] This is validated by numerical simulation of the position-dependent spin phase, carried out with the Spinach framework that simultaneously accounts for spin and space variables. With this approach, 2D SQ-MQ correlation spectra can be collected in a single scan of less than one second, instead of several minutes for the conventional approach (Fig. 1). This is demonstrated with a maximum quantum analysis of a mixture of poly-aromatic compounds. We also analyse the sensitivity of this ultrafast 2D MQ NMR approach, and the benefits of using a triple-axis gradient probe for its implementation.

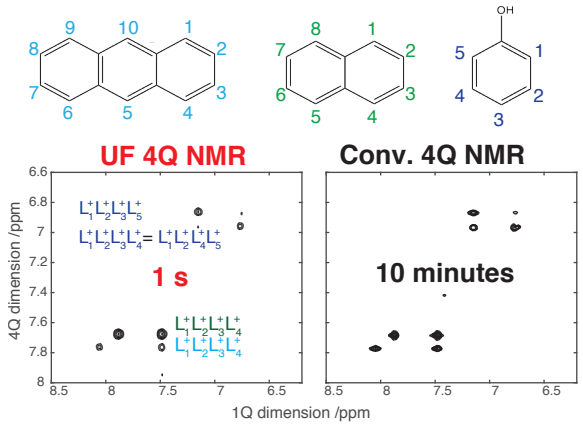

Fig. 1 1Q-4Q 2D correlation spectrum for a model mixture of 3 aromatic compounds. The UF version is acquired in a single scan.

We then show how spatial encoding of the chemical-shift dimension can be used to accelerate three-dimensional diffusion-ordered NMR spectroscopy (3D DOSY) experiments.[5] The conventional implementation of 3D DOSY requires two incremented dimensions, which results in experiment durations of several hours. Using an ultrafast acquisition of 2D correlation spectra for each gradient increment, the experiment duration is reduced to less than 5 min. This is illustrated here with the acquisition of 3D DOSY COSY data on a mixture of small molecules, which gives a separation of individual COSY spectra (Fig. 2). We compare the concatenated (DOSY – ufCOSY) and incorporated (ufCOSY – iDOSY) implementation of the sequences, and analyse the influence of gradient non-uniformity and ways to address them.

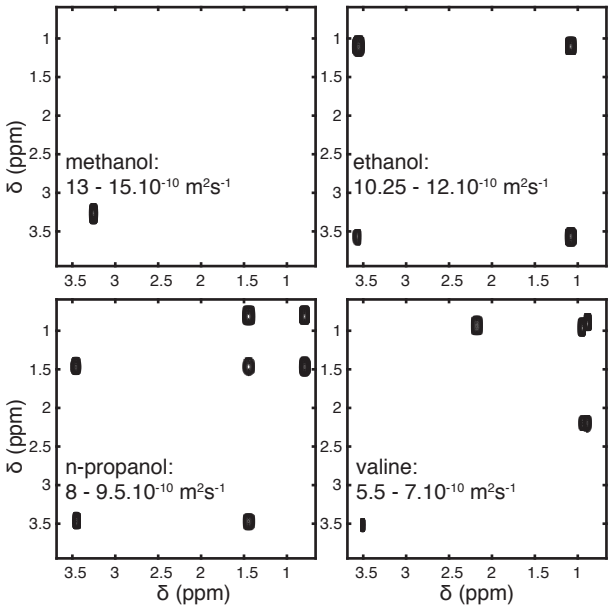

Fig. 2 COSY spectra of the components of a mixture, as separated with a 3D ufCOSY-iCOSY experiment.

These accelerated experiments will be particularly relevant for the monitoring of solution mixtures that evolve in time and/or are hyperpolarised.

References

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