NMR Supersequences for the Characterisation of Small Molecules

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The structure characterisation of small molecules by NMR spectroscopy continues to represent one of the major applications of this analytical technique and routinely employs well established 2D correlation experiments such as COSY, HSQC, HMBC, TOCSY, NOESY/ROESY and variants. Now established as the leading techniques, attention has turned to developing experimental methods that allow the faster collection of these data sets. Traditionally, these 2D data are acquired as a series of individual experiments and for each of these by far the longest period within the pulse sequence is the recovery (relaxation) delay in which excited magnetisation returns toward its equilibrium state between each transient. Herein, we describe an alternative approach to data collection by recording multiple 2D data sets nested as individual modules within a single "supersequence". This requires only a single recovery delay for each series of modules, and so allows for significantly reduced data collection times. The methods are especially well suited to the routine collection of characterisation data to support synthetic chemistry programmes.

The proposed technique is outlined schematically in Figure 1 [1] and shows the concatenation of mutiple modules following the single recovery delay. We term this approach NOAH (*NMR by Ordered Acquisition using ^{1}H-detection*). Conceptually, this relies on the sequential sampling of distinct pools of magnetisation by each module in turn, such that the output from one module is sampled as the input to the next (Figure 2). The method is suitable for conventional NMR spectrometers and requires no specialised hardware.

In this presentation we describe the general NOAH concept and its practical implementation. We shall also present some recent sequences optmised for the characterisation of small molecules [2] and new variants of NOAH supersequences that demonstrate the versatility of the approach. We demonstrate the combination of NOAH with non-uniform sampling (NUS) and the use of NOAH data in combination with computer-assisted structure elucidation (CASE) protocols.

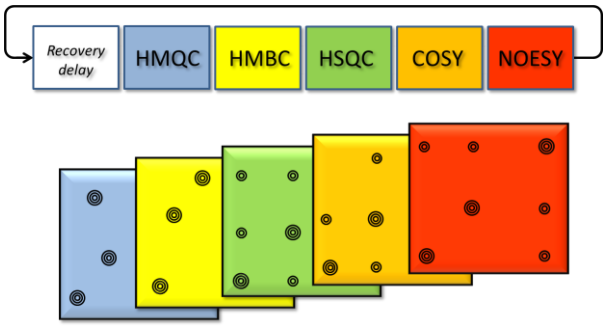

Figure 1. ***Upper***: Schematic representation of a NOAH supersequence, here comprising a (^{1}H, ^{13}C, ^{15}N) NOAH-5 experiment made up of five nested modules. A single recovery delay is employed prior to data collection. ***Lower***: Each NOAH module yields a separate 2D data set that is processed and analysed as for conventional data.

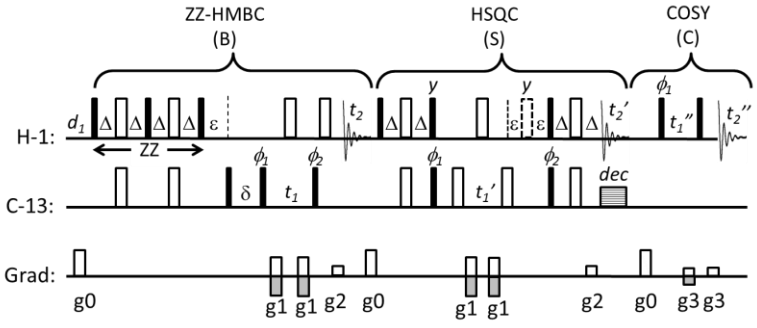

Figure 2. Outline of the (^{1}H, ^{13}C) NOAH-3 BSC supersequence yielding individual HMBC, edited HSQC and COSY data sets from one experiment. Different magnetisation reservoirs are sampled by each module in turn.

References:

1. Ē. Kupče and T. D. W. Claridge, *Angew. Chem. Int. Ed. Eng*., 2017, 56, 11779-11783.
2. Ē. Kupče and T. D. W. Claridge, *Chem. Comm*. 2018, 54, 7139-7142.