Optimizing *J*-modulated ADEQUATE experiments through homonuclear decoupling (HD) and non-uniform sampling (NUS)

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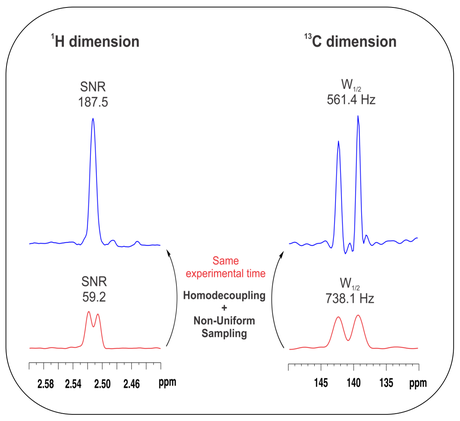
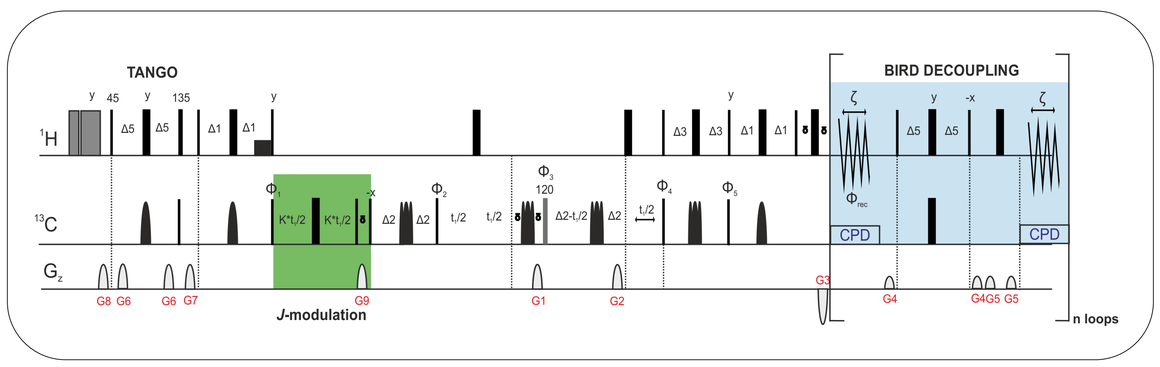
ABSTRACT



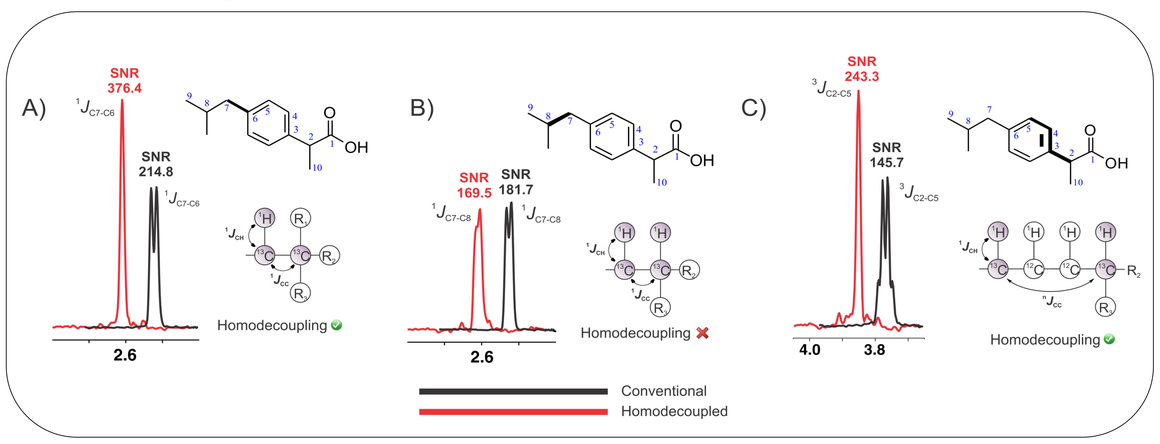
Homonuclear ^{13}C–^{13}C couplings at natural abundance can be measured using the *J*-modulated ADEQUATE experiment. To somewhat ameliorate F_1 digitization requirements, a scaling factor was incorporated into the original pulse sequence. Non-Uniform Sampling (NUS) provides an obvious avenue to further facilitate the acquisition of $^{1}J_{CC}$ and $^{n}J_{CC}$ homonuclear coupling constant data.

We introduce homonuclear decoupling (HD) analogous to that described for the 1,1-HD-ADEQUATE and 1,n-HD-ADEQUATE experiments and evaluate the combination of non-uniform sampling and HD on the acquisition of both $^{1}J_{CC}$ and $^{n}J_{CC}$ homonuclear ^{13}C–^{13}C coupling constants using ibuprofen as a model compound.

METHODOLOGY



Pulse sequence for *J*-modulated homonuclear decoupling (HD)-ADEQUATE. The pulse sequence is fundamentally similar to the recently reported pulse sequence for 1,1-HD-ADEQUATE and 1,n-HD-ADEQUATE., which employs 'chunked' data acquisition analogous to the procedure used with pure shift HSQC experiments (blue boxed region). A *J*-scaling factor (green boxed region) is used to resolve J_{CC} along F_1.



For $^{1}J_{CC}$ couplings In ADEQUATE experiments, there are two possible situations that lead to different results. First, for the observed $^{1}J_{CC}$ coupling pathway, the protonated carbon via which the coupling will be observed can be adjacent to either a quaternary or protonated carbon. In the former case, shown in A), the proton used for detection will not have a vicinal coupling to another proton on ^{13}C. Hence, all other vicinal and long-range couplings to the detected proton will be refocused by the BIRD-180° element applied during acquisition, collapsing the detected proton to a singlet. As an example, for the C7–C6 correlation, the H7 doublet used to detect the carbon–carbon correlation will be collapsed to a singlet with a corresponding increase in signal to noise (S/N) (from 215:1 to 376:1) as shown for the 1,1-HD-ADEQUATE spectrum of ibuprofen. In contrast, as shown B), the H7 proton used to detect the C7–C8 correlation will not be collapsed because the H7 methylene and H8 methine protons both reside on ^{13}C.

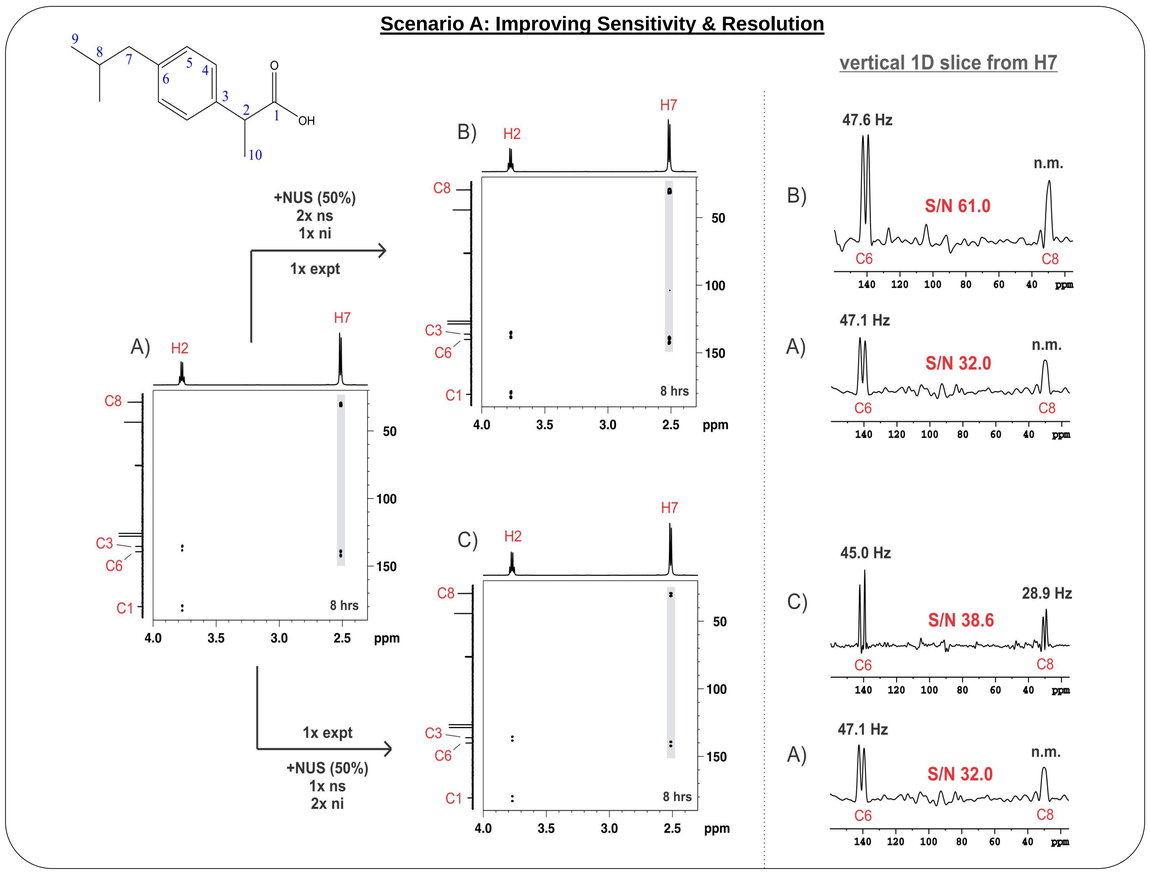
For long-range correlations, $^{n}J_{CC}$ will be decoupled except for the small homonuclear proton–proton coupling between the remote proton(s) on ^{13}C, which generally will not be observed given the typical resolution in this type of experiment (see C)).

CONCLUSIONS

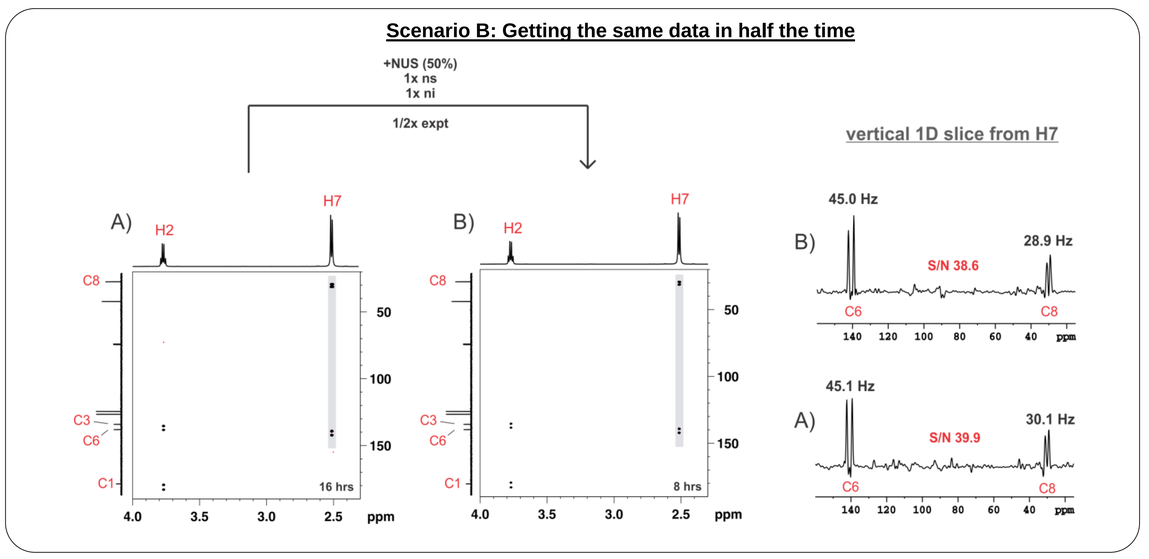
- **The extension of homonuclear decoupling to quaternary carbons in both the 1,1- and 1,n-ADEQUATE experiments affords higher-sensitivity versions of these experiments that can be applied to challenging structure elucidation problems when more sensitive techniques fail, as is the case of the complex alkaloid cryptospirolepine**
- **Combining both HD and NUS for the acquisition of ^{n}J-modulated ADEQUATE data allowed the successful visualization of carbon-carbon coupling constants as small as 2.3 Hz for the $^{2}J_{C2\text{-}C4}$ coupling of ibuprofen. In tandem, homonuclear decoupling and non-uniform sampling may help to facilitate the challenging measurement of carbon-carbon homonuclear coupling constants.**

RESULTS

J-modulated 1,1-HD-Adequate & NUS

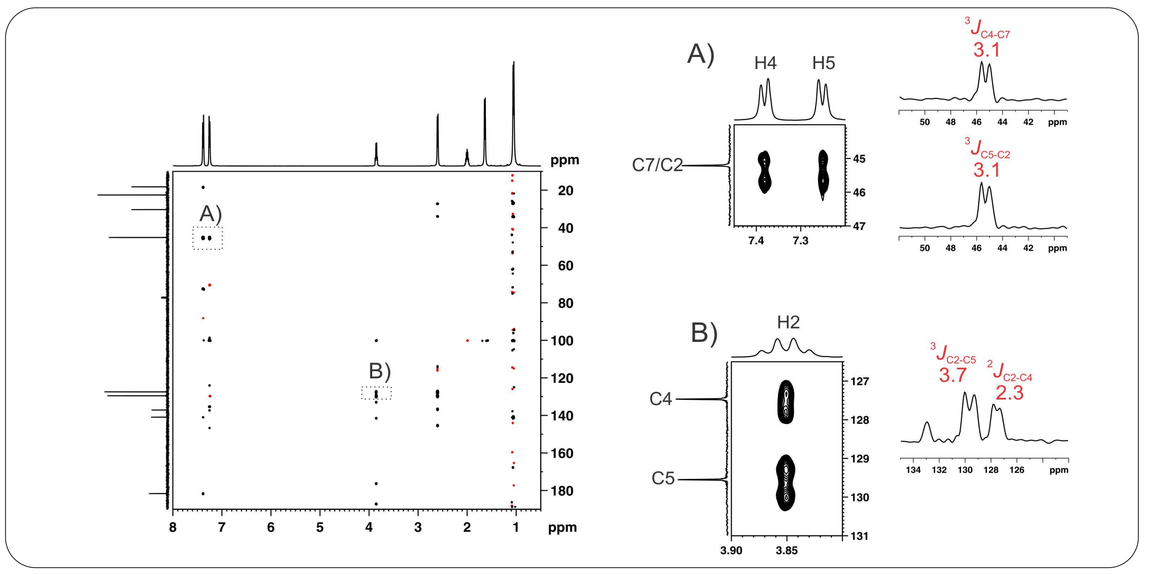


Comparison of conventionally sampled and 50% non-uniformly sampled *J*-modulated 1,1-HD-ADEQUATE spectra. All experiments were performed using identical data acquisition times with the scaling factor K = 10. Three sets of conditions are compared. A.) Data were acquired using 128 t_1 conventional increments and 96 scans/increment. B) Data were acquired using 50% NUS of 128 t_1 increments (64 increments actually acquired) with 192 scans/increment. C.) Spectrum with 50% NUS of 256 t_1 increments (128 increments actually acquired) and 96 scans/increment. Each experiment consumed 8 h 16 min of spectrometer time. Note that the H7 slice form panel B affords approximately twice the s/n and same the same F1 resolution as the slice from panel A. Panel C offers twice the F_1 resolution along and the same s/n as the data from panel A.



Comparison of conventionally sampled and 50% non-uniformly sampled *J*-modulated 1,1-HD-ADEQUATE spectra. A) Conventionally sampled spectrum, ni = 256 with 96 transients/t_1 increment, giving an acquisition time of 16 h. B) Spectrum acquired with 50% NUS of the data with 128/256 increments acquired with 96 transients/t_1 increment, giving an acquisition time of 8 h

J-modulated 1,n-HD-Adequate + Non-Uniform Sampling



5 Hz ^{n}J-Modulated 1,n-HD-ADEQUATE. The data were acquired using 50% NUS of 256/512 increments with 256 transients accumulated/t_1 increment giving a total acquisition time of 57 h. A) Expansion showing the collapsed H4 and H5 doublets for the $^{n}J_{CC}$ for the C4-C7 and C5-C2 homonuclear couplings. B) Expansion showing the collapsed H2 quartet with correlations to the C4 and C5 resonances. The trace shows the small $^{3}J_{C2\text{-}C5}$ = 3.7 and $^{2}J_{C2\text{-}C4}$ = 2.3 Hz couplings.

12th EUROMAR Conference. 3rd-7th July2016. Aarhus (Denmark)