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Communication

Recording ^{13}C-^{15}N HMQC 2D sparse spectra in solids in 30 s

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ABSTRACT

We propose a dipolar HMQC Hadamard-encoded (D-HMQC-H$_n$) experiment for fast 2D correlations of abundant nuclei in solids. The main limitation of the Hadamard methods resides in the length of the encoding pulses, which results from a compromise between the selectivity and the sensitivity due to losses. For this reason, these methods should mainly be used with sparse spectra, and they profit from the increased separation of the resonances at high magnetic fields. In the case of the D-HMQC-H$_n$ experiments, we give a simple rule that allows directly setting the optimum length of the selective pulses, versus the minimum separation of the resonances in the indirect dimension. The demonstration has been performed on a fully ^{13}C,^{15}N labelled f-MLF sample, and it allowed recording the build-up curves of the ^{13}C-^{15}N cross-peaks within 10 min. However, the method could also be used in the case of less sensitive samples, but with more accumulations.

1. Introduction

Presently, nearly all the two-dimensional (2D) spectra observed in Nuclear Magnetic Resonance (NMR) are recorded with the same principle: the acquisition during a time, t_2, of a series of signals (free induction decays or FIDs) for numerous evolution times, t_1, during which the spin system is subject to a selected interaction. After a 2D Fourier Transform (FT), the frequency ($F1$, $F2$) 2D spectrum is then observed and analyzed. Most of the time, the step for the evolution time, Δt_1, is kept constant. Along F1, the resolution and the spectral width, SW1, are then the inverse of the maximum evolution time, $t_{1,max}$, and of Δt_1, respectively. As a result, when the resonances are narrow and when they span over a large frequency range, the number of required t_1 steps, $m = t_{1,max}/\Delta t_1$, is large, and hence also the experimental time, T$_{exp}$. Provided the sensitivity is sufficient to observe the signals of interest in a few scans, the situation is commonly described as sampling limited. For example, this is the case when ^{13}C spectra of well crystallized compounds are recorded under magic angle spinning (MAS) to enhance the resolution, especially at high magnetic fields because of the proportionality between the frequency range and the field.

One way to decrease T$_{exp}$ is to use non-linear sampling of the evolution time, and on average the typical gain in time with respect to the linear t_1 sampling is of ca. 2 [1].

In the case of homo-nuclear correlation (HOMCOR) spectra, the m value can be decreased, and hence also T$_{exp}$, by using along $F1$ the prior knowledge provided by the directly detected signal along $F2$; this is known as the Covariance scheme [2]. This method has been used in solid-state NMR with either linear or non-linear sampling [3].

The prior knowledge is also used in the Hadamard spectroscopy to dramatically reduce T$_{exp}$ in sparse spectra. In this case the time saving is achieved by excluding empty spectral regions that contain no useful information. Indeed, when dealing with sparse spectra, two particular ways can be used to reduce T$_{exp}$. Both methods use selective excitations of the N species indirectly detected along $F1$, and hence they both require a previous acquisition of the 1D spectrum of this nucleus to know its resonance frequencies. In the first method, each of the N resonances is excited selectively, and the corresponding N FIDs are recorded separately. In the second method, n FIDs are observed, each related to a multi-selective simultaneous excitation of the N resonances encoded according to a Hadamard matrix, [H$_n$] [4], where the size of this matrix, n, is either a power of 2 or a multiple of 4 larger than or equal to N. After a Hadamard decoding processing, the N individual FIDs can be retrieved and used to reconstruct the 2D spectrum of interest. It can be shown that using the Hadamard

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encoding-decoding process, instead of N consecutive single excitations, allows gaining a factor of up to n for T_{exp} to achieve the same signal-to-noise ratio (S/N). In both cases, the 2D spectrum of interest can be reconstructed from the individual traces. As a result, the 2D spectrum is obtained with only n steps, instead of $m = t_{1,max}/\Delta t_1$ in case of the conventional way. Unlike the Fourier matrix, the Hadamard matrix is real rather than complex, which considerably simplifies the Hadamard transform. More importantly, it reduces the number of Hadamard encoding steps by a factor of two. For the same reason, it improves the S/N of the experiment by a factor $\sqrt{2}$ as compared to that obtained with a classical FT of a similar selective frequency encoding experiment [4c,4d].

The main limitation of these two methods is to obtain a selective excitation for each resonance. Indeed, when two resonances are separated by $\Delta\nu$, their selective excitation requires a pulse of minimum duration in the order of $1/\Delta\nu$. Therefore, when on a spectrum the minimum separation between two close resonances, $\Delta\nu_{min}$, is very small, the selective excitation of each of these two resonances requires very long pulse lengths, in the order of $\tau_{sel} \approx 1/\Delta\nu_{min}$. These long excitations may lead to a large signal decrease due to losses occurring during τ_{sel}, particularly in solids where the T_2' values are often in the *ms* range. One way to increase the S/N may appear to be reducing the length of the Hadamard encoding pulses. However, when doing this the two closest resonances are not separately excited, and their signals are weighted mixtures of the responses of the two species. This is still more difficult with two partly overlapping resonances, and in this case only a common response of the two sites can be observed.

In two previous works [5], we have demonstrated in solids on ^{13}C labeled amino-acids the validity of multi-selective Hadamard excitations in the cases of ^{13}C-^{13}C correlations based either on through-bond [5b] or through-space [5a] recouplings, and of ^{13}C-^{1}H CPMAS hetero-nuclear correlations (HETCORs) [5a].

In this communication, we would like to extend the Hadamard scheme to the case of ^{13}C-^{15}N D-HMQC (Dipolar Hetero-nuclear Multiple-Quantum Correlation) indirect detection 2D method. Indeed, it has been shown that this through-space HETCOR method is very simple and very robust in the case of high abundance nuclei [6]. As a test sample, we have chosen the fully ^{13}C and ^{15}N labeled f-MLF tri-peptide, N-formyl-Met-Leu-Phe. The molecule and the 1D CPMAS ^{13}C and ^{15}N spectra are shown in Fig. 1, together with the ^{13}C and ^{15}N assignments and their isotropic chemical shifts given in Table 1 [7]. The three ^{15}N resonances are well separated, whereas the ^{13}C spectrum is more crowded due to the presence of 19 different resonances. It must be noted that in Fig. 1c, most of the ^{13}C resonances are broadened by the $^{1}J_{13C-13C}$ couplings in this fully labeled sample.

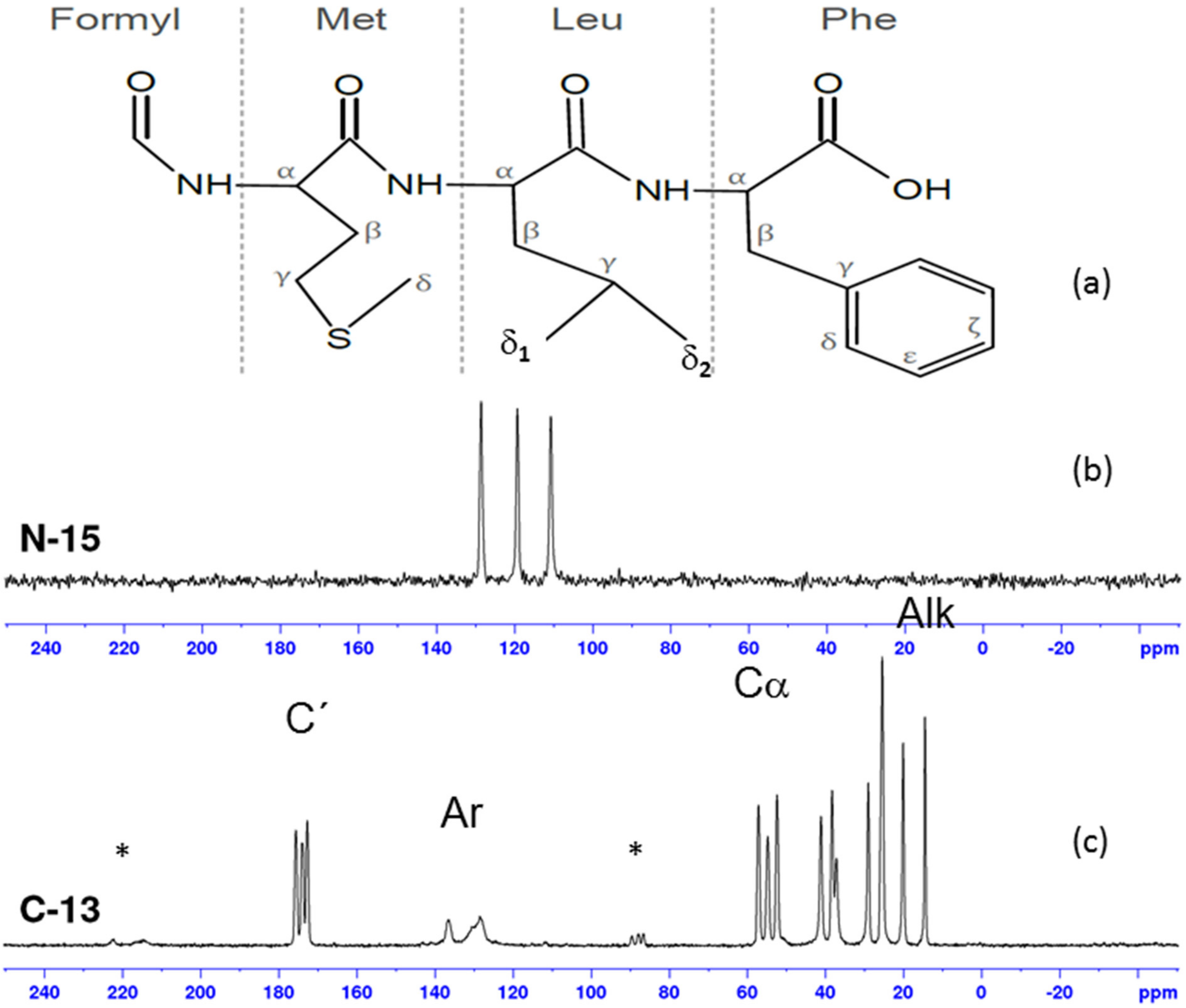

Fig. 1. f-MLF: (a) molecule, and ^{15}N (b) and ^{13}C (c) MAS spectra observed at 14.1 T with ν_R = 13 kHz. The labelling and assignment of ^{13}C and ^{15}N resonances have been given in Ref. [7]. In (c), the * indicate spinning sidebands of C′ and Ar carbons.