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Ultrafast Solid-State 2D NMR Experiments via Orientational Encoding

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2D NMR[1] enables the characterization of a wide variety of chemical and biochemical systems in liquids and solids; in the latter case, usually in combination with MAS.[2] Recent years have witnessed a growing interest in speeding up multidimensional acquisitions by departing from schemes whose duration might be defined by sampling requirements, rather than by sensitivity constraints. Proposals for accelerating 2D NMR include among others non-FT schemes[3] as well as "ultrafast" techniques enabling the acquisition of arbitrary 2D NMR spectra within a single scan.[4] Ultrafast NMR replaces the serial $\phi_e(t_1) = \Omega_1 t_1$ time increments used in traditional 2D spectroscopy[5] by a single-scan encoding of the indirect-domain interactions Ω_1 along an ancillary, inhomogeneously broadened ω_{inh} frequency domain. A robust way of imposing this kind of encoding in liquid-phase experiments has proven to involve the use of pulsed magnetic field gradients, for which $\omega_{inh}(z) = \gamma G z$. In combination with a frequency-incremented train of selective RF pulses sweeping a range ω_{inh}^{max} over a time t_1^{max}, a spatially dependent pattern $\phi_e(z) \approx t_1^{max}\Omega_1\omega_{inh}(z-z_o)/\omega_{inh}^{max}$ can then be imposed, containing the full information expected from the indirect-domain evolution but encoded now along a spatial axis. The repetitive readout of such encoding monitored as a function of t_2 leads to a series of echoes that, following suitable processing, can reveal the full 2D NMR correlation being sought within a single scan. Still, despite this scheme's generality, we found that its demands usually fail to materialize when involving MAS. Multiple hardware-dependent factors appear to conspire against the realization of gradient-based ultrafast 2D MAS NMR experiments, including a tilting of the gradient's direction from an exact magic-axis alignment, and spinning-related instabilities preventing a reliable formation of gradient echoes. As a result, we found that although commercially available probes incorporating MAS and gradients succeed in selecting coherence pathways from rotating solids and in executing ultrafast 2D NMR on static samples, they often fail to yield quality single-scan 2D MAS traces—even when the rotated sample is a liquid.

Driven by this handicap we explore an alternative source of broadening capable of facilitating the encoding entrusted so far to field gradients, relying this time on the intrinsic inhomogeneities $\omega_{inh}(\Phi) = \delta_{aniso} f(\eta,\Phi)$ arising from anisotropies in the spin interactions. If combined with a train of rotor-synchronized frequency-shifted RF pulses, this broadening could endow different orientations Φ within the sample with inequivalent t_1 evolution times, $\phi_e(\Phi) \approx t_1^{max}\Omega_1\omega_{inh}(\Phi - \Phi_o)/\omega_{inh}^{max}$, in a fashion akin to that underlying the z-encoding of Ω_1 (Figure 1). The resulting orientational encoding is here explored as a mean to accelerate 2D solid-state MAS NMR, using as a test case experiments involving half-integer $S \geq 3/2$ nuclei. These species were chosen due to their reliance on 2D MAS methods to provide high-resolution spectra and due to the large anisotropies associated with their e^2qQ/h couplings.[6] Obtaining high-resolution NMR information from these spins usually requires removing both first- as well as second-order effects, a task that 1D MAS NMR fails to achieve owing to the multiple spatial ranks involved in the latter. Over the years a number of solutions have been proposed to deal with this complication, mostly on the basis of 2D NMR schemes that refocus the anisotropic evolution experienced by spins over the course of t_1, by an analogous anisotropic evolution acting during t_2.[7] While such 2D experiments initially involved correlating $+1/2 \leftrightarrow -1/2$ transitions at different spinning angles, current implementations focus on correlating different $m \leftrightarrow m'$ transitions within the $-S \leq m,m' \leq +S$ manifold while subjecting the sample to conventional MAS. It is one such family of high-resolution experiments, derived from central/satellite correlations, that was targeted in the present orientational encoding test. This 2D STMAS experiment removes all second-rank anisotropies by means of accurate sample spinning, and refocuses the remaining fourth-rank anisotropies by correlating the satellite-transitions' evolution over the course of t_1 (e.g., the $\pm 3/2 \leftrightarrow \pm 1/2$ transition for $S = 3/2$ nuclei) with a central $+1/2 \leftrightarrow -1/2$ evolution during t_2. As the anisotropies associated with these transitions differ solely by a constant factor R, the dephasing undergone by the spins for a given t_1 delay will echo after a time $t_2 = Rt_1$. FT of the time-domain signal resulting from a parametric incrementation of t_1 thus yields high-resolution spectra devoid of all anisotropic broadenings. Orientational encoding could enable a "parallelization" of this 2D scheme by replacing the single hard pulse originally exciting the ST's, with a train of N_1 rotor-synchronized and selective RF pulses applied at equidistant offsets $\{O_j = O_i + j\Delta O\}_{j=1,N_1}$ (Figure 2). These pulses will have to be short compared to the rotor period T_r but long enough to select a specific frequency range within the full span of e^2qQ/h; care should therefore be given to their effective bandwidth, which in the present case will be given by usual inverse pulse width considerations and by the MAS-driven frequency sweeps that first-order quadrupolar anisotropies undergo during the pulses' duration. Minimizing the bandwidth ΔO (and thereby maximizing the number N_1 of elements that can be fitted within the inhomogeneity) leads to $\tau_p \approx [4\pi T_r/(e^2qQ/h)]^{1/2}$ pulse lengths; the exact RF pulse shapes for maximal excitation can be found numerically from these conditions. This kind of excitation will endow different crystallites with a progression of $\{t_1(j)\}_{j=1,N_1}$ encoding times within a single scan; subjecting the excited

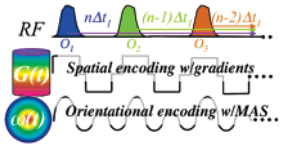

Figure 1. Extending the idea of NMR encoding along a spatial dimension with the aid of selective RF pulses and echoing gradients (center)[4] to an analogous encoding imposed as a function of crystallite orientation using intrinsic spin anisotropies subject to MAS.

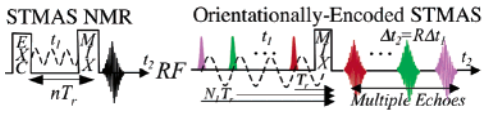

Figure 2. Extension of STMAS to an orientationally encoded "ultrafast" version, operating on the basis of a rotor-synchronized RF excitation train and the detection of multiple isotropically encoded echoes within one scan.

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coherences to a conventional mixing sequence correlating the satellite and central transitions results in a train of second-order echoes from which an isotropic spectrum can be reconstructed. At this point, however, a difference emerges between the single-scan 2D STMAS experiment just described and typical gradient-based ultrafast acquisitions, concerning the character of the echoes arising in the direct domain. Whereas a single kind of inhomogeneity (the field gradient) acted throughout the latter, two kinds will now be present: a first-order broadening employed to impart the orientational encoding, and a second-order anisotropy originating the subsequent direct-domain echoes. This in turn will impose differences in the nature and the processing needs of the resulting signals, which will now consist of N_1 echoes separated by $R\Delta t_1$ intervals. Each of these echoes will span a time width that is inversely proportional to the spread of the second-order quadrupole effect, while encoding in their progression the isotropic evolution of the different sites. To obtain the desired correlation spectrum, the resulting data array thus needs to be spliced, rearranged into a 2D matrix as a function of time variables $0 \leq \tau \leq R\Delta t_1$ and $\{t_2(j) = (j - 1)R\Delta t_1\}_{j=1,N_1}$ characterizing the anisotropic central-transition MAS and the isotropic evolutions respectively, and 2D FT'd. Moreover, by contrast to spatially encoded experiments where gradients allowed us to control the time widths spanned by these multiple echoes, this is no longer the case upon relying on an orientational encoding governed by intrinsic anisotropies. Only changes in the Δt_1 increments can consequently be used to properly satisfy the sampling requirements. Given the rotor-synchronized nature of STMAS experiments, this in turn implies manipulating the T_r period separating the encoding pulses; although the ensuing spinning rate change could be made a priori arbitrary, we found experimentally that decreasing MAS rates beyond ~10 kHz led to rapidly decaying central-transition echoes and to a concomitant loss in spectral sensitivity. Therefore, rather than achieving a sufficient separation between the echoes by a theoretically correct but poorly performing slow-spinning route, this problem was circumvented by doubling the number of independent orientationally encoded experiments to two. The opportunity then arose for achieving an appropriate number N_1 of echoes, sufficiently separated to be spliced yet at the same time keeping a high spinning rate, by collecting two data sets with Δt_1 increments set apart by $\Delta t_1/2$ differences—each experiment devoted to the collection of complementary increments in the ST evolution. As can be appreciated from Figure 3C–E, splicing and interleaving these echo trains into a single data set provides high-resolution 2D spectra within just two such sets of t_1-incremented phase-cycled 1D scans.

The results in Figure 3 illustrate initial examples of the potential carried by orientational encoding to speed up 2D MAS NMR acquisitions. Although this may not be as important a goal in solid- as in liquid-state experiments, reducing these acquisitions down to a single scan (or as was here demonstrated, to just a few scans) might still be useful in a variety of instances, including studies on unstable systems, experiments on hyperpolarized solids, or measurements on very slowly relaxing spins. It should be noted that other routes for accelerating 2D solid-state experiments down to single scans have been demonstrated in the past based on alternatives related to the *k*-walk MRI idea, including recent proposals concerning half-integer quadrupolar nuclei.[8] Such methods are usually efficient sensitivity-wise, yet at least judging from our experience with ultrafast NMR, the orientational encoding principle discussed here is probably more general in terms of applicability. Therefore, while prompted by technical challenges, we believe that these encoding alternatives could have merits of their own in studies of solids and semisolids.

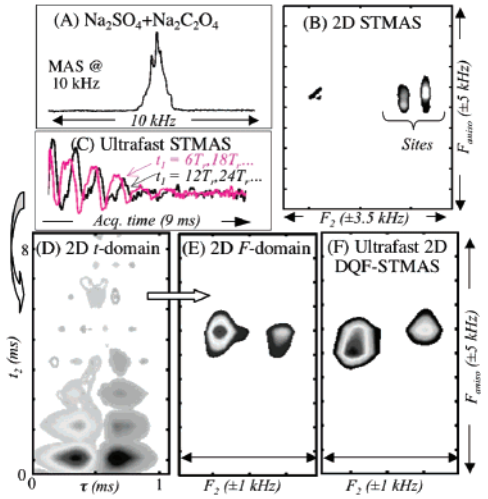

Figure 3. Speeding-up capabilities of orientational encoding illustrated with ^{23}Na MAS NMR results recorded on a 14.1 T Varian Infinity+. (A) Single-pulse central transition spectrum. (B) *z*-Filtered 2D STMAS experiment; 32 t_1's with an 8-scan phase cycling per increment. (C) Signals arising from an orientationally encoded analogue of STMAS derived from the scheme in Figure 2 ($\tau_{pulse}^{exc} = 2.5\ \mu s$, $\gamma B_1^{exc} = 20$ kHz, $\Delta O = 400$ kHz, $\gamma B_1^{mix} = 200$ kHz, $\Delta t_1 = 12T_r$) with two phase-cycled experiments encoding eight increments each and having their initial t_1 values differing by a $\Delta t_1/2$ delay. (D, E) Two-dimensional time- and frequency-domain data arising upon splicing signals in (C) according to their t_1 values, rearranging them along their respective τ/t_2 evolutions and processing them as described in the text. The resulting spectrum arises from just two sets of phase-cycled 1D measurements. (F) Same as (E) but based on DQF–STMAS.[7e]

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(1) Abbreviations: 2D NMR, two-dimensional nuclear magnetic resonance; MAS, magic-angle spinning; FT, Fourier transform; e^2qQ/h, quadrupole coupling constant; ST, satellite transition; RF, radio frequency.

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