Communication

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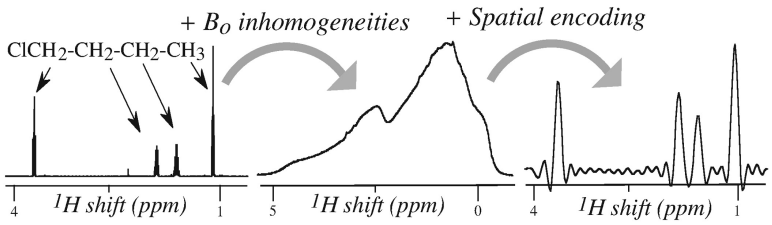

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Spatial Encoding and the Acquisition of High-Resolution NMR Spectra in Inhomogeneous Magnetic Fields

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Nuclear magnetic resonance (NMR) delivers detailed molecular-level information via interactions that affect the fine structure of the spectral line shapes. Particularly important among these are the chemical shifts and the J couplings,[1] interactions that are orders of magnitude smaller than the main Zeeman coupling to the external field B_o. This in turn demands highly homogeneous fields for proper chemical characterizations, with heterogeneities in B_o typically spanning under one part in 10^8. Achieving such degree of homogeneity is not trivial, particularly when considering that it needs to be attained over a relatively large volume and within a short interval following the sample's insertion. The routine accomplishment of this goal comes at a cost both in the price of NMR systems and in the size demanded by NMR magnets. Moreover, instances arise where reaching such extreme homogeneities is simply unattainable, as when dealing with spatially heterogeneous tissues or employing "inside-out" magnet arrangements such as those in remote NMR characterizations. Given these challenges and the important gains that could result from overcoming them, a number of proposals have been made to retrieve high-resolution NMR spectra under inhomogeneous B_o conditions.[2] One of the earliest and still most widely used alternatives relied on using two-dimensional (2D) multiquantum correlations.[2a−c] Overhauser-based intermolecular 2D correlations were also demonstrated as a possible route to achieve such an end;[2d] more recently, Pines et al. demonstrated that $\Delta B_o(z)$ dependencies could be compensated using radio-frequency (RF) fields possessing B_o-like spatial inhomogeneities.[2e] The present study discusses yet another option for achieving narrow lines in the presence of B_o heterogeneities, which unlike previous propositions operates on a single-scan basis and can narrow away inhomogeneities possessing arbitrary spatial dependencies. This new approach relies on the spatial encoding of NMR interactions, a protocol that we have recently proposed for acquiring 2D NMR spectra within a single scan.[3]

Spatial encoding monitors spin evolution in an indirect fashion, by replacing the usual $\phi = \Omega_1 t$ modulation underlying Fourier transform (FT) NMR by an analogous spatial modulation of the Ω_1 interactions.[3a,b] This can in turn be achieved in a number of manners, the simplest of which involves applying a train of frequency-shifted RF pulses while in the presence of a longitudinal field gradient G_e (Figure 1A). This in effect partitions the sample into N_1 independent spin packets positioned at z_j coordinates, whose evolution frequencies become encoded along the geometry of the field gradient according to $\phi(z_j) = C\Omega_1(z_j - z_{N_1})$, $C \approx 2T_pG_e/\Delta O$. The resulting winding of magnetizations can be subsequently uncoiled by an acquisition field gradient G_a, which will reveal the evolution frequencies by creating distinct echoes whenever $k = \int G_a(t')\,dt' = -C\Omega_1$. It follows that this spatial encoding approach can, just as traditional continuous-wave (CW) or FT NMR alternatives, provide conventional-looking NMR spectra. Unlike these other alternatives, however, the spatial decoding process unraveling these spectral data can last arbitrarily short acquisition times T_a, as well as be efficiently reversed by manipulating the sign of the G_a acquisition gradient.

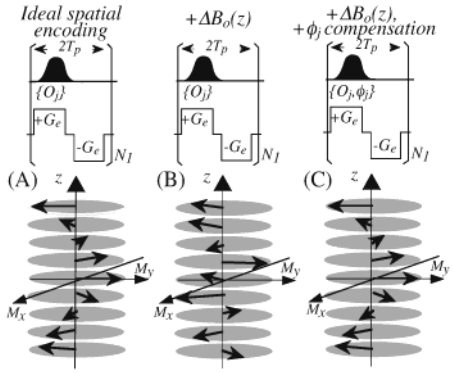

Figure 1. (A) Ideal magnetization winding created by a spatial encoding procedure, involving N_1 selective pulses of duration T_p applied at an offset increment $\Delta O = |O_j - O_{j+1}|$. (B) Distortions induced by spatial inhomogeneities ΔB_o on the ideal spiral. (C) Reinstatement of the winding's ideality via appropriate ϕ_j phase shifts in the spatially encoding RF pulses.

To appreciate how these features can help compensate field heterogeneities, it is illustrative to compare the consequences that ΔB_o effects—assumed uniaxial for the sake of simplicity—will impart on FT and on spatially encoded NMR experiments, respectively. In the former case, spins at different spatial locations will be jointly excited and then evolve with a range of different precession frequencies, eventually interfering destructively with one another. Also spatially encoded NMR experiments will reflect field inhomogeneities, as each of the spatial elements involved in the Ω_1 encoding precesses with a phase depending both on the internal interactions being sought as well as on the artificial ΔB_o (Figure 1B). Upon uncoiling the various spin packets into which the sample has been partitioned will thus fail to interfere in the construction of sharp echoes, and a low resolution k-signal will result. Such a k distribution signal may not necessarily resemble its conventional CW or FT NMR spectral analogues, yet also as in these cases its Ω_1 information will have been lost. And yet despite this similar end result, the comparison just made highlights a difference that can be exploited to compensate for the effects introduced by ΔB_o: whereas in pulsed FT NMR field heterogeneities blur the information being sought over the course of the whole data acquisition time, the cumulative effects imparted by field heterogeneities on space-encoded acquisitions solely matter over a short moment in time, proximate to the instant of the k-axis echo formation. Furthermore, at this point in time the consequences of ΔB_o will be well-defined: the distortions imparted into the helical magnetization pattern being sought will be given by additional $\Delta\phi(z_j) \approx C{\cdot}\Delta B_o(z_j){\cdot}(z_j - z_{N_1})$ precession phases. This in turn suggests a route capable of compensating for the ΔB_o distortions, based on subtracting from the individual spin packets upon their RF excitation these additional phase shifts incurred by the field nonidealities (Figure

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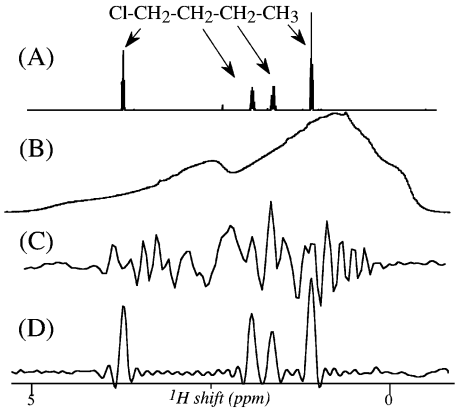

Figure 2. (A) ^{1}H FT NMR spectrum of $C_4H_9Cl/CDCl_3$ recorded in a homogeneous field. (B) Idem, but in the presence of ~1.5 kHz field inhomogeneities artificially introduced by detuning the spectrometer's $\{z^i\}_{i=1-5}$ shim sets. (C) Spatially encoded ^{1}H NMR spectrum recorded under identical inhomogeneous conditions as (B). (D) Same experiment but upon adding proper $\{\phi_j\}_{j=1,N1}$ phase corrections to the spatially encoding RF excitation pulses, adapted from $\Delta B_o(z)$ field maps as explained in Figure 3. Notice that the *sinc*-like peak shapes in this trace reflect the limited duration of the spatial encoding, rather than the effects of field inhomogeneities. As all remainder experiments in this communication, these spectra were collected at 11.75 T within a single transient using a Varian iNova NMR console and probe. The spatial encoding proceeded as in Figure 1 with $N_1 = 64$ square pulses, $T_p = T_a = 0.2$ ms, $\Delta O = 5$ kHz, $G_e = G_a =$ 40 G/cm.

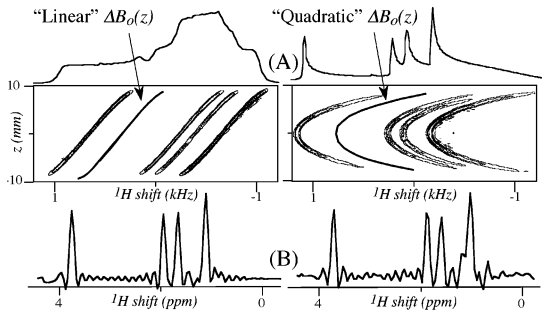

Figure 3. (A) 2D EPSI profiles measured in preparation of the high-resolution spatially encoded NMR acquisitions, illustrated for C_4H_9Cl and field patterns dominated by z and z^2 inhomogeneities. Bold curves indicate the fitted $\Delta B_o(z)$ functions assumed for the phase compensations; shown on top are the corresponding conventional 1D traces. (B) ΔB_o-compensated spatially encoded spectra obtained for each of the field patterns.

1C). Figure 2 illustrates the potential of this simple procedure to retrieve high-resolution NMR data, using ^{1}H NMR data sets recorded on a 1% *n*-butyl chloride/$CDCl_3$ solution as example. As shown here, field inhomogeneities impair to similar extents resolution in the FT and in the spatially encoded NMR spectra, yet a simple phase correction of the encoding pulses can account for these distortions in almost their entirety (Figure 2D).

From a practical standpoint, a necessary intermediate step for implementing the compensation just described entails determining the average field distortions ΔB_o experienced by spin packets as a function of their z positions in the sample. During the present study, these determinations were carried out using echo-planar spectroscopic imaging (EPSI) NMR, a protocol capable of yielding 2D shift-position correlations within the course of a single scan.[4] The top panels of Figure 3 illustrate the spatially resolved shift information yielded by this sequence for different kinds of artificially induced field inhomogeneities. This figure also highlights another feature of our new scheme: its absence of demands on the geometry subtended by $\Delta B_o(z)$ for its proper compensation.

Starting from the physical principles just described, numerous improvements and variations become possible. An evident choice for enhancing experimental sensitivity consists of introducing a train of refocusing 180° pulses over the course of the data acquisition; given the relatively short T_a times required to collect the spatially encoded spectra, this would enable the acquisition of numerous spectra within the natural transverse relaxation decay of the spins. Co-adding such data sets would then substantially increase the overall per-scan sensitivity of the experiment. An additional improvement could result from extending the single-axis encoding employed in this work to the use of orthogonal triple-axis gradients. In combination with multiple-axis spatial encodings,[3c] the phase-shift proposition hereby described would enable the compensation of ΔB_o effects throughout the sample volume instead of solely along a z-axis. The resulting procedure would then resemble the improvements in field homogeneity normally carried out via 3D field mapping procedures,[5] except for the fact that corrections would be dialed in as phase shifts in the RF excitation pulses rather than as currents applied into a large set of linearly independent shimming coils. Although evidently more involved than the alternative exemplified in Figure 1, such an approach could prove valuable for improving nonaxial ΔB_o distortions in cases where spinning away transverse heterogeneities is not viable. A third possibility involves exploiting the kind of scheme that we have hereby discussed to compensate not just for static field inhomogeneities, but also dynamic drifts in the overall magnetic field strength over the course of an experiment. Even in the absence of B_o locking or of field homogeneity circuitry, this could then be used to impart both inter- and intrascan acquisition stability. Last but not least, it is worth addressing the compensation ability of the proposed scheme. If implemented in the discrete RF excitation mode described here, narrowing factors on the order of N_1 can be imparted on inhomogeneously widened peaks. On the other hand simulations indicate that, at least in the absence of flow or diffusion, larger field distributions could be dealt with by replacing the discrete spatial encoding mode described in this communication by continuous spatial encoding alternatives. Spectral resolutions on the order of 0.1 ppm could thus be achieved, even when dealing with fields heterogeneities spanning ca. 10−100 ppm over the sample as a whole. These alternatives, as well as further extensions of the methodology introduced here, will be described in more detail in a coming publication.

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