

# Three-dimensional phase-encoded chemical shift MRI in the presence of inhomogeneous fields

Vasiliki Demas\*, Dimitris Sakellariou†, Carlos A. Meriles†, Songi Han†, Jeffrey Reimer\*, and Alexander Pines†\*

Departments of \*Chemical Engineering and †Chemistry, University of California, Berkeley, CA 94720-1460

Contributed by Alexander Pines, April 30, 2004

A pulse sequence consisting of an excitation pulse and two adiabatic full-passage pulses with scaled relative peak amplitudes is combined with phase encoding to recover chemical shift information within 3D images in a 1D inhomogeneous static magnetic field with a matched *rf* field gradient. The results are discussed in the context of *ex situ* magnetic resonance and imaging. The future directions of our research in implementing the *ex situ* technique in a real one-sided system are also discussed.

The advantages to conducting magnetic resonance in inhomogeneous magnetic fields have been well recognized mainly owing to the potential application to “outside the magnet” NMR and MRI. Various efforts have been made to study molecular dynamics (1) and imaging (2) in the presence of magnetic field inhomogeneities. The majority of these efforts, with stray field imaging (3, 4) and the NMR MOBILE Universal Surface Explorer (MOUSE) (5, 6) being the most predominant, have allowed for imaging and relaxation measurements. Spectral information, such as the chemical shift, has yet to be obtained with such devices. It has been demonstrated that chemical information lost in inhomogeneous magnetic fields can be recovered by use of specially crafted pulses in the presence of matched *rf* and static magnetic fields (7). Our objective is to exploit and refine the *ex situ* methodology in combination with imaging techniques to obtain image information together with spatially localized spectroscopic information in an inhomogeneous field outside the magnet, and thus to develop a useful tool for scanning chemical and mechanical properties of materials. In this communication we present high-resolution spectroscopic and image information in a model environment where a 1D, linear, magnetic-field inhomogeneity is imposed. This is the first approximation to a one-sided system, toward which future efforts of this work are guided. Existing portable NMR systems possess large nonlinear gradients, which make the application of this technique hard. However, much effort is going toward designing hardware (*rf*-coil geometries together with one-sided magnets) to allow the present technique to be used in real *ex situ* situations. In addition the technique described in this article may be easily modified to selectively signal from small areas of large objects, allowing us to select regions where the inhomogeneities are tractable.

Inhomogeneities in the static field result in Larmor frequency ( $\omega_0$ ) variations; spins with smaller  $\omega_0$  will lag during precession. Inhomogeneities in the *rf* field result in different spins orienting at different rates,  $\omega_1$ , during excitation pulses. One strategy for recovering information in *ex situ* magnetic resonance is to play these two nonidealities against one another. If the  $B_0$  and  $B_1$  inhomogeneities have the same spatial dependence, pulses could be designed so that stronger  $B_1$  fields place spins with faster precession frequencies in the *xy* plane behind slower spins. When the spin system is then left to evolve, a “nutaton” echo is formed when the faster spins “catch up” to the slower ones. The situation is slightly more complicated when the spins also evolve under the chemical shift interaction. In spatially matched static and *rf* fields, a significantly different characteristic dephasing occurs because

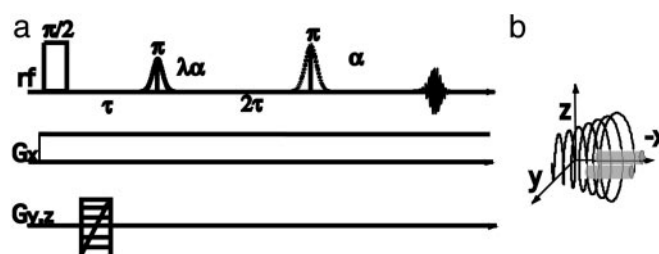


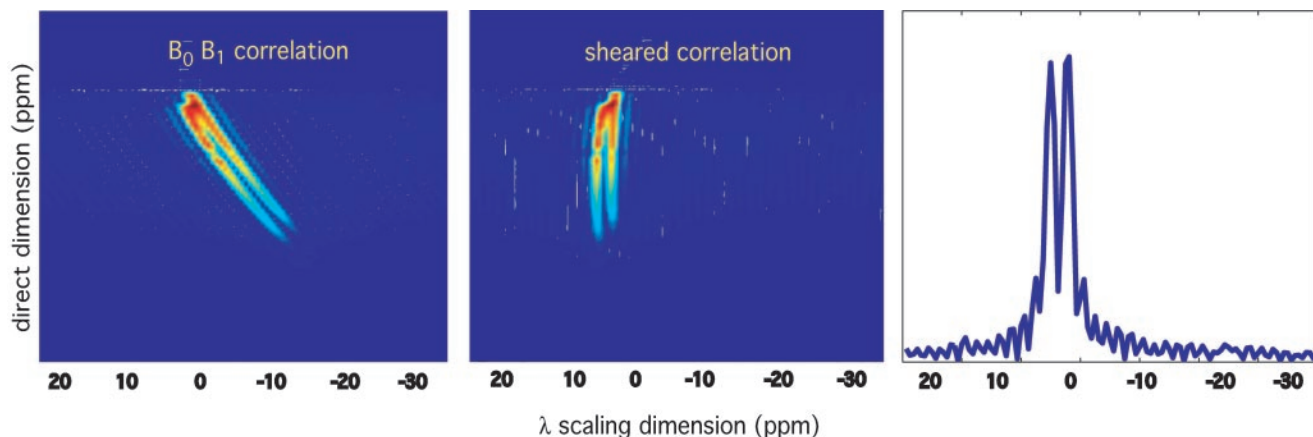
Fig. 1. Experimental scheme for chemical shift MRI in the presence of inhomogeneous fields. (a) Pulse sequence for the static and *rf* gradient fields. Two scaled adiabatic  $\pi$  pulses follow an excitation pulse. The static field gradient along  $x$  is applied during all experiments to emulate the natural inhomogeneity of an *ex situ* environment. Phase encoding is used to image the other two dimensions, and the overall experiment is repeated for different scaling of the two adiabatic pulses. (b) Experimental setup. Two tubes (one filled with water and the other with oil) were placed inside a conical solenoidal coil producing a  $B_1$  spatial profile that matched the linear magnetic field gradient along  $x$ . See ref. 7 for the experimental details.

of chemical shift and field inhomogeneities; whereas static field inhomogeneities are compensated by a matched  $B_1$  profile, the signal phase modulation due to chemical shift is preserved. Modulation of the nutation echo amplitude due to the chemical shift can be recovered, as described by using  $z$ -rotation composite pulses (7, 8) to form nutation echoes (9, 10). In this communication we apply this same strategy but use adiabatic pulses that compensate over a broader range of inhomogeneities (11).

The pulse sequence consists of a conventional hard excitation pulse (12  $\mu$ s), followed by a delay  $\tau = 8$  ms to allow for spin precession, and two adiabatic  $\pi$  pulses of 4-ms duration each, separated by double the time interval,  $2\tau$  (Fig. 1a). The maximum amplitude of the first adiabatic pulses is scaled by  $\lambda$  relative to the maximum amplitude of the second adiabatic pulse. It has been shown that the overall phase given to the signal after the application of two adiabatic pulses with the same frequency sweep, but different maximum amplitude, is proportional to the *rf* field and the scaling factor  $\lambda$ , but independent of frequency offset  $\Delta\omega = \omega_0 - \omega_1$  (11) over the range where the adiabatic condition holds. A 1D gradient along the  $x$  direction is turned on throughout the experiment to emulate, to a first approximation, the inherent inhomogeneity of a true *ex situ* magnet, whereas the amplitude of the gradient pulses along the  $y$  and/or  $z$  directions is varied to obtain image information along these dimensions. A complete set of imaging experiments is repeated for a range of different values of  $\lambda$ . For each scaling value  $\lambda$ ,  $B_1$  inhomogeneities compensate for  $B_0$  inhomogeneities, but the refocusing corresponds to a different evolution time for the chemical shift. Incrementing  $\lambda$  thus introduces a new time dimension which,

\*To whom correspondence should be addressed. E-mail: pines@cchem.berkeley.edu.

© 2004 by The National Academy of Sciences of the USA



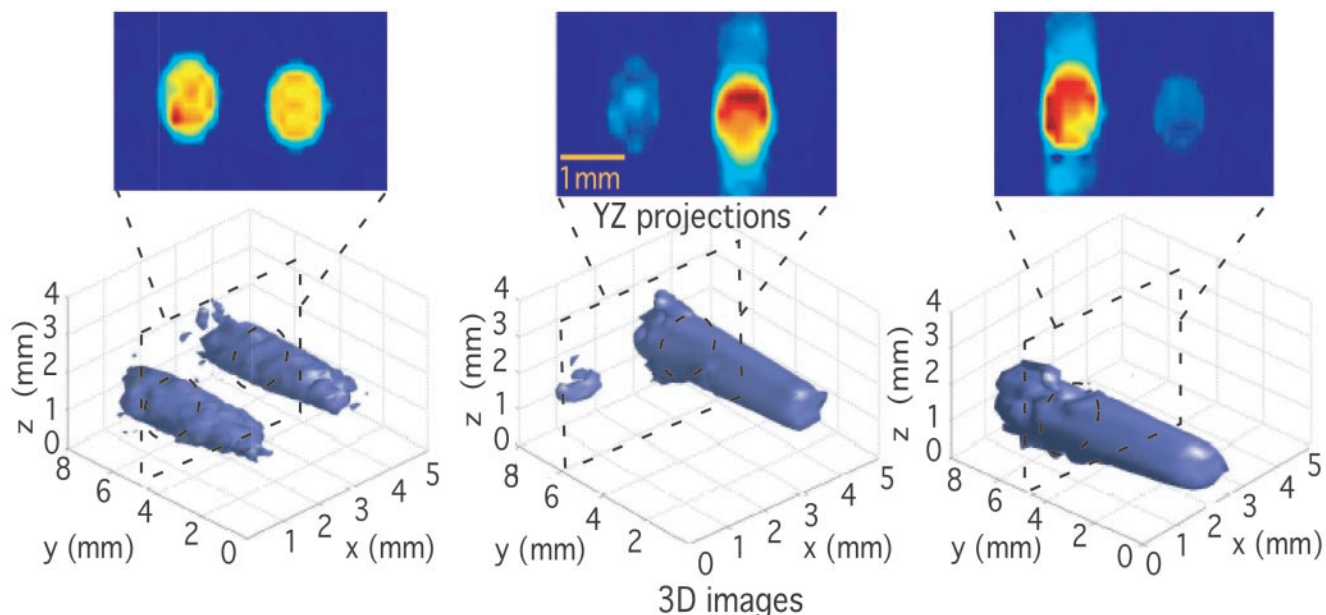
**Fig. 2.** Chemical shift information can be recovered in inhomogeneous fields by proper correlation of  $B_0$  and  $B_1$  fields. (Left) The direct and scaling dimensions are selected to yield the correlation of the  $B_1$  field and the static magnetic field. They show linear correlation indicated by the two lines for both chemical species. (Center) The data are then sheared so that the spectrum can be recovered on projection. (Right) The recovered 1D proton spectrum. Chemical shifts are referenced with respect to the water signal at 4.8 ppm.

after Fourier transformation, yields the NMR spectral information (11).

In practice the inhomogeneities present in *ex situ* environments are larger than the ones we used, as well as nonlinear. We have shown in the past that composite pulses can perform very well in high gradient cases, provided enough *rf* power is available (to cover the inhomogeneity bandwidth), because such pulses are primarily insensitive to diffusion. The static gradient strength that we can correct for then depends on the maximum *rf* power. On the other hand, it has been shown that long adiabatic pulses can operate over an extremely large bandwidth without the need of high *rf* amplitude. Of course, such long pulses are sensitive to diffusion, and future studies should focus on the limitations of these pulses as a function of gradient strength and diffusion coefficients. The pulses we are currently using can correct for 100-kHz offset. We believe that the ideal pulse scheme will depend on the magnet design

(because not all open magnets will be tractable) and will incorporate *rf* efficiency, short-length, and broadband behavior together with tunability. Even though for the proof-of-principle experiments described herein we have imposed linear gradients giving a well controlled linear matching, one needs to consider that in actual cases perfect matching might be difficult to achieve because of the magnet design. We believe that the solution to this problem will have to address the design of the magnet and the *rf* coil in one step. A first-order approach is to limit the signal acquisition to regions where the correlation is good at the expense of signal to noise. Even though this might be possible to achieve either using pulses (correlation selective pulses) or physically (separate coils for excitation and detection), our goal in the future is to optimize the *rf*-coil geometry together with the magnet geometry to provide the best possible matching.

The experimental arrangement consists of a conventional 4.2-T magnet (180 MHz proton Larmor frequency) with the



**Fig. 3.** *yz* projections and 3D images of the sample (as a subset of the 4D data set) correlated with chemical shift. Either both tubes (trace at 14 ppm), or the water (trace at chemical shift of 16 ppm water) and the oil (trace at chemical shift 12 ppm oil) tubes are selectively displayed depending on chemical shifts.

