Improvement of Spectral Resolution by Spectroscopic Imaging

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Abstract. We propose to use three-dimensional spectroscopic imaging (SI) to increase the spectral resolution for biological samples for which strong susceptibility effects (or poor magnetic homogeneity) cause significant line broadening. Due to susceptibility effects (or poor field homogeneity) the SI voxel spectra even from a uniform sample are shifted with respect to each other and much less broadened than the total sample spectrum. Realignment of the spectra from individual voxels prior to their coaddition produces a total-volume spectrum with significantly narrower lines.

1 Introduction

Resolution and, thus, the information content of nuclear magnetic resonance (NMR) spectra critically depend on the magnetic field homogeneity. In macroscopically heterogeneous samples with irregular geometry, the magnetic field homogeneity is affected by the susceptibility effects \cite{1,2} which cannot be eliminated by magnetic field shimming. The susceptibility effects could be eliminated by magic angle sample spinning which is limited to small and robust samples. Spectral filtering is another frequently used method for resolution enhancement. However, resolution enhancement filters dramatically reduce the signal-to-noise ratio (SNR). Therefore, additional methods for line narrowing with minimal loss of SNR are highly desirable.

Spectroscopic imaging (SI) is a technique that provides high-resolution spectra from individual volume elements (voxels) of the sample \cite{3-6}. It is an ideal method to obtain information about the spatial variation of the NMR spectrum across the sample. However, the sensitivity losses, which are increasing with spatial resolution, restrict its use only to cases with favorable SNR. Frequently, SI is complemented by other spatially selective spectral methods (VSE \cite{7}, CARVE \cite{8}, etc.) which minimize sensitivity losses by providing spectra from larger-sized voxels. The SI uses traditional spectral excitation and detection with phase-encoding gradients
to provide spatial encoding. The number of voxels is identical to the number of phase encoding steps. Because the total-sample signal is constant, the increase of spatial resolution (number of voxels) decreases the SNR per voxel. To improve the SNR, it may be useful to coadd signals from several voxels or to use volume-selective excitation. Either method is prone to line broadening due to magnetic field inhomogeneity.

The sensitivity drop in the SI voxel spectra is caused by the two related effects. One is purely geometrical; the increase of spatial resolution reduces the volume of a single voxel and thus reduces the voxel signal. The other is the signal attenuation caused by phase-encoding gradients. Large gradients induce large signal dephasing which leads to mutual cancellations of the signals from different sample regions.

In samples with regular geometry (or in small volumes), variations of the static magnetic field can be compensated by appropriate shims. However, in geometrically irregular and macroscopically inhomogeneous samples, variations of the static magnetic field are hard to compensate. The variability of the field within the voxel is much smaller than across the whole sample volume. Then, individual voxel spectra have narrower lines than the spectra recorded from the whole sample volume. Due to the field inhomogeneity, the average voxel field varies and the voxel spectra are shifted relatively to each other. Thus, the SI spectra from different voxels of the homogeneous sample region have identical spectra with narrower lines but relatively shifted from voxel to voxel. Since the volume of individual voxels is much smaller than the volume of the sample, the SNR of the voxel spectra are considerably lower than the SNR of the spectrum from the whole sample [9]. To regain the SNR, the spectra obtained by SI have to be coadded. Plain coaddition yields a spectrum identical to the standard spectrum of the whole sample (see Eq. (2)). However, when individual voxel spectra are co-aligned before summation, the resulting spectrum has significantly narrower lines compared with the standard one-dimensional (1-D) spectrum from the same sample volume.

For spectral alignment, corresponding shifts need to be calculated. The shifts can easily be calculated from the relative positions of the prominent lines in the voxel spectra. Calculated shifts are proportional to the magnetic field variations (inhomogeneities) in the sample and can be used for the static magnetic field mapping [10].

Let us consider the SNR of coadded spectra. Suppose that immediately after the excitation pulse the time domain signal from the sample has an amplitude $S(t = 0)$ and a noise $\sigma$. The time-domain SNR for a one-pulse experiment is then simply $\text{SNR}_1 = S(t = 0)/\sigma$. In the 3-D SI experiment, signals $\hat{S}_j(t)$ from $M^3$ different k-space points are acquired, where $\hat{S}_j(t)$ denotes time-domain signals from k-space points $k_j$. During the inverse Fourier transformation (FT) the k-space signals are multiplied by corresponding weights and summed to obtain time-domain signals from voxels at different positions $r_i$

$$S_i(t) = \frac{1}{M^3} \sum_{j=1}^{M^3} \hat{S}_j(t) \exp(-i \mathbf{r}_i \cdot \mathbf{k}_j).$$
Suppose the signals $S_i$ are coadded directly without alignment of spectral lines to obtain the signal from the whole sample

$$S_z(t) = \sum_{i=1}^{M^3} S_i(t) = \frac{1}{M^3} \sum_{j=1}^{M^3} \hat{S}_j(t) \left[ \sum_{i=1}^{M^3} \exp(-ir \cdot k_j) \right] = \frac{1}{M^3} \sum_{j=1}^{M^3} \hat{S}_j(t) M^3 \delta_{j,1} = \hat{S}_1(t). \quad (1)$$

The result of Eq. (1) is rather surprising as it tells that only the signal $\hat{S}_1(t)$ from the k-space center ($k_1 = 0$) contributes to the final signal $S_z(t)$. The signal $\hat{S}_1(t)$, which is acquired at zero-phase encoding gradient, is also identical to the signal $S$ acquired by the nonselective excitation pulse sequence. Signals from all other k-space points are canceled out during the summation. Therefore, if we would not be interested in aligning spectra before coadding them, there would not be any sense for acquiring signals from k-space points other than $k_1 = 0$ since all these signals do not contribute to the final signal. An equation resembling Eq. (1) holds for the transformation of noise during the coaddition of the SI signals:

$$\sigma_z = \sum_{i=1}^{M^3} \sigma_i = \frac{1}{M^3} \sum_{j=1}^{M^3} \bar{\sigma}_j \left[ \sum_{i=1}^{M^3} \exp(-ir \cdot k_j) \right] = \frac{1}{M^3} \sum_{j=1}^{M^3} \bar{\sigma}_j M^3 \delta_{j,1} = \bar{\sigma}_1.$$

Again, the noise $\bar{\sigma}_i$ is identical to the noise $\sigma$ in the one-pulse experiment. So we have $S_z(t) = \hat{S}_1(t) = S(t)$ and $\sigma_z = \bar{\sigma}_1 = \sigma$ from where follows that the time-domain SNR of directly coadded SI signals is identical to the SNR of the one-pulse experiment signal. As signals $S_z$ and $S$ are identical also at later times and not only at $t = 0$, the frequency-domain SNR of both signals is identical as well

$$\text{SNR}_z = \text{SNR}_1. \quad (2)$$

When spectra are aligned before they are coadded, the expression for the signal from voxels is somewhat different that in Eq. (1). Namely, to shift a spectrum for the frequency $\Delta \omega_i$ to align it with a reference signal, its time-domain signal has to be multiplied by the factor $\exp(i \Delta \omega_i t)$, so we have

$$S_z(t) = \sum_{i=1}^{M^3} S_i(t) \exp(i \Delta \omega_i t) = \frac{1}{M^3} \sum_{j=1}^{M^3} \hat{S}_j(t) \left[ \sum_{i=1}^{M^3} \exp(-ir \cdot (k_j - \Delta \omega_j t)) \right]. \quad (3)$$

Here time $t$ is measured from the center of the echo in the SI sequence. Spectral alignment before signal coaddition does not influence the time-domain SNR as this is defined by the ratio between the signal $S_z$ at $t = 0$ and the noise $\sigma$ at that time; Eq. (3) therefore turns into Eq. (1) when $t = 0$. The difference in $S_z$ emerges at $t > 0$, when also terms other than $\hat{S}_1$ contribute to the final signal. Namely, factors $\exp(i \Delta \omega_i t)$ are no longer equal to 1 when $t > 0$ and the sum in square brackets of Eq. (3) is nonzero also for points other than $k_1 = 0$. As a consequence of line alignment before signal coaddition the time-domain signal $S_z(t)$ becomes significantly longer compared with the signal without line alignment, which yields narrower lines in the spectrum of the signal $S_z(t)$ when the spectra are aligned before coaddition.
than when they are not. Coadded aligned SI spectra may have therefore a much higher frequency-domain SNR than directly coadded unaligned SI spectra.

2 Materials and Methods

Experiments were performed on a microimaging system (TecMag) equipped with a 2.35 T horizontal-bore magnet (Oxford) and 50 G/cm microgradients (Bruker). The sample (a cylindrical plastic container, 18 mm in diameter and 12 mm in length, filled with ethanol) is placed with the cylinder axis along the direction of the static magnetic field in a microprobe with a diameter of 25 mm. The 1-D NMR spectrum was obtained in a single scan acquired in 210 ms with 512 complex points, with 17 μs excitation pulse. A 3-D spin-echo SI experiment (Fig. 1) is performed with matrix of 16 by 16 by 16, 210 ms of acquisition time, 512 complex points, 2.4 ms of echo time and 1 s of repetition time, with 17 μs of excitation and 34 μs of refocusing pulse. The total SI experiment time was 4096 s. After data acquisition, the SI spectra were obtained by 4-D FT. To emphasize spectral improvements by spectral coalignment, all spectra were reconstructed without zero filling or any other type of signal postprocessing. The voxel spectra were coaligned by pairwise matching positions of the voxel biggest line (CH₃ group line) with the line from the central voxel. All M³ voxel spectra were coadded upon coalignment. For comparison, the voxel spectra were also coadded without alignment. Finally, from the voxel alignment shifts a map of the static magnetic field in the sample was calculated.

Fig. 1. Schematic diagram of the SI sequence that was used in the experiment. The data acquisition begins at the top of the spin echo.
3 Results

Figure 2a shows the 1-D spectrum obtained by the one-pulse excitation sequence. Because of the sample uniformity and cylindrical shape the major cause of line broadening (30 Hz) is mostly poor shimming. Figure 2b shows the sum of the SI voxel spectra of the same sample under identical instrumental conditions. The spectrum without alignment appears practically identical to the single-pulse 1-D spectrum from the whole sample (Fig. 2a). The average line width of 35 Hz is similar to the line width of the 1-D spectrum. The realignment of the voxel spectra before their coaddition narrows the lines almost 3 times (from 35 to 13 Hz) with threefold improvement of the SNR (from 400 to 1200).

Figure 3 depicts a static magnetic field distribution $\Delta B_0$ in the coronal cross section through the sample. The distribution map was calculated from spectral shifts ($\Delta \omega$) obtained while coaligning the SI voxel spectra ($\Delta B_0 = \Delta \omega / \gamma$). The magnetic field inhomogeneity in Fig. 3 ranges from +45 Hz, in both face centers of the cylindrical sample, to −30 Hz, in the central rim. The magnetic field offset $\Delta B_0$ was set to zero in the center of the sample. For illustration, shown are the SI spectra from the volume center, the face center and the sample exterior.

![Graphs showing proton spectra of ethanol](image)

Fig. 2. Proton spectra of ethanol stored in a cylinder which were acquired by a single-scan one-pulse sequence (a) and the SI sequence with a matrix of 16 by 16 by 16 (b). The SI spectra were coadded without spectral alignment (dashed) and with spectral alignment (solid).
Fig. 3. Magnetic field mapping by SI. The top image depicts magnetic field in the coronal slice through the sample (the slice position is indicated on the scheme on the right). The field was calculated from shifts of spectral lines during the process of spectral alignment. Single-voxel spectra, shown below the field map, correspond to different characteristic points of the sample that are indicated by arrows. The effect of the magnetic field inhomogeneity can be clearly seen also from the spectra; spectral structure is preserved; however, the spectra are shifted from voxel to voxel.

4 Discussion

High-resolution spectra of biological samples are rich sources of information only if spectral lines can be resolved enough to be characterized individually. In diamagnetic liquids, the spectral lines are broadened mostly by instrument imperfection and deteriorated resolution is improved by various methods. The most obvious is the use of resolution enhancement filters. Their spectral resolution is improved at the expense of sensitivity. When sensitivity is intrinsically low, resolution enhancement filtering is of limited value. The method presented in this paper utilizes SI for improvement of spectral resolution. In SI the resolution is improved at the expense of both the spatial information and the sensitivity. In a homogeneous sample (or homogeneous regions of a heterogeneous sample) the spatial information is irrelevant so the total effect is that SI provides resolution enhancement with less severe sensitivity losses compared with the filtering method. The SI method for improving the spectral resolution could be useful for recording high-resolution spectra from a homogeneous part of larger samples including in vivo spectroscopy, homogeneous liquid samples that are difficult to shim and magnetic field mapping.
The method used for spectral coalignement is based on aligning the prominent line of each spectrum with the same line of the reference spectrum. This approach is limited to spectra with at least one prominent well-resolved line, like, for example, in vivo brain spectra. In the $^{31}$P spectrum a very good reference is the creatine phosphate line; and in $^1$H spectra, N-acetyl aspartate. For complex spectra without suitable reference line, the spectra may be coaligned by use of the correlation between the current and the reference spectrum or by calculating the first momentum of the spectra. The spectral coalignement may be considered equivalent to the magnet shimming. In shimming, the static magnetic field variations over the sample are minimized by an appropriate combination of electric currents through shim coils. Thus, shimming keeps the voxel spectra aligned during data acquisition. In the SI method, the spectral alignment is achieved in the postprocessing. The SI method may have a practical advantage when the field variability has a complex spatial profile (which may be) impossible to shim. For the SI method, in principle, there are no such limitations.

The SI resolution enhancement method is most efficient when the field inhomogeneity varies slowly across the sample. Then the achieved line narrowing is roughly proportional to the (linear) SI spatial resolution. However, the SI method fails if the total gradient variation occurs at a spatial scale commensurate (or smaller) with the voxel size. This may happen in a system with a microscopic susceptibility variation like in lungs, cell suspensions, emulsions, etc. Then the voxel size does not affect the voxel spectrum line width. The SI method usually has modest spatial resolution to keep experimental time manageable. A consequence is the appearance of cutoff artefacts which manifest in the SI spectrum as a spectral spillover from neighboring voxels. This is in complete analogy to the apodization error in spectroscopy. The spillover can be controlled by multiplying k-space data with a suitable filtering function.

A major drawback of the SI method is that the SNR of the final spectrum does not increase with the square root of the number of signal acquisitions. It is approximately equal to the SNR of the 1-D spectrum obtained from a single scan. In spite of this, the SI method is useful since it exhibits sensitivity losses far less than the resolution enhancement filtering. An alternative approach to SI is to use standard volume excitation methods to get a spectrum from each voxel separately. Because in the SI method data from all voxels are recorded all the time, for $N$ voxels the SI spectrum would have an $N^{1/2}$ better SNR than a spectrum resulting from sequential recordings from all the voxels.

5 Conclusion

In this paper, we propose to use SI to improve the spectral resolution for inhomogeneous samples, which are difficult to shim. The resolution enhancement is achieved at the expense of spatial information.

The major advantage of the proposed method is that it is insensitive to the type of the static magnetic field inhomogeneity. Even with best sample shim-
ming the spectral resolution can still be improved by the use of this method. Therefore, the SI method can be used in conjunction with shimming and resolution enhancement filtering to further improve the spectral resolution. The real advantage and usefulness of the method depends on the type of resolution enhancement filter used and the properties of the field map across the sample volume. Here we used an empirical approach to demonstrate the feasibility and usefulness of the method. A full account on theoretical analysis and comparison with other resolution methods will be reported elsewhere.

References


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