Edge Enhancement by Diffusion: Microscopic Magnetic Resonance Imaging of an Ultrathin Glass Capillary

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Abstract

Diffusion can improve magnetic resonance imaging on a microscopic length scale by *edge enhancement* which acts against diffusional blurring. We demonstrate the effect *edge enhancement* and we provide an appropriate mathematical description using Kubo's *line shape function* formalism. We apply the the-

ory to make specific predictions for *edge enhancement* in a two-dimensional phantom system. In particular, we determine the corresponding *line shape function* and use it to reconstruct an MRI image of water in an ultrathin ($50\,\mu$m) capillary tube. We explain how a corresponding experiment can be realized with micro coils capable of receiving adequate FID signals from microscopically small sample volumes.

Introduction

The resolution of MRI devices is presently advancing towards the theoretical limit of about one micron [1, 2, 3]. The achievable signal to noise ratio and blurring due to diffusion are known factors that limit resolution. In a previous paper [4] we have investigated the role of diffusion in microscopic MRI. We show that in the presence of compartmental barriers, diffusion can cause useful distortions of the frequency spectrum of the FID signal similar to *motional narrowing* in NMR spectroscopy which can improve the visibility of those barriers in reconstructed images by an effect called *edge enhancement*. As the name suggests, this effect only occurs within a few microns of a boundary. Consequently, to actually observe *edge enhancement*, one would need a spatial resolution of several microns, a resolution which has recently been achieved

for the first time [2, 5]. In this letter we want to suggest an experiment which can verify the existence of the *edge enhancement* effect.

We intend for the explicit predictions of microscopic MRI images provided below to serve as a guide for experiments on phantom systems. Phantom systems seem especially promising because they allow control of many parameters and can easily be described mathematically. Control of parameters will not only be a convenience, but will play an integral role in the interpretation of experimental results. Since MRI at micrometer resolution is a recent innovation, it is difficult to know what are artifacts and what are 'real' attributes of the images. The theory presented here predicts how real attributes, e. g., *edge enhancement*, vary with experimental parameters, e. g., the field gradient, thereby allowing one to eliminate image artifacts.

Recent technological improvements have made it possible to detect *edge enhancement* in experiments. Advances in microscopic NMR imaging have enabled two- and three-dimensional images to be acquired from samples of dimensions of the order of 500–1000 microns. We propose an ultrathin glass capillary, filled with water as a possible sample. Due to the small sample volume such an experiment will not be without difficulties. Microscopic radio frequency coils of diameter less than 1 mm have been specifically designed for NMR imaging of such small samples [6]. Through such devices the proposed

experiment has become feasible.

Theory

In MRI the image reconstruction of an object is generated from the object's response to a radio-frequency pulse that dealigns the object's magnetization from its equilibrium value which is proportional to the applied, external magnetic field

$$\vec{H} = (H_o + Gz)\hat{z} \ . \tag{1}$$

The field gradient G provides a spatial dependence of the nuclear Larmor frequency $\Omega(\vec{r}) = \gamma|\vec{H}(\vec{r})|$, where γ is the gyromagnetic ratio of the nuclei responsible for the magnetization (usually water protons). The spatial dependence of $\Omega(\vec{r})$ encodes spatial information into the frequency profile. The precise nature of that encoding comprises a major focus of this work.

The Line Shape Function

In [4] we derived the *line shape function* which describes the frequency response of the *transverse* magnetization $m_\perp = m_x + im_y$ of water protons (spins) undergoing confined diffusion in a field gradient.[1] The frequency response is

[1]The theory applied is relevant only for T_2-weighted images.

obtained by Fourier-transforming the observed free induction decay (FID) in the standard manner. A theoretical description of the FID can be based on the diffusion-Bloch equation [7]

$$\partial_t m_\perp = (\nabla \cdot D\nabla - i\Omega(\vec{r}) - \frac{1}{T_2})m_\perp \ . \tag{2}$$

An overall solution[2] for $m_\perp$ in frequency space is the *line shape function* $I(\omega)$ for a spin ensemble diffusing in a linear gradient field,

$$\begin{aligned} I(\omega) &= \frac{1}{2\pi}\mathrm{Re}\int_{-\infty}^{+\infty} dt\ e^{i\omega t} M(t) \\ &= \frac{1}{2\pi}\mathrm{Re}\ \langle 1\ \frac{1}{\hat{D} + i(\Omega(z) - \omega) - 1/T_2}\ p_o\rangle \ , \end{aligned} \tag{3}$$

where D is the diffusion constant of the medium and T_2 is the native relaxation time for water protons. $M(t)$ is the spatial integral of $m_\perp$ and the brackets $\langle \ldots \rangle$ denote the spatial average. Expression (3) is suitable for a numerical treatment [4, 10]. The initial magnetization $m_\perp(z, 0)$ is equal to the (normalized) equilibrium distribution $p_o(z)$.

Numerical Solution for Two-Dimensional Diffusion

By a discretization scheme, expression (3) can be evaluated numerically for the case of one-dimensional diffusion [4]. In the terminology used here, *one-*

[2]We will give only a brief sketch of the solution here; for a more detailed description we refer to [4, 8, 9].

dimensional means that, of the three spatial degrees of freedom of the water protons, a knowledge of only one suffices to specify the properties of the protons. A cube filled with water for which one set of edges is aligned with the magnetic field in z-direction would be an example. Each proton can be described well by only its z-coordinate. A cylinder aligned along the x-axis as shown in Fig. 1 can be considered a two-dimensional example. Since, by symmetry, every two-dimensional cross section is equivalent, two coordinates are sufficient to describe the system. For a two-dimensional geometry an approximation to (3) can be found by averaging over the spatial dimension orthogonal to the field gradient (z-axis) and accounting for the eliminated dimension through an equilibrium distribution. This distribution represents a projection of the proton density onto the z-axis. Appropriate distributions are

Place Fig. 1 here

$$p_o(z) \propto \begin{cases} 1 & \text{linear geometry} \\ \sqrt{r^2 - z^2} & \text{circle of radius } r. \end{cases} \tag{4}$$

The approximation assumes that all protons with the same z-coordinate show identical diffusional behavior. It ignores that diffusion along the z-axis is restricted to some degree by the dependence of the capillary boundary on the y-coordinate.

To discover the validity of this assumption, we compared *line shape function* calculations using an approximate discretization scheme for (3) with

Monte Carlo simulations which provide essentially exact results.[3] Figure 2 shows the results to be very similar. We will, hence, employ in the following (3) to evaluate the frequency response of spin ensembles and use this response to obtain MRI images.

Diffusion-Enhanced Frequency Spectra

To demonstrate the effects of *motional narrowing* on frequency spectra and to understand the impact of these effects on reconstructed images, we investigate the situation of water protons, homogeneously distributed in a cylindrically bounded diffusion space, as can be realized by a water-filled glass capillary. We take the capillary to be oriented perpendicular to the gradient field as in Fig. 1, and the other parameters are as listed in Table 1. Figure 2 presents frequency spectra measured across a capillary for four different diffusion constants which are representative of those occurring in biological tissues. Comparing these spectra the effect of diffusion on the *line shape function* is readily discerned. Spectrum (c) corresponds to diffusion in pure water for which we provide a reconstruction below.

Place Tab. 1 here

Place Fig. 2 here

For slow diffusion (Fig. 2 a) the spectrum closely reflects the spin density

[3]The simulation program is described in [4]

across a cylindrical capillary as given by (4). It is undistorted across the center and shows small peaks close to the boundaries. An image reconstruction done from the spectrum in Fig. 2 c will show a brightened ring at the position corresponding to the peaks. This remarkable feature means that the boundary can easily be discerned in an image even if there is no intrinsic contrast between the inside, the boundary and the outside medium.

The spectra in Figs. 2 (b) and 2 (c) reveal that as the diffusion constant increases, the two peaks located at the boundaries in Fig. 2 (a) move toward the center. For very high diffusion constants, the two peaks merge and, in the limit of *motional narrowing*, produce the single peak observed in Fig. 2 (d). Again, the deviations from the undistorted spectrum—in this case, the peaks—will result in bright rings or spots in a reconstruction. These rings do not directly represent the object, but rather they indicate the existence of a barrier. To infer the actual size of the object, the diffusion constant must be known.

We note that the overall shape of the spectra resulting from the theory of *line shape functions* and those obtained through simulations agree well in Fig. 2. The fluctuations in the simulated spectra are due to finite samples and can be reduced by larger samples. It should be noticed, however, that there are some deviations in the two prediction methods. While the peaks are at about the same position for the simulated spectra and for the spectra calculated from

the *line shape function*, the relative amplitudes of the peaks differ, and it can be seen that the simulation does not predict as pronounced peaks as does the *line shape function*. Since both methods employ some approximations it is not clear which description is more accurate. Experiments may help to clarify this issue.

To predict the position of the peaks relative to the boundary we have introduced a parameter [4]

$$q = \sqrt[3]{\frac{\pi D}{\gamma G r^3}} \tag{5}$$

that gives an estimate of the extent of *motional narrowing*. It tells one how far the peaks move inwards from the outer boundary in units of the radius r. A q-value of zero corresponds to no narrowing, a value of 1 indicates extreme narrowing where only a single peak is observed. The q-values of 0.11, 0.24, 0.53, and 1.14 for Fig. 2 (a) through (d), respectively, agree well with the peak positions shown.

The parameter q explicitly shows how the narrowing is affected by the experimentally accessible parameters r, D, and G. For example, increasing the gradient will lower q which means that the bright rings will move outwards and become weaker whereas for a lower gradient they move inwards. The experimentalist has, therefore, a means of determining whether the appearance of rings and spots is being caused by *motional narrowing* or due to some other

cause of artifacts, such as susceptibility fluctuations or improper tilt of the probe.

Reconstruction

In this section we present two-dimensional reconstructions for the circular diffusion domain (cross section through the capillary) investigated above. As input data we used spectra calculated from the *line shape function* algorithm to avoid artifacts caused by noise which would arise from simulated spectra due to their jaggedness.

A single frequency spectrum contains all the information necessary to reconstruct the two-dimensional structure of the corresponding original. We use available reconstruction software [11] which employs a backprojection algorithm. For reconstructions obtained from FID signals the diffusion effects discussed here are independent of the particular reconstruction method used. This is because diffusion makes its mark on the frequency spectrum, the sole input of any reconstruction technique.

Reconstruction of Two-Dimensional Images

To demonstrate edge enhancement in a reconstructed image, we show the calculated reconstruction of a water-filled glass capillary with a 50 μm diameter in a 8 G/cm gradient field. The bright ring appears with a diameter of approximately 34 μm, corresponding to a q-value of 0.32. From Eq. (5) one would expect $q = 0.30$ which shows how helpful the q-value can be in predicting image characteristics.

Place Fig. 3 here

Our results have motivated us to suggest experiments which would specifically look for *edge enhancement*. Particularly illuminating would be images of water-filled glass capillaries, not more than about 200 μm in diameter.[4] The achievable signal-to-noise ratio in an NMR experiment is proportional to the sample volume. Consequently, special radio frequency coils are necessary for imaging samples less than 1 mm in diameter. A size reduction of the radio frequency coil improves coil-sample coupling and increases the coil sensitivity. It has been shown previously [6] that pixel resolutions less than 10 microns can be achieved using such coils. Solenoidal radio frequency coils of diameter 100–800 microns have been constructed and tested [5]. Initial measurements of spectroscopic linewidth, using samples of water within capillary tubes, in-

[4] A specific design of such an experiment has been suggested by Peck, Webb, and Magin [5]

dicate that a pixel resolution less than 3 microns is attainable [5]. With these and forthcoming improvements in experimental hardware and know-how, we can expect that conclusive results will soon become available.

Conclusion

Before *motional narrowing* effects are investigated in microscopic MRI of biological tissues, it should be highly profitable to look for such effects in controllable phantom systems such as a water-filled glass capillary. We have provided here explicit predictions to help guide such investigations. In other model systems, like a film of water between glass plates (1D case) or liposomes with a highly impermeable membrane (3D case), edge enhancement should also be observable. Such observations would demonstrate the viability of *motional narrowing* effects for edge enhancement in microscopic MRI.

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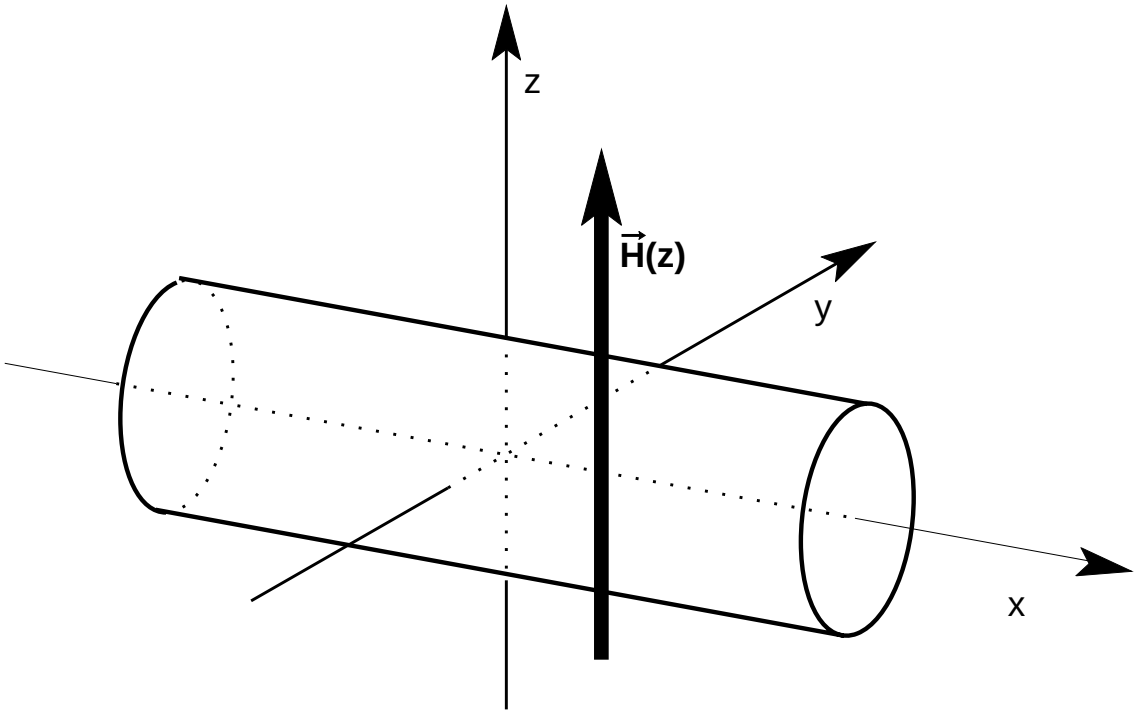

Figure 1: Proposed setup for a capillary experiment.

diameter	$40\,\mu$m
diffusion constant	$3 \cdot 10^{-4\cdots-7}\,\mathrm{cm}^2/\mathrm{s}$
field gradient	$8\,\mathrm{G/cm}$

Table 1: Parameters used for the spectra shown.

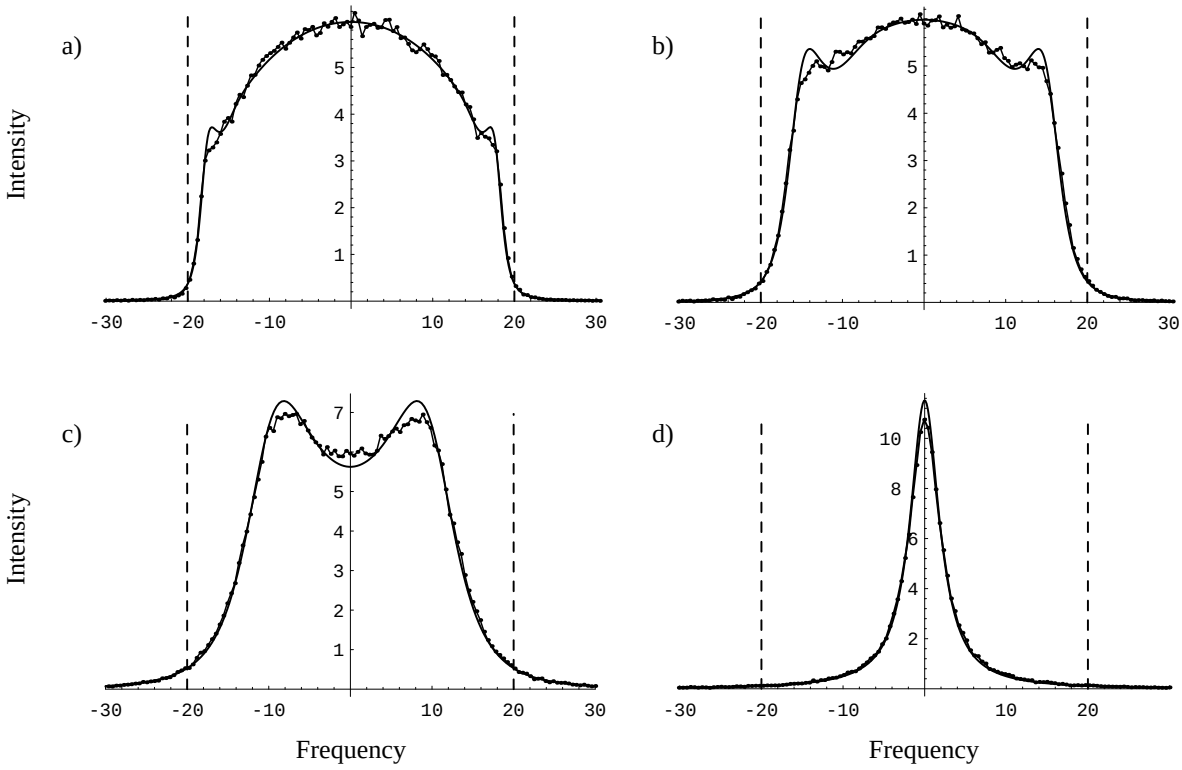

Figure 2: Frequency spectra $I(\omega)$ for two-dimensional diffusion in a disk of diameter $40\,\mu$m with the field and the gradient in the plane of the disk. The smooth curves correspond to the *line shape* function evaluated from a discretized form of Eq. (3). The jagged curves have been determined by Monte Carlo simulation.[3] The bounds of the diffusion domain (disk) are indicated by vertical dashed lines. The frequency is shown as $\omega/\gamma G$ in μm. The parameters have been chosen according to Table 1. The diffusion constants assumed are: a) $3 \cdot 10^{-7}$, b) $3 \cdot 10^{-6}$, c) $3 \cdot 10^{-5}$, and d) $3 \cdot 10^{-4}\,\mathrm{cm}^2/\mathrm{s}$. 100 000 particles were monitored in the Monte Carlo simulations.

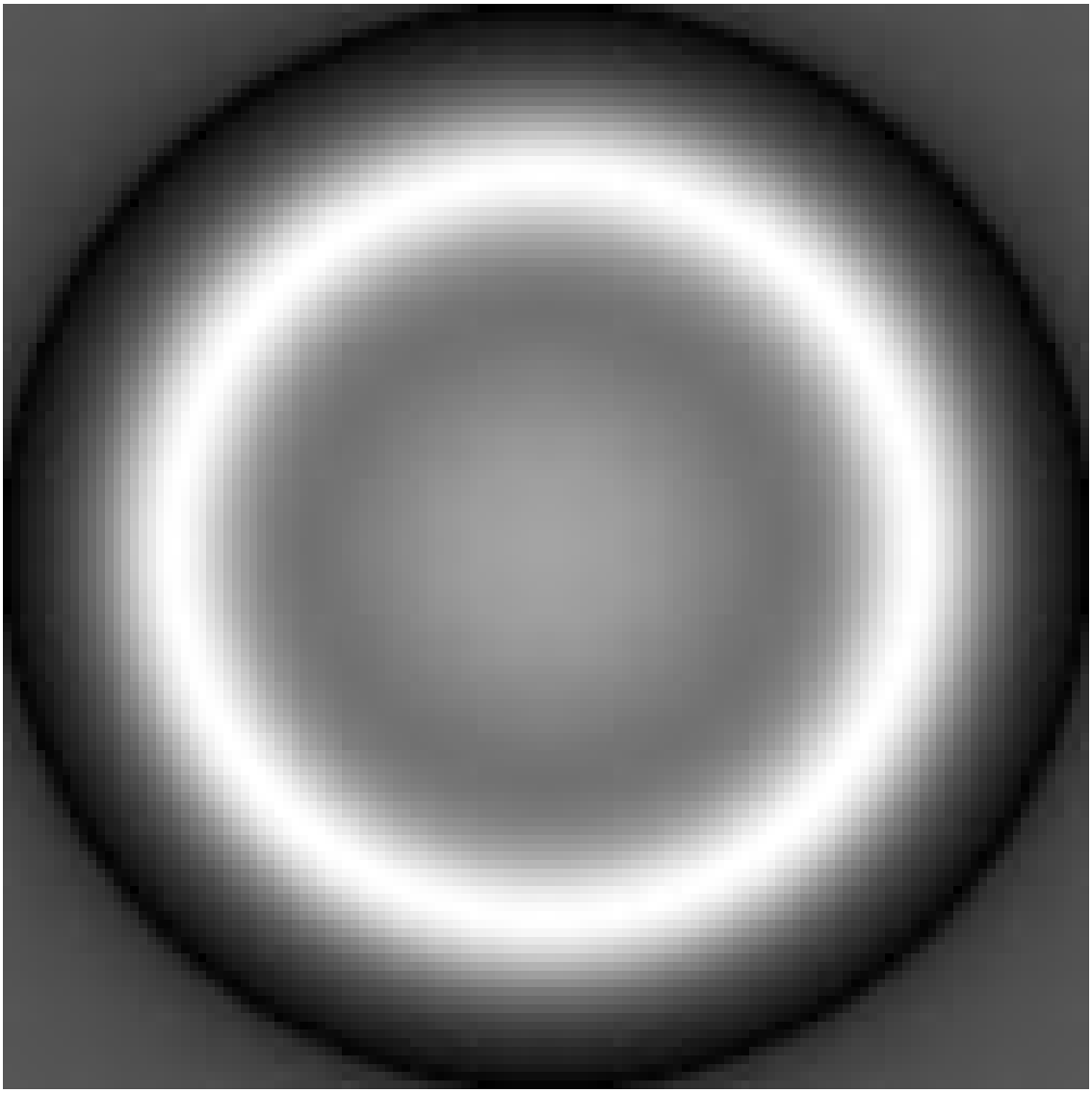

Figure 3: Reconstructed cross section of a 50 μm capillary filled with water. The frequency spectrum was calculated according to the *line shape function* in a 8 G/cm gradient with 0.4 μm resolution. The length of the frame corresponds to 50 μm, the diffusion constant is that of water, 3×10^{-5} cm^2/s