

Computer Simulations and Experimental Tests of Surface-to-Volume Measurements using ^3He NMR

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Introduction:

Hyperpolarized ^3He diffusion NMR is a powerful tool to probe lung microstructure at a length scale inaccessible by k -space MRI. In the short time scale limit, time-dependent diffusion measurements are sensitive to the surface-to-volume ratio (S/V) of the surrounding structure. Because of the high ^3He diffusion coefficient and the small size of alveoli, such measurements are challenging in the lung because the short-time scale limit cannot easily be reached due to hardware limitations. The feasibility of lung S/V measurements was assessed in a recent paper by Conradi et al [1], in which it was determined that S/V can likely be measured with 10-20% accuracy. To further explore this matter, we conducted experimental tests in a one-inch glass sphere containing hyperpolarized ^3He . In addition, we wrote a computer simulation capable of exploring simple and complex structures. The usefulness of a simulation is especially manifested in its ability to probe both, the regime that the experiment cannot reach and the regime that is too complex to allow analytical solutions. Both regimes were simulated and deviations from analytical solutions are discussed.

Methods:

We conducted the experimental part of this work using a commercial Siemens MRI scanner along with a custom ^3He radio-frequency coil. We measured the diffusion coefficient at different diffusion times by fitting the exponential signal decay as a function of b -value. Whereas for physical experiments one is typically concerned with reducing noise sources that arise due to equipment imperfections, our simulation is instead limited by statistical noise. For a typical noble gas MRI the order of magnitude of molecules is Avogadro's number. In a simulation such statistics cannot be achieved. Furthermore, within the duration of a typical scan-sequence, any one molecule undergoes many more collisions and direction changes than can be accounted for. In writing a diffusion simulation one therefore has to make a compromise between detail and feasibility. Therefore we employed an acceleration factor, which multiplies the time that we scatter the molecule. Care was taken in two regards: First, the distance traveled was calculated from the appropriate distribution function. Second, we made sure the maximum diffusion step was at least 2 orders of magnitude smaller than the surrounding structure. Other features are: proper reflection at boundaries, isotropic scattering probability, and molecular diffusion during the gradients. In order to test the simulations for accuracy, several analytical results in the literature have been explored:

- 1) By simulating q -space NMR for restricted diffusion in a simple box, we attempted to reproduce the periodic resonance phenomena as derived by Callaghan et al. [2]. In addition, we simulated the case of an array of connected boxes (separation of four times the box dimension) in order to verify that these resonances were further modulated by the reciprocal lattice as predicted by Callaghan.
- 2) We simulated b -value measurements to determine S/V inside a simple box with unequal side lengths ($A=2*B=3*C$). Since the free diffusion signal attenuation in the small time scale limit is reduced by the ratio of molecules within striking distance ($\sqrt{D_0t}$) of the boundary surfaces, one can write the time dependent diffusion coefficient as:

$$\frac{D(t)}{D_0} = 1 - \alpha \frac{S}{V} \sqrt{D_0 t}$$

Here α is a constant of proportionality. Therefore, one can relate the ratio of the slopes from a $D(t)$ vs. \sqrt{t} graph to the ratio of surface areas.

- 3) Using the same technique as in 2) we extracted S/V of a sphere. Mitra et al [3] have determined α to be $4/(9\sqrt{\pi})$ for a sphere. This particular simulation was also accompanied by ^3He diffusion NMR experiments inside a one-inch sphere. In addition to the regime achievable by experiment, we also simulated the narrow pulse regime as well as purposefully violating it by increasing the width of the diffusion gradients.

Results/Discussion:

The resonances for a simple box are shown in Fig1. Observe that the locations of these resonances in Fig1 reveal the connection length between boxes as discussed by Callaghan [2]. Second, the sensitivity of diffusion MRI to surface to volume was studied. We found that the simulated ratio of surfaces was: $A/B=1.93$ $B/C=1.4$. These results are within 3.5% and 6.7% of the expected ratios and hence give a good indication of the sensitivity of diffusion MRI to surface areas. Finally, the results for the different simulations done inside a one-inch sphere are shown in Fig2. Shown here are the time dependent diffusion constants as a function of diffusion time. The three different regimes were studied. The red circles are taken in the strict narrow pulse approximation. The blue triangles are within a regime that we were able to measure with an experiment. The corresponding experimental data is shown in black triangles. Finally, the green squares indicate a regime that purposefully violates the narrow pulse approximation. Using the above equation, one can use the slope to calculate the S/V values (expected is 2.36cm^{-1}). The results were as follows: Narrow pulse regime: 2.37cm^{-1} . Experimental regime: 2.87cm^{-1} . Experimental data: 2.91cm^{-1} . Narrow pulse violation: 3.07cm^{-1} . The simulation reproduces the theoretical limit and the experimental data well. We also note that the experimental S/V is within 23% in rough agreement with [1].

Outlook:

A future objective of the simulation is to define a threshold criterion for which diffusion MRI becomes a useful tool for S/V measurements. We will also continue to complement such simulations with experimental studies. We hope to use these results for qualitative or even quantitative corrections if one has to operate outside the ideal regime. In addition, our simulation can be used to explore more complex geometries using both q -space and b -value measurements.

References:

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