Analysis of Local Spatial Magnetization Frequency Sheds New Light on Diffusion MRI

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Intended audience MR physicists, signal and image processing researchers.

INTRODUCTION A thorough understanding the process of restricted diffusion in the presence of a magnetic field gradient is required for a correct interpretation of the measurements attained by any given diffusion MR scan. A number of results exist indicating to that the commonly used concept of q-space holds an oversimplification of the process [1,2,3]. We present a novel local frequency analysis of the process showing that this is indeed the case and discuss some important consequences.

THEORY AND METHOD To carry out the experiment we used an infinitesimally generated nearest neighbor approach. For restricted diffusion in 1 dimension, this method was validated by analytical methods. The only assumption made is that a quantized space-time can provide a good approximation of the continuous process. Quantizing the diffusion process it can be expressed as:

$$\mathbf{m} = \mathbf{A}^K \mathbf{m}_0 \qquad \text{where} \qquad \mathbf{A} = G^{\frac{1}{2}} D\, G^{\frac{1}{2}}$$

Here **m** is a complex vector of length N holding the magnetization vectors for each unit, **A** is an NxN complex matrix and *K* is the number of diffusion time steps. **A** can be expressed in term of a real tri-diagonal matrix, *D*, and a complex diagonal matrix, *G*. The off-diagonal terms in *D* specifies the relative amount of spins that move to the adjacent units in one time step. Conservation of mass requires that all columns in *D* sum to unity. *G* specifies the spin phase increment occurring during one time step. The diagonal terms in *G* are given by exp(*igx*) where x is the spatial position of the corresponding unit and *g* is the applied gradient strength. The sequence simulated is the standard single PFG sequence: 1. A gradient, *g*, is applied during a time δ. 2. A gradient free time, Δ – δ, follows. 3. A gradient of –*g* is applied during a time δ. To analyze the diffusion process the local spatial frequency of the magnetization, ω(*x*), was computed. The definition is given by:

$$w(x) = \frac{\partial \arg(\mathbf{m})}{\partial x}$$

RESULTS In the experiments presented here the compartment was quantized to consist of 60 adjacent identical units. The off diagonal terms in *D* were set to 0.002. Δ was set to corresponds to a diffusion propagator standard deviation of 0.8 times the compartment size. This was the shortest time possible for the diffusion to properly average the compartment magnetization. This Δ required *K* = 500 000 time steps for the *D* used. The length of δ was varied logarithmically from 0.0001 Δ to 1 Δ, corresponding to *K* ranging from 50 to 500 000. Simulating 2000 instances (40 δ, 50 *g*) took 13 seconds on a good laptop. Figure 1 visualizes compartment magnetization for *g* corresponding to 2.60 cycles across the compartment using the short pulse approximation (SPA). SPA predicts a complex exponential magnetization across the compartment. Even though δ is very short the simulated magnetization clearly deviates from a perfect spiral and the total number of cycles is only 2.20. Figure 2 shows the compartment magnetization when varying δ. The well known edge effects [2,3,4] are noticeable already for δ = 0.001 Δ and increase to be extreme roughly at δ = 0.1 Δ. For longer δ the averaging effect of the diffusion effectively prevents a build up of a strong local magnetization. The black line indicates the location of δ = 0.05 Δ, the value used to render figure 1.

Figure 3 shows the local frequency dependence on δ for the same *g* as in figure 2. For lengths up to δ = 0.001 Δ the SPA is valid and the local frequency constant across the compartment. For longer δ the local frequency consistently decreases as the position approaches the compartment edges. The distance from the edge at which the decrease begins increases with increasing δ and at δ = 0.1 Δ this 'edge' effect reaches all the way to the center of the compartment. For longer δ the local frequency is everywhere much lower than predicted by the SPA. Figure 4 shows the local frequency dependence on *g* for δ = 0.05 Δ. For reference the transparent plane shows the SPA prediction. For low *g* there is a slight decrease in local frequency when the compartment edge is approached. As *g* increases the local frequency drop gets more pronounced and the effect spreads toward the compartment center. At a *g* corresponding to 7 cycles across the compartment the 'edge' effect reaches all the way to the center. The black lines in figures 3 and 4 indicate the location of δ = 0.05 Δ, thus showing the same function but in different contexts.

DISUSSION AND CONCLUSION The results above show that the commonly used SPA is a poor candidate for modeling and interpretation of data obtained by present clinical scanners. The decrease of the local spatial frequency of the magnetization at the compartment edges is substantial at clinical values of δ (typically δ = 0.5 Δ) and will have a major impact on compartment size and shape estimates. The typically low anisotropy reported in clinical examinations may in fact not reflect the actual tissue microstructure but be a consequence of the inadequacy of the model used. We have shown that the basis functions that correspond to clinical diffusion sequences are in fact very far from the SPA predicted Fourier basis and, to complicate things further, it is clear that the basis created will be dependent on the geometry of each individual compartment present in one voxel. Thus, to quote a giant in the field, *"…the concept of q-space no longer has any meaning…"* ([1] p356).

However, diffusion MRI scans will continue to hold a lot of information and following the leads presented above we feel confident that models better suited for extracting micro structure properties from the measured data can be found.

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References: [1] P. Callaghan 1991. [2] P. Mitra and B. Halperin, JMR, 1995. [3] J. Stepisnik *et. al.* JMR, 1999. [4] I. Åslund and D. Topgaard, JMR 2009.

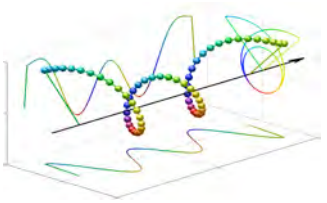

Figure 1. Positions in the complex plane of 60 magnetization vectors across the compartment for one gradient strength and δ=0.05Δ. Colors indicate phase angle. The real part is plotted on the 'back' plane and the imaginary part on the bottom plane.

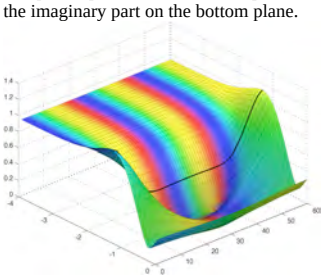

Figure 2. Magnetization across the compartment (y-axis, positions 1 to 60) for d from 0.001Δ to 1.0Δ (x-axis, log10 scale). Z-axis shows magnitude, colors indicates phase. The black line marks δ=0.05Δ.

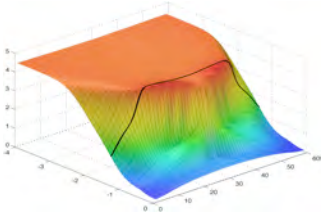

Figure 3. Color and height shows the local spatial frequency of the magnetization for a given gradient strength. x- and y-axis same as in Figure 2. The black line marks δ=0.05Δ.

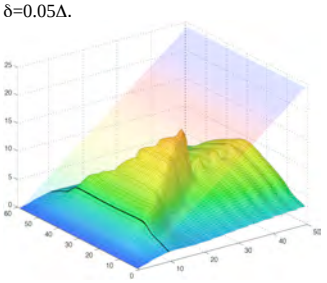

Figure 4. Color and height shows the local frequency for different positions across the compartment for δ=0.05Δ. Spatial position (1-60) is indicated on the x-axis. The y-axis indicates the applied gradient strength. The black line marks the *g* used in figures 1, 2 and 3.