Published in final edited form as:

Conf Proc IEEE Eng Med Biol Soc. 2010 ; 2010: 2710–2713. doi:10.1109/IEMBS.2010.5626530.

A New Model for Diffusion Weighted MRI: Complete Fourier Direct MRI

Alpay Özcan[Senior Member, IEEE]

Biomedical MR Laboratory, Mallinckrodt Institute of Radiology, Washington University in Saint Louis, School of Medicine, Box 8227, St. Louis MO 63110, USA. ozcan@zach.wustl.edu

Abstract

The diffusion weighted MR signal is modeled using particle methods. The model shows that the signal is the Fourier transform of the distribution function of the number of spins at the initial time at a given position with a given displacement integral value. The distribution function is computed via Fourier transform steps that keep the Hermitian property of the signal in order to guarantee that the distribution function is real valued. The function, which depicts the tissue microstructure ‘as it is’ without being tied to any expansions, transformations and assumptions such as Markovian property or symmetry about the spin motions, is displayed using isosurfaces overlaid on the spin density map for a fixed baboon brain sample.

I. INTRODUCTION

The magnetic resonance imaging (MRI) is a protocol that is inherently dependent on the position of the magnetic spins. When the spin relaxation times are neglected, the Bloch equations [1] that describe the dynamical evolution of the transverse spin magnetization admit the solution described by a rotating magnetization vector m_i written in complex number form:

$$m_i(t) = \exp(-\mathcal{J} \gamma \Omega_i) m_i(t_0). \quad (1)$$

Here, γ is the gyromagnetic ratio, the initial transverse magnetization is $m_i(t_0)$,

$$\Omega_i = \int_{t_0}^t G(x_i, \tau) \cdot x_i(\tau) d\tau \quad (2)$$

describes the angle as a function of the magnetic field gradient vector $G(x, t) \in \mathbb{R}^3$, and the time dependent position of the i^{th} spin packet is given as:

$$x_i(t) = x_i(t_0) + w_i(t) \quad (3)$$

with the continuous (because particles cannot disappear and reappear at a different point) function w_i denoting the displacement from the initial position i.e. $w_i(t_0) = 0$. In essence, the equations (1) and (3) are the solution of a dynamical system described jointly by the Bloch equations and the equation of motions for each particle.

Although the effect of w_i is considered negligible for a regular pulse sequence, it was shown by Stesjkal and Tanner [2] that the inclusion of diffusion encoding magnetic gradients, as in Fig. 1, enhances the effect of the spin motion on the MR signal. In the past, several partial

differential equation (PDE) based methods such as Callaghan's q -space [3] followed by the diffusion spectrum imaging (DSI) [4], diffusion tensor imaging (DTI) [5], [6], high angular resolution diffusion weighted imaging (HARDI) [7], the Generalized DTI (GDTI) [8] have been proposed to model the diffusion weighted (DW) MR signal.

In this manuscript, the DW-MRI signal is modeled using particle methods similar to the work of McCall et al. [9] to overcome the restricting symmetry conditions of the existing methods imposed either by their inherent properties, e.g. DTI ellipsoids and HARDI spherical harmonics that are symmetric functions, or by the simplifications used in the technique, such as the utilization of the complex signal's magnitude in DSI that causes the resulting DSI orientation distribution (ODF) function to be symmetric by the properties of the Fourier transform.

II. SIGNAL FORMATION

The first step for deriving the expression of the signal is the computation of Ω_i in (2) which is dependent on the magnetic field gradient vector $G(x_i, t)$. $G(x_i, t)$ has different time functions and components depending on the pulse sequence in utilization. For example, the pulsed gradient spin echo (PGSE) sequence shown in Fig. 1 have rectangular pulses defined in each of the imaging axes labeled by the read-out, phase encode and slice select gradients, $G_{ro} = [g_{ro1}, 0, 0]$, $G_{pe} = [0, g_{pe2}, 0]$, $G_{ss} = [0, 0, g_{sl3}]$ as well as a diffusion encoding component, $k_D \in \mathbb{R}^3$.

The initial time t_0 for the computations is the end time of the radio frequency (RF) excitation period. During the application RF pulse the magnetization is not yet completely tipped to the transverse plane and the slice select gradient has a fixed value. Statistically speaking, the latter implies that the effect of the spin motion during this time period will be constant for each acquisition and will reflect consistently only on $m_i(t_0)$, the initial magnetization.

With this point in consideration, when (2) is computed for PGSE pulse sequence of Fig. 1, the following expression is obtained:

$$\Omega_i = k_{mr} \cdot x_i(t_0) + k_D \cdot W_i^d + k_{rw} \cdot W_i^{rw} + W_{i,1}^{acq} (k_{mr1}) g_{ro1} - \Delta t_{ro} G_{ss} \cdot x_i(t_0), \quad (4)$$

where the last part is a constant since the slice select axis component of $x_i(t_0)$ is the slice position in the physical space. The variables originating from the pulse sequence parameters are:

$$k_{mr}(t, G_{pe}) = (t - t_{acq} - \Delta t_{ro}) G_{ro} - \Delta t_{ro} G_{pe} \quad (5)$$

$$k_{rw} = \left[-g_{ro1}, \frac{k_{mr2}}{\Delta t_{ro}}, -g_{sl3} \right], \quad (6)$$

with the time t and the phase encoding gradient g_{pe2} becoming a function of $k_{mr} = [k_{mr1}, k_{mr2}, k_{mr3}]$:

$$t = \frac{k_{mr1}}{g_{ro1}} + t_{acq} + \Delta t_{ro} \quad \text{and} \quad g_{pe2} = -\frac{k_{mr2}}{\Delta t_{ro}}$$

since g_{ro} is constant. The k -space variables multiply the following three integrals corresponding to the displacement integrals for diffusion (d), analog to digital conversion acquisition (acq) and initial rewind (rw) gradient time periods respectively

$$W_i^d = \int_{t_{d3}}^{t_{d4}} w_i(\tau) d\tau - \int_{t_{d1}}^{t_{d2}} w_i(\tau) d\tau, \quad (7)$$

$$W_i^{acq}(t) = \int_{t_{ucq}}^t w_i(\tau) d\tau, \quad (8)$$

$$W_i^{rw} = \int_{t_0}^{t_{ro}} w_i(\tau) d\tau. \quad (9)$$

These quantities are the MR observables of the spin motions and show that DW-MRI measures the displacement integral values of the spins rather than their displacements, contrary to the existing literature. Moreover, for the diffusion phenomenon, the narrow pulse approximation is not appropriate at any scale due to the Brownian nature of w_i which makes it nowhere differentiable.

In conclusion, the MRI scanner acts as a time-delay linear system with the input-output pair (w_i, W_i) as depicted in Fig. 2.

III. COMPLETE FOURIER DIRECT (CFD) MRI

The DW-MRI signal is the sum of the individual magnetizations with $m_i(t_0) = m_0 \in \mathbb{R}$:

$$S_{cfd}(k_{mr}, k_D, k_{rw}) = m_0 \sum_i \exp(-\mathcal{J} \gamma \Omega_i). \quad (10)$$

Since the focus of MRI is the location dependent properties, rather than having a spin by spin sum as in (10), the summation is carried out as an integral of the signal originating from the infinitesimal volume element $dx dW$:

$$S_{cfd}(k_{mr}, k_D, k_{rw}) = \int P_{cfd}^{total}(x, W) \exp(-\mathcal{J} \gamma \Omega_i) dx dW. \quad (11)$$

where $P_{cfd}^{total}(x, W)$ is the distribution of the number of spins at the initial position x having spin displacement integral values of $W = [W^d, W^{acq}, W^{rw}]$. By (4) and (11), S_{cfd} is the

Fourier transform of P_{cfd}^{total} :

$$S_{cfd}(k_{mr}, k_D, k_{rw}) = \mathcal{F}\{P_{cfd}^{total}\}(k_{mr}, k_D, k_{rw}) \quad (12)$$

with the nonlinearities introduced by W_1^{acq} .

The equation (12) elucidates the most important property of S_{cfd} : Since P_{cfd}^{total} is a real valued function, the signal S_{cfd} must be a Hermitian function by the properties of Fourier transform [10].

Although the domains of the Fourier pair of (12) are at least eight dimensional spaces (nine for volume imaging), among the MRI observables described in (7)–(9) the most informative one for the spin motion is W_d . Its distribution is given by marginalizing P_{cfd}^{total} :

$$\begin{aligned} P_{cfd}(x, W^d) &= \int P_{cfd}^{total}(x, W^d, W^{rw}) dW^{rw} \\ &= \mathcal{F}_{(k_{mr}, k_D)}^{-1} \{S_{cfd}(k_{mr}, k_D, 0)\}. \end{aligned} \quad (13)$$

P_{cfd} resides in a five dimensional space (six for volume imaging). However, due to the affine relationship between k_{rw} and k_{mr} in (6), k_{rw} cannot be sampled at 0. In this manuscript, the estimation of P_{cfd} is achieved by applying systematic phase corrections in each dimension that guarantee the Hermitian property. The corrections assure that, amid noise, nonlinearities introduced by W_1^{rw} and $k_{rw} \neq 0$, the estimated P_{cfd} is real valued.

This is accomplished by first executing the Fourier transform in k_{mr} ,

$$I_{k_{mr}}^{complex}((x_{ro}, x_{pe}), k_D) = \mathcal{F}_{k_{mr}}^{-1} \{S_{cfd}(k_{mr}, k_D, k_{rw})\}. \quad (14)$$

and applying up to the second order polynomial corrections at each value of k_D systematically:

$$I_{k_{mr}}(x, k_D) = I_{k_{mr}}^{complex}(x, k_D) \exp(-\mathcal{J}(r_{ro}(x_{ro}) + r_{pe}(x_{pe}))), \quad (15)$$

using the polynomials that are obtained from the angle of $I_{k_{mr}}^{complex}(x, 0)$ in the signal regions along the center lines of the image at $k_D = 0$:

$$\begin{aligned} r_{ro}(x_{ro}) &\approx \angle I_{k_{mr}}^{complex}((x_{ro}, 0), 0) \\ r_{pe}(x_{pe}) &\approx \angle I_{k_{mr}}^{complex}((0, x_{pe}), 0). \end{aligned}$$

This portion of the corrections rectifies the phase shifts created by shifting of the echo time from the middle of the acquisition period and the phase shifts in the phase encode direction caused by the shaking of the whole sample.

The computations are completed by evaluating the Fourier transform in each k_D -dimension, one by one

$$P_{cfd}(x, W^d) = \mathcal{F}_{k_D}^{-1} \{I_{k_{mr}}(x, k_D)\} \quad (16)$$

while applying appropriate phase corrections that preserve the Hermitian property, $I_{k_{mr}}(x, -k_D) = I_{k_{mr}}^*(x, k_D)$, at each step. It is important to note that the corrections are *not* applied on a pixel by pixel basis but systematically throughout each of the dimensions.

IV. VISUALIZATION OF P_{cfd}

For two dimensional MR slices P_{cfd} is a five dimensional positive valued function, which makes its visualization challenging. The strategy of this manuscript is to show the number of spins with low mobility, i.e. $P_{cfd}(x, 0)$ as the background image and to overlay on it the isosurfaces of the normalized P_{cfd} :

$$\bar{P}_{cfd}(x, W^d) = \frac{P_{cfd}(x, W^d)}{P_{cfd}(x, 0)} \quad (17)$$

that corresponds to the displacement integrals. The normalization is possible because a majority of the spins have small displacements due to diffusion. Moreover, if there is coherent spin motion, its effect—the shifting of the maximum point of P_{cfd} —will be eliminated by the phase corrections. So at any position x , the maximum of P_{cfd} is attained around $W^d = 0$.

The isosurface at the location x is formally defined as

$$\{W^d \in \mathbb{R}^3 : \bar{P}_{cfd}(x, W^d) = c\}$$

with the level value c ($1 \geq c > 0$). The level value is constant for all of the pixels. This provides a single scale presentation of the spin motion enabling the comparison of tissue microstructure at different positions.

The choice of the level value c is critical for the information content of the presentation. For example, if c is close to 1 the isosurfaces will only depict the spins with low mobility, which do not provide any information about the structure of the environment. On the other hand if c is chosen to be small the isosurfaces will be affected by noise. An appropriately small value of c corresponds to the small number of spins that have traveled long enough paths to describe the microstructure of their surroundings. The choice depends on the properties of the sample. For example, when the experiments were carried on a water sample, for a large range of c -values the isosurfaces were spherical. On the other hand, for the baboon brain sample of Section V, although for large level values the isosurfaces look like spheres on all of the pixels, as the value is lowered the microstructural properties appear at locations containing different types of tissues. With extremely lower values, all of the isosurfaces become disconnected and noisy. This is observed for larger values in the areas containing cerebrospinal fluid (CSF) as expected.

V. EXPERIMENTAL SETUP AND RESULTS

A fixed baboon brain immersed in 4% paraformaldehyde was used for the experiments. The primate was prematurely delivered at 125th day and sacrificed at 59th day after delivery. All animal husbandry, handling, and procedures were performed at the Southwest Foundation for Biomedical Research, San Antonio, Texas. Animal handling and ethics were approved to conform to American Association for Accreditation of Laboratory Animal Care (AAALAC) guidelines. Further details of the sample preparation are described in [11].

The experiments were carried out on a 4.7 Tesla MR scanner (Varian NMR Systems, Palo Alto, CA, USA) with a gradient system of bore size of 15 cm, maximum gradient strength of 45 gauss/cm and rise time of 0.2 ms using a quadrature birdcage coil (Varian NMR Systems, Palo Alto, CA, USA) with 108/63mm diameter sizes.

CFD-MRI data were obtained using the standard pulsed gradient spin-echo multi-slice sequence with in-house modifications that store all of the relevant parameters. k_{mr} -space is sampled to result in images of 128×128 pixels with a field of view $64 \times 64 \text{ mm}^2$ and 0.5 mm slice thickness. k_D -space is sampled in a uniformly spaced Cartesian grid in a cube $[-25\text{G/cm}, 25\text{G/cm}]^3$ with $11 \times 11 \times 11$ voxels, i.e. 5G/cm sampling intervals at each dimension. In regular MRI terms, 1331 images per slice were obtained. The repetition time $T_R = 1 \text{ s}$, echo time $T_E = 56.5 \text{ ms}$, diffusion pulse separation $\delta = 30 \text{ ms}$ and diffusion pulse duration $\delta = 15 \text{ ms}$ were used.

After the acquisition, the data were transferred from the MR scanner's computer to a two quad core 2.3GHz Intel Xeon® cpu and 8GB memory Dell Precision Workstation 490 running Windows XP® 64-bit operating system. The DWI data were placed in a 5-dimensional array and the discrete Fourier transform was computed along with the phase corrections as described in Section III. Afterwards, isosurfaces were computed as in Section IV. In-house Matlab® (Mathworks, Natick, MA USA) programs were used to accomplish all of the computations and display the graphics and maps.

Figure 3 presents the background image described in Section IV for the sample used in the experiments. It should not be confused with the spin echo image obtained without any diffusion encoding gradients. It depicts the number of spins with low mobility ($W^d \sim 0$) at each location. For that reason, the image is not an anisotropy map. For example, if a mixture of mineral oil and water—both isotropic—was the sample, the areas of mineral oil would appear brighter because of the lower spin mobility in the oil.

In Fig. 3, the inner capsule, the corpus callosum and the pons are the brightest areas because the myelinated axon tracts reduce the value of the displacement integral W^d . In the grey matter, which contains neuronal cell bodies, dendrites, axons, glial cells and capillaries, the intensity is lower due to the longer travel paths. The CSF in the ventricles appears as the darkest since the spins do not tend to stay around their initial positions and execute long travels in a liquid.

These points are emphasized including the geometric aspects in Fig. 4 with the isosurfaces overlayed on the area of interest marked in Fig. 3 around the junction of the corpus callosum and the inner capsule. The isosurfaces on the corpus callosum and the inner capsule follow the nerve bundles with a clear alignment and special shape illuminating the tracts. Moreover, at the intersection they have shapes elucidating the crossing fibers. The isosurfaces of the grey matter have rounder shapes in accordance with the organization of the tissue structure. The CSF isosurfaces have a 'noisy' appearance as the level value c was chosen low for the description of the tissue structure.

An important consideration about the presentation is that as the isosurfaces are three dimensional objects, the single viewpoint presented in Fig. 4 (due to space limitations) is not sufficient to gain a full appreciation of the information content provided by CFD-MRI. The visualization in three dimensions from different angles displays detailed aspects of the tissue microstructure and geometry.

VI. CONCLUSION

The aim of modeling the effect of spin motion on the MRI signal is to extract information about the microstructure from the motion of the spins. The complicated geometry of the environments makes it impossible to justify even the essential assumptions, such as the Markovian property because the past encounters of the particles with different mediums, obstacles and barriers makes their present and future positions dependent on their past. CFD-MRI's advantage is to present the information as it is, without any assumptions on the nature of the motion that use intermediary fits and transforms. An immediate outcome of the approach, is the ability to represent the motion properties in an asymmetric, unconstrained, unrestricted fashion as in Fig. 4.

Acknowledgments

This work was supported, in part, by the Washington University Small Animal Imaging Resource, a National Cancer Institute funded Small Animal Imaging Resource Program facility (U24-CA83060) and by the NIH/NINDS grant Biomarkers and Pathogenesis of MS (P01-NS059560).

REFERENCES

1. Haacke, EM.; Brown, RW.; Thompson, MR.; Venkatesan, R. Magnetic Resonance Imaging: Physical Principles and Sequence Design. John Wiley and Sons; 1999.
2. Stejskal EO, Tanner J. Spin diffusion measurements: Spin echoes in the presence of a time-dependent field. The Journal of Chemical Physics. 1965 Jan; vol. 42(no. 1):288–292.
3. Callaghan, PT. Principles of Nuclear Magnetic Resonance Microscopy. Oxford University Press; 1991.
4. Wedeen VJ, Hagmann P, Tseng W-YI, Reese TG, Weisskoff RM. Mapping complex tissue architecture with diffusion spectrum magnetic resonance imaging. Magnetic Resonance in Medicine. 2005 Dec; vol. 54(no. 6):1377–1385. [PubMed: 16247738]
5. Basser PJ, Mattiello J, LeBihan D. Estimation of the effective self-diffusion tensor from the NMR spin echo. Journal of Magnetic Resonance Series B. 1994; vol. 103:247–254. [PubMed: 8019776]
6. Mattiello J, Basser PJ, LeBihan D. Analytical expressions for the B matrix in NMR diffusion imaging and spectroscopy. Journal of Magnetic Resonance Series A. 1994; vol. 108:131–141.
7. Frank LR. Anisotropy in high angular resolution diffusion-weighted MRI. Magnetic Resonance in Medicine. 2001 Jun; vol. 45(no. 6):935–1141. [PubMed: 11378869]
8. Özarslan E, Mareci TH. Generalized diffusion tensor imaging and analytical relationships between diffusion tensor imaging and high angular resolution diffusion imaging. Magnetic Resonance in Medicine. 2003 Nov; vol. 50(no. 5):955–965.
9. McCall DW, Douglass DC, Anderson EW. Self-diffusion studies by means of nuclear magnetic resonance spin-echo techniques. Berichte der Bunsengesellschaft für Physikalische Chemie. 1963; vol. 67(no. 3):336–340.
10. Bracewell, RN. The Fourier Transform and its Applications. 3rd ed.. McGraw Hill; 2000.
11. Kroenke CD, Bretthorst GL, Inder TE, Neil JJ. Diffusion MR imaging characteristics of the developing primate brain. NeuroImage. 2005 May; vol. 25(no. 4):1205–1213. [PubMed: 15850738]

Fig. 2.

The DW–MRI signal from a signals and systems perspective describing the MRI observables of the diffusion phenomenon.

Fig. 3.

The background image represents $P_{cfd}(x, 0)$ of the baboon brain of Section V. The brighter areas indicate the high number of spins with lower displacement integral values. The inner capsule, corpus callosum and the pones are the areas with such properties. The box shows the junction of the inner capsule with the corpus callosum displayed on Fig. 4.

Fig. 4.

The isosurfaces for a level value of 0.14 around the corpus callosum and the inner capsule junction. The areas with high spin mobility, i.e. spaces filled with cerebrospinal fluid have noisy isosurfaces. The ones on the ventricles near the corpus callosum are purposely not shown to unveil the shape of the isosurfaces that align with the fiber tracks of the corpus callosum.