Published in final edited form as:

Proc IEEE Int Symp Biomed Imaging. 2011 March 30; 2011: 931–934. doi:10.1109/ISBI.2011.5872556.

COMPARISON OF THE COMPLETE FOURIER DIRECT MRI WITH EXISTING DIFFUSION WEIGHTED MRI METHODS

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Abstract

The Complete Fourier Direct (CFD) MRI method introduced in earlier work for modeling the diffusion weighted MRI signal is compared with the existing methods. The preservation of Hermitian symmetry in the diffusion weighted MRI signal without affecting its energy is the key point that differentiates CFD–MRI from the existing methods. By keeping the correct Fourier relationship intact, the joint distribution function is represented ‘as it is’, without any constraints, e.g. being symmetric. The necessity to model or assume models for spin motion and try to fit the model to the samples of the Fourier transform as in case of model matching methods is not required because the Discrete Fourier Transform applied to correctly processed signal in CFD–MRI gives more accurate results.

Index Terms

Diffusion Weighted Magnetic Resonance Imaging; Fourier Transform

1. INTRODUCTION

The diffusion weighted magnetic resonance imaging (DW–MRI) is an indispensable and versatile technique with wide application areas. The advancements have propelled the initial utilization of DWI measures, e.g. apparent diffusion coefficient in early detection of ischemia [1] to a multitude of highly crucial areas in research and clinical imaging, such as in cancer diagnosis [2], follow–up on treatment, pre–and post–operative assessment for different organs (e.g. fiber tracking before brain surgery), monitoring of neurological diseases and neonatal development.

Yet, there does not exist a clear consensus on a single model that describes adequately DW–MRI signal. This inconsonance originates mainly from the existing methods’ inadequacy of identifying the microstructure of geometrically complicated regions, such as the junction of nerve bundles or fiber tract crossings, from the experimental data. Therefore, a new perspective is necessary for the effective extraction and effective interpretation of different levels of information that will ultimately lead to the improvement of health care.

The starting point and the basis of the existing DW–MRI methods is invariably the work of Stejskal and Tanner [3]. Therein the attenuation of the spin–echo NMR *signal peak* under the influence of the additional motion sensitizing magnetic field gradients is described. This is achieved by including the self–diffusion process of the spins in the partial differential equations (PDE) that model the formation of the NMR signal. The outcome of these experiments is the *scalar* diffusion coefficient of the entire sample.

There appears to be two avenues for the path from DW–NMR to DW–MRI in the literature:

1. **Model matching methods** initiated by diffusion tensor imaging (DTI) [4, 5] and further expanded with high angular resolution diffusion weighted imaging (HARDI) [6], diffusion orientation transform (DOT) [7] and two versions of the generalized DTI (GDTI) [8, 9].
2. **Spectral methods** originating from Callaghan's q -space [10] followed by the diffusion spectrum imaging (DSI) [11], and Q-ball imaging [12].

With the exception of the GDTI version in [9], all of the DW-MRI methods are restricted to report physically symmetric quantities because either they assume such models in the case of model matching or they use the magnitude of the signal in the Fourier transform in the case of spectral methods. It is difficult to imagine that the motion of the spins in a biological environment populated with different types of fluids, barriers and tissue would be symmetric at any given location, e.g. at the fiber junctions. For the same reasons, important assumptions used in the derivation of these mathematical models, such as the Markovian property, are impossible to justify.

The Complete Fourier Direct (CFD) MRI [13] provides an *unconstrained general model* allowing the data to indicate if there exists truly any structure that shapes the models, e.g. symmetry, which is much sounder than using models with pre-assumed restrictions. Consequently, the experimental data from a fixed baboon brain described in Section 5 point that this is not the case.

2. BRIEF OVERVIEW OF CFD-MRI

In this section, the CFD-MRI method, which is introduced in [13], is briefly summarized. In Complete Fourier Direct MRI, rather than using the conventional PDE formulation, the mathematical model of DW-MRI signal formation is constructed using particle methods in the spirit of the work of McCall et al. [14]. The construction does not possess any assumptions on the type of motion.

The MRI signal originates from all of the spin magnetizations $M(t) = \sum_i m_i(t)$ where the evolution of the transverse magnetization of the i^{th} spin is described by a rotating magnetization vector, $m_i(t) = \exp(-j \gamma \Omega_i) m_i(t_0)$. Here, γ is the gyromagnetic ratio. The transverse magnetization vector, m_i , is written in complex number form with $m_i(t_0)$ denoting

the initial magnetization tipped to the transverse plane; $\Omega_i = \int_{t_0}^t G(x_i, \tau) \cdot x_i(\tau) d\tau$ describes the phase as a function of the magnetic field gradients $G(x, t) \in \mathbb{R}^3$, and the time dependent position of the spin, $x_i \in \mathbb{R}^3$. The motion of i^{th} spin is given by $x_i(t) = x_i(t_0) + w_i(t)$ where $w_i(t) \in \mathbb{R}^3$ represents the displacement of the spin from its initial position with $w_i(t_0) = 0$. The function $w_i(t)$ could express any kind of displacement such as Brownian motion, molecular movement in biological tissue with different medium and obstacles, coherent motion or any combination of these.

It is shown in [13] that the DW-MRI signal, S_{cfid} , is the Fourier transform of the joint distribution function $P_{cfid}^{total}(x, W)$, of the number of spins with the initial position $x \in \mathbb{R}^3$ at time initial time t_0 possessing the displacement integral values of $W \in \mathbb{R}^7$. In mathematical terms the Fourier transform of the total CFD distribution function P_{cfid}^{total} evaluated at the frequencies specified by (k_{mr}, k_D, k_{rw}) : $S_{cfid}(k_{mr}, k_D, k_{rw}) = \mathcal{F}\{P_{cfid}^{total}\}(k_{mr}, k_D, k_{rw})$. Here, k_{mr} is the usual MRI k -space variable defined by the imaging gradients, k_D is a vector equal to the motion sensitizing magnetic field gradients and k_{rw} is an affine function of k_{mr} [13].

The most relevant of the displacement integrals is the one originating from the motion

sensitizing gradients $W_i^d = \int_{t_{d3}}^{t_{d4}} w_i(\tau) d\tau - \int_{t_{d1}}^{t_{d2}} w_i(\tau) d\tau$ where the time points t_{di} denote the turn on–off times of the motion sensitizing gradients. W^d is recovered by marginalizing the joint distribution: $P_{cfd}(x, W^d) = \mathcal{F}_{(k_{mr}, k_D)}^{-1} \{S_{cfd}(k_{mr}, k_D, 0)\}$. However, the affine dependence of k_{rw} makes it impossible to fix $k_{rw} = 0$ and to experimentally sample in $(k_{mr}, k_D, 0)$ subspace.

The solution is to estimate P_{cfd} by rectifying of the undesirable effect of k_{rw} –sampling which is achieved by applying systematic phase corrections at each dimension of the Fourier space during its computation. The corrections are specifically chosen to re-establish Hermitian symmetry during the execution of the Fourier Transform. This is the central idea of the CFD–MRI: As P_{cfd}^{total} is the count of the spins, it is real valued. Therefore, S_{cfd} is Hermitian symmetric.

Since the domain of P_{cfd} is the five dimensional real space ($\mathbb{R}^5$), its visualization is challenging. The visualization is realized by using two components: the presentation of the number of spins at the initial time at each location, $P_{cfd}(x, 0)$, as the background image and the three dimensional distribution of the displacement integral values represented by the isosurfaces as in Fig. 1. The isosurfaces are defined by a level value c i.e. $\{W^d \in \mathbb{R}^3 : \bar{P}_{cfd}(x, W^d) = c\}$ using the normalization of P_{cfd} at each location $\bar{P}_{cfd}(x, W^d) = \frac{P_{cfd}(x, W^d)}{P_{cfd}(x, 0)}$.

3. COMPARISON WITH THE EXISTING METHODS

The Fourier relationship between the signal and the joint distribution function provides a complete understanding of the model matching methods. The methods start by applying DFT to the data in the first l (imaging) dimensions. Thus the first l independent variables are the physical location. The three remaining untransformed variables are the independent variables of the Fourier reciprocal of the spin displacement integral space. The goal of the model matching methods is therefore to fit the preferred model to the displacement integrals' distribution function's Fourier transform which is sampled at the (vector) values defined by the motion sensitizing gradients. It is natural that the fit is limited theoretically and numerically by the accuracy and amount of information that the models can capture. In CFD–MRI, the application of DFT to the entirety of data prevails over these problems.

Moreover, the Markovian property, i.e. independent increments, is a necessary condition for the b –value calculations. An isotropic sample possesses the Markovian property and therefore the b –value is an exact adjustment factor to calculate the (isotropic) diffusion matrix, D , of spin displacement w from its integral W^d that has a covariance equal to

$E[W^d (W^d)^T] = \delta^2 (\Delta - \frac{\delta}{3}) D$ (see Section 5). In the case of a biological tissue sample, the adjustment of b –value becomes an *approximation*. Since CFD–MRI directly obtains the joint distribution function, the statistical properties of W^d are *completely* available. The subtle point that guarantees this is the CFD frequency, $k_D = G_D$, that does not involve δ , unlike the q –space variable [10]: $q = (2\pi)^{-1} \gamma \delta G_D$.

The Fourier relationship has also been investigated in Callaghan's q –space [10], tying the signal to the 'average propagator'. In [10], parallel to the historical development of the DW models, the theory is first developed for the NMR experiments (see [10, Chap. 6]) using the polarized neutron scattering analogy. However, the translation to MRI is presented (see [10, Chap. 8]) asserting without proof that the imaging and displacement portions of the signal are separable (see [10, Chap. 8, pp. 440]). The derivations of the CFD signal in [13]

demonstrate to the contrary. The imaging gradients embed the Fourier space in an affine manner into a larger dimensional space. In addition, they show that the inseparability partially accounts for the non-Hermitian nature of the q -space signal model “reflecting the effects of phase shifts as well as phase spreading” as mentioned in [10, Chap. 8, pp. 440].

The signal out of the MR scanner is *not* the Fourier transform of the desired joint distribution function. It does not possess the Hermitian property. This indicates that it is not sufficient to fit a model to the complex valued data without the appropriate systematic phase corrections, for example as in GDTI [9].

In addition, using the magnitude of the DW-MRI signal, as in the case of DSI [11], does not count as a phase correction. The Fourier transform of the magnitude (a real valued function) gives a complex valued (thus physically meaningless) Hermitian probability function in the motion space. Therefore another application of the magnitude is necessary to obtain a real valued and forcefully center symmetric function. This has happened when the complex signal from the fixed baboon brain sample was processed with DSI methodology exactly as described in [11]. The magnitude was forcefully taken to calculate the DSI's orientation distribution function (ODF) [11, Eq. 20] presented in Fig. 2 which resulted in a center symmetric ODF. Moreover, if the raw data are first treated with the CFD phase corrections re-establishing the Hermitian property, DSI will immediately result in a center symmetric ODF. In brief, the usage of magnitude in DSI calculations causes the results to be center symmetric. In contrast, Fig. 2 demonstrates that by preserving the Hermitian property, CFD-MRI captures correctly the crossing fibers at the corpus callosum and external capsule junction without having symmetry restrictions therein. This is also true for the structural information extracted from the white matter and the corpus callosum by the isosurfaces.

4. CONCLUSION

The theoretical derivations of CFD-MRI [13] established the relationship between the signal and the correct physical quantities. This in turn provided the correct guidance for the estimation of the joint distribution function. The preservation of Hermitian symmetry without affecting the energy of the signal is the key point that differentiates CFD-MRI from the existing methods. By keeping the the correct Fourier relationship intact compared to the spectral methods, the joint distribution function is represented ‘as it is’, without any constraints, e.g. being symmetric. This property also abolishes the necessity to model or assume models for spin motion and try to fit the model to the samples of the Fourier transform as in the model matching methods. In conclusion, the Discrete Fourier Transform applied to correctly processed signal in CFD-MRI yields more accurate and more informative results.

5. EXPERIMENTAL SETUP

A fixed baboon brain immersed in 4% paraformaldehyde was used for the experiments. The primate was prematurely delivered on the 125th day and sacrificed on the 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 explained in [15].

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 cylindrical quadrature birdcage coil (Varian NMR Systems, Palo Alto, CA, USA) with 63 mm inner diameter. CFD-MRI data were obtained using the standard pulsed-gradient spin-echo multi-slice sequence. The k_{mr} -space

was 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. The k_D -space was sampled in a uniformly spaced Cartesian grid in a cube $[-30 \text{ G/cm}, 30 \text{ G/cm}]^3$ with $11 \times 11 \times 11$ voxels, i.e. 6G/cm sampling intervals at each dimension. The repetition time $T_R = 1 \text{ s}$, echo time $T_E = 56.5 \text{ ms}$, diffusion pulse time offset $\Delta = 30 \text{ ms}$ and diffusion pulse duration $\delta = 15 \text{ ms}$ were used.

In-house Matlab® (Mathworks, Natick, MA USA) programs were used for all of the computations and to display the graphics and maps using a two quad core 2.3GHz Intel Xeon® cpu and 8GB memory Dell Precision Workstation 490 running Windows XP® 64-bit operating system.

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. Moseley ME, Cohen Y, Mintonovitch J, Chileuitt L, Shimizu H, Kucharczyk J, Wendland MF, Weinstein PR. Early detection of regional cerebral ischemia in cats: Comparison of diffusion- and T2-weighted MRI and spectroscopy. *Magnetic Resonance in Medicine*. May; 1990 14(2):330–346. [PubMed: 2345513]
2. Xu, Junqian; Humphrey, Peter A.; Kibel, Adam S.; Snyder, Abraham Z.; Narra, Vamsidhar R.; Ackerman, Joseph JH.; Song, Sheng-Kwei. Magnetic resonance diffusion characteristics of histologically defined prostate cancer in humans. *Magnetic Resonance in Medicine*. Apr; 2009 61(4):842–850. [PubMed: 19215051]
3. Stejskal EO, Tanner JE. Spin diffusion measurements: Spin echoes in the presence of a time-dependent field. *The Journal of Chemical Physics*. Jan; 1965 42(1):288–292.
4. Basser, Peter J.; Mattiello, James; LeBihan, Denis. Estimation of the effective self-diffusion tensor from the NMR spin echo. *Journal of Magnetic Resonance Series B*. 1994; 103(3):247–254. [PubMed: 8019776]
5. Mattiello, James; Basser, Peter J.; LeBihan, Denis. Analytical expressions for the B matrix in NMR diffusion imaging and spectroscopy. *Journal of Magnetic Resonance Series A*. 1994; 108(2):131–141.
6. Frank, Lawrence R. Anisotropy in high angular resolution diffusion-weighted MRI. *Magnetic Resonance in Medicine*. June; 2001 45(6):935–1141. [PubMed: 11378869]
7. Özarslan, Evren; Shepherd, Timothy M.; Vemuri, Baba C.; Blackband, Stephen J.; Mareci, Thomas H. Resolution of complex tissue microarchitecture using the diffusion orientation transform (DOT). *Neuro Image*. July; 2006 31(3):1086–1103. [PubMed: 16546404]
8. Özarslan, Evren; Mareci, Thomas H. Generalized diffusion tensor imaging and analytical relationships between diffusion tensor imaging and high angular resolution diffusion imaging. *Magnetic Resonance in Medicine*. Nov; 2003 50(5):955–965. [PubMed: 14587006]
9. Liu, Chunlei; Bammer, Roland; Acar, Burak; Moseley, Michael E. Characterizing non-gaussian diffusion by using generalized diffusion tensors. *Magnetic Resonance in Medicine*. May; 2004 51(5):924–937. [PubMed: 15122674]
10. Callaghan, Paul T. *Principles of Nuclear Magnetic Resonance Microscopy*. Oxford University Press; 1991.
11. Wedeen, Van J.; Hagmann, Patric; Tseng, Wen-Yih Isaac; Reese, Timothy G.; Weisskoff, Robert M. Mapping complex tissue architecture with diffusion spectrum magnetic resonance imaging. *Magnetic Resonance in Medicine*. Dec; 2005 54(6):1377–1385. [PubMed: 16247738]
12. Tuch, David S. Q-ball imaging. *Magnetic Resonance in Medicine*. Nov; 2004 52(6):1358–1372. [PubMed: 15562495]

13. Özcan, Alpay. A new model for diffusion weighted MRI: Complete fourier direct MRI. Proceedings of the 32st Annual International Conference of the IEEE EMB Society; Buenos Aires, Argentina. Sept. 2010; p. 2710-2713.
14. McCall, David W.; Douglass, Dean C.; Anderson, Ernest W. Self-diffusion studies by means of nuclear magnetic resonance spin-echo techniques. *Berichte der Bunsengesellschaft für Physikalische Chemie*. 1963; 67(3):336–340.
15. Kroenke, Christopher D.; Larry Bretthorst, G.; Inder, Terrie E.; Neil, Jeffrey J. Diffusion MR imaging characteristics of the developing primate brain. *Neuro Image*. May; 2005 25(4):1205–1213. [PubMed: 15850738]

Fig. 1.

The isosurfaces ($P_{cfd}(x, W^d) = 0.17$) picked from the area around the corpus callosum (CC) and external capsule (EC) junction are shown overlayed on the image defined by $P_{cfd}(x, 0)$. Starting from left bottom going clockwise, the sample pixels are from cerebrospinal fluid (CSF), CC, White Matter (WM) and CC and EC junction respectively. Notice that the isosurfaces of the CSF pixels are immersed in noise because of the isotropic nature creating a dispersed distribution compared to more structured pixels.

Fig. 2.

The comparison of P_{cfd} (first row in each subfigure) with the Diffusion Spectrum Imaging Orientation Distribution Function (DSI-ODF) (second row) shown from different viewpoints in $\mathbb{R}^3$ at each subfigure. Both functions are calculated from the same data on the right junction of the corpus callosum (CC) and the external capsule (EC), from the pixels of Fig. 1. The isosurface ($\bar{P}_{cfd} = 0.17$) captures the asymmetric structure of the fiber crossings while the ODF is constrained to be symmetric for all of the pixels. Note that in CSF, ODF detects structure which is not present in reality as indicated by CFD.